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ORIGINAL WORK

Continuous Electroencephalogram Evaluation of Paroxysmal Events in Critically Ill Patients: Diagnostic Yield and Impact on Clinical Decision Making

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Abstract

Background: Continuous electroencephalogram (cEEG) monitoring has been widely used in the intensive care unit (ICU) for the evaluation of patients in the ICU with altered consciousness to detect nonconvulsive seizures. We investigated the yield of cEEG when used to evaluate paroxysmal events in patients in the ICU and assessed the predictors of a diagnostic findings. The clinical impact of cEEG was also evaluated in this study.

Methods: We identified patients in the ICU who underwent cEEG monitoring (>6 h) to evaluate paroxysmal events between January 1, 2018, and December 31, 2019. We extracted patient demographics, medical history, neurological examination, brain imaging results, and the description of the paroxysmal events that necessitated the monitoring. We dichotomized the cEEG studies into those that captured habitual nonepileptic events or revealed epileptiform discharges (ictal or interictal), i.e., those considered to be of positive diagnostic yield (Y+), and those studies that did not show those findings (negative diagnostic yield, Y−). We also assessed the clinical impact of cEEG by documenting changes in administered antiseizure medication (ASM) before and after the cEEG.

Results: We identified 159 recordings that were obtained for the indication of paroxysmal events, of which abnormal movements constituted the majority ($n=123$). For the remaining events ($n=36$), descriptions included gaze deviations, speech changes, and sensory changes. Twenty-nine percent (46 of 159) of the recordings were Y+, including the presence of ictal or interictal epileptiform discharges ($n=33$), and captured habitual nonepileptic events ($n=13$). A history of epilepsy was the only predictor of the study outcome. Detection of abnormal findings occurred within 6 h of the recording in most patients (30 of 46, 65%). Overall, cEEG studies led to 49 (31%) changes in ASM administration. The changes included dosage increases or initiation of ASM in patients with epileptiform discharges ($n=28$) and reduction or elimination of ASM in patients with either habitual nonepileptic events ($n=5$) or Y− cEEG studies ($n=16$).

Conclusions: Continuous electroencephalogram monitoring is valuable in evaluating paroxysmal events, with a diagnostic yield of 29% in critically ill patients. A history of epilepsy predicts diagnostic studies. Both Y+ and Y− cEEG studies may directly impact clinical decisions by leading to ASMs changes.

Keywords: Paroxysmal activities, Continuous EEG, Critically ill, Diagnostic yield, Seizure treatment

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Introduction

Continuous electroencephalogram (cEEG) monitoring is invaluable in the diagnosis of nonconvulsive seizures (NCSs) in patients with altered mental status (AMS). Up

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to 19% of patients in the intensive care unit (ICU) with AMS had seizures on cEEG, of whom the majority (92%) were experiencing NCS [1]. cEEG use has been increasing, as it is recommended to identify NCS in critically ill patients by the American Clinical Neurophysiology Society task force [2].

The cEEG is also recommended by the American Clinical Neurophysiology Society to evaluate paroxysmal events, including motor and autonomic spells, as well as unexplained paroxysmal increases in intracranial pressure [2]. However, previous studies have included heterogenous patient populations in whom the majority of cEEG studies were used to investigate AMS and the detection of NCS [1]. Overall, the use of cEEG for the assessment of paroxysmal events has received less attention. For example, in a study of cEEG in three major medical centers, 5,792 cEEG sessions were analyzed and only 12% cEEG were used to evaluate paroxysmal events [3]. A similar Fig. (12.9%) was reported in a study of noncritically ill hospitalized patients [4]. Although the use of cEEG in the detection of NCS or nonconvulsive status epilepticus in AMS has been confirmed, the value of cEEG in the diagnosis of paroxysmal events is less studied. Furthermore, besides its value in diagnosis, the impact of cEEG on the clinical management also warrants investigation.

Here, we studied the diagnostic yield of cEEG for the investigation of paroxysmal events. We defined diagnostic yield positivity (Y+) to be the detection of either interictal or ictal epileptiform discharges or a habitual nonepileptic event. We also investigated factors that were associated with an increased likelihood of a Y+study. Finally, we studied the impact of cEEG on clinical treatment by identifying antiseizure medication (ASM) changes following the cEEG studies.

Methods

Study Population and Data Collection

We retrospectively reviewed consecutive ICU cEEG performed at the George Washington University Hospital (Washington, DC) between January 1, 2018, and December 31, 2019. A cEEG study was requested by an intensivist and cEEG was recorded by using Natus video monitoring system (Natus, Middleton, WI). Twenty-one electrodes were placed according to the International 10–20 System. Criteria for inclusion in the analysis were at least 6 h of continuous video EEG monitoring and an indication for assessment of paroxysmal events in the ICU. We excluded the studies that were used to evaluate persistent AMS or the management of status epilepticus. Patients often remain unconscious after cardiac arrest. In our hospital, patients undergo cEEG monitoring post arrest, per American Heart Association recommendation (class I) [5]. Therefore, these patients were excluded from current study, which focused on the indication of paroxysmal events. The use of EEG in patients with cardiac arrest, particularly the prognostic value of cEEG, has been extensively investigated in other studies [6]. For patients with multiple cEEGs during the study period, we included only the first cEEG in the study.

Demographic information, the primary admission diagnosis, and the pertinent neurologic medical history (seizure history, ASM use, past brain surgeries) were extracted from the hospital electronic medical records. Physical examination findings were dichotomized by the presence or absence of focal neurological deficits. Focal deficits included any documented focal motor, sensory, reflex changes, or aphasia. Findings such as diffuse weakness, diffuse hyperreflexia, and tremor were not included. Brain imaging studies were characterized by the presence or absence of focal abnormalities known to be associated with seizures, such as subdural hematoma, subarachnoid hemorrhage, and brain tumor, among others. Chronic findings, such as chronic microvascular changes, were not included.

cEEG reports were also reviewed to extract the indications, durations, and results of the EEG. The results were categorized as Y+if they included any epileptiform discharges (interictal or ictal) or a captured habitual nonepileptic event. An event similar in semiology to the paroxysmal event that prompted the cEEG study is considered a habitual event. Otherwise, the diagnostic yield was considered negative (Y−).

We reviewed the charts to determine the impact of cEEG on clinical decision making, which we inferred from cEEG-based ASM changes. This was accomplished by adding the number of patients with ASM discontinuation or decrease in cEEG with nonepileptic events or Y−studies to those with medication initiation or escalation in cEEG with epileptiform discharges. The study was approved by the George Washington University Institutional Review Board.

Statistical Analysis

We used the Mann–Whitney *U*-test to compare differences between two independent groups when the dependent variable was continuous but not normally distributed, such as age. Binary variables were compared by using the χ^2 test. Significant variables ($p<0.10$) in the univariate χ^2 analysis were then included in multivariate logistic regression models to identify independent predictors of diagnostic tests, and the odds ratios were calculated. Statistical analysis was performed by using SPSS Statistics (version 22; IBM, Armonk, NY) with $p<0.05$ being considered significant.

Results

Patient Characteristics and Paroxysmal Activities

A total of 159 cEEG evaluations were included in this cohort. Primary admission diagnoses for patients who underwent cEEG monitoring included intracranial bleeding (either intraparenchymal hemorrhage or subarachnoid hemorrhage, $n=35$), brain tumor (either primary or metastatic, $n=19$), and brain trauma or subdural hematoma ($n=17$). A complete list of the admission diagnoses is shown in Table 1. Clinical characteristics are summarized in Table 2. In this cohort, 86 patients were men (54.1%), and the mean age was 59 years (range 22–92). There was no significant difference in age (mean age 59.4 vs. 57.4 years, respectively, $p>0.05$) or sex ratio (men 53% vs. 56%, respectively, $p>0.05$) between two subgroups of patients with the primary diagnoses of neurological or nonneurological disorders. Thirteen patients (8.2%) had a history of epilepsy and 57 patients (36%) had brain surgeries. A total of 101 patients (63%) were intubated during the cEEG evaluation, and focal neurological deficits were identified in 74 (47%) patients. Abnormal focal radiologic findings were noted in 102 (64%) patients.

Regarding the indications, most studies were performed to evaluate abnormal motor symptoms ($n=123$), and the description included transient shaking, twitching, jerking, convulsion, nonpurposeful automatism, posturing or stiffness, and episodic gaze deviation occurring in the setting of abnormal movements. As for events without motor phenomena ($n=36$), the description included isolated gaze deviation ($n=16$), speech changes ($n=9$), sensory changes or hallucinations ($n=3$), staring episodes ($n=2$), or a combination of those symptoms ($n=6$) (Table 2).

Table 1 Primary admission diagnoses

Admission diagnoses	*n*
Intracranial hemorrhage	35
Brain trauma or subdural hematoma	19
Brain tumor or brain metastasis	17
Stroke	10
CNS infection or encephalitis	9
Seizure-like activity	6
Other CNS disorder[a]	4
Syncope	7
Gastrointestinal disease	9
Respiratory or cardiovascular disease	11
Systemic infection	4
Postoperative state[b]	15
Others[c]	13
Total	159

CNS, central nervous system

[a] Including vasculitis, hydrocephalus, and cerebral venous thrombosis

[b] Including cardiovascular, orthopedic, and general surgery

[c] Including trauma, bleeding, metabolic derangement, anaphylactic, and angioedema

Table 2 Demographic and patient characteristics

Characteristic	Y − EEG	Y + EEG	*p* value
Age (range 22–92) (yr)	58	61	0.28
Sex, n (%)			
Male	62 (55)	24 (52)	0.86
Female	51 (45)	22 (48)	
Semiology, n (%)			
Motor	82 (73)	41 (89)	0.02
Nonmotor	31 (27)	5 (11)	
History of epilepsy, *n* (%)			
Yes	3 (3)	10 (22)	< 0.001
No	110 (97)	36 (78)	
History of brain surgery, *n* (%)			> 0.99
Yes	41 (36)	16 (35)	
No	72 (64)	30 (65)	
Intubated, n (%)			
Yes	72 (64)	29 (63)	> 0.99
No	41 (36)	17 (37)	
Focal deficit on examination, *n* (%)			
Yes	54 (48)	20 (43)	0.73
No	59 (52)	26 (57)	
Abnormal image[a], *n* (%)			0.72
Yes	71 (64)	31 (67)	
No	40 (36)	15 (33)	
Total (159)	113	46	

EEG, electroencephalogram, Y −, negative diagnostic yield, Y +, positive diagnostic yield

[a] Two patients did not have image studies during the admission

cEEG Findings

The duration of cEEG studies varied from 6 to 720 h (median 33 h). The duration of most recordings was 6 h to 3 days (Fig. 1a). In this cohort, 46 patients (29%) had a Y + cEEG, which included epileptiform discharges ($n=33$) or nonepileptic habitual events ($n=13$). There was no significant difference in diagnostic yield (31% vs. 25%, respectively, $p>0.05$) between patients with a primary diagnosis of a neurological disorder versus patients with nonneurologic disorders. Diagnostic findings occurred within the first 6 h of the recording in 65% of the Y + studies ($n=30$). Nine and five patients had initial diagnostic findings within the first 12 and 24 h, respectively. For the remaining two patients, the initial findings occurred after 24 h of the recording (Fig. 1b).

There was no significant difference in age, sex, presence or absence of brain surgery history, focal neurological deficits, or imaging abnormalities among patients who

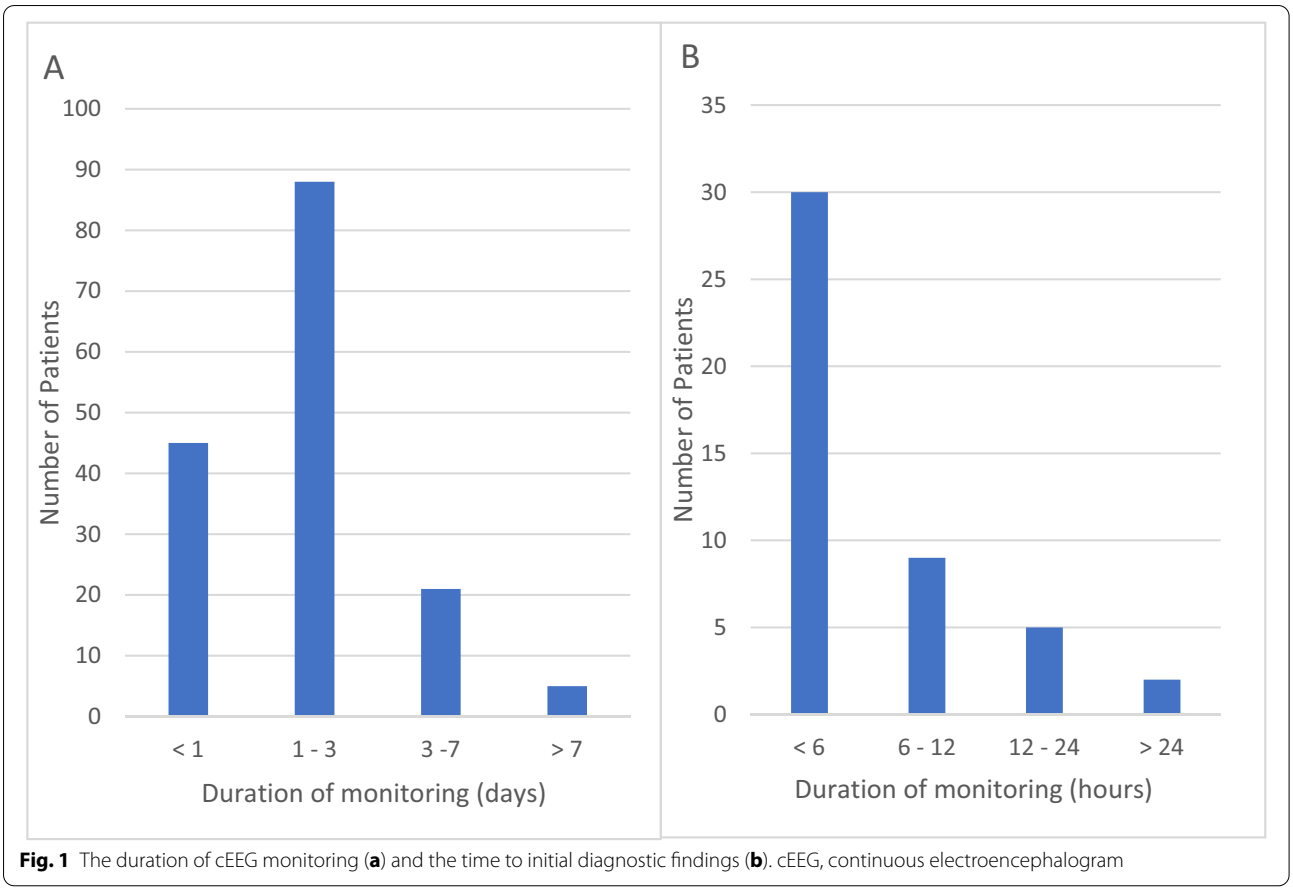

Fig. 1 The duration of cEEG monitoring (**a**) and the time to initial diagnostic findings (**b**). cEEG, continuous electroencephalogram

Table 3 Multivariable logistic regression model

Parameter	Hazard ratio (CI)	*p* value
History of seizure	9.2 (2.4–35.8)	0.001
Motor components	2.7 (0.97–7.8)	0.058

CI, confidence interval

had Y + or Y − cEEG findings (Table 2). The presence of epilepsy history and a motor semiology were associated with the Y + EEG findings in univariate studies (Table 2). Multivariate logistic regression analysis identified the presence of epilepsy history as the predictor of Y + finding (odds ratio 9.2, 95% confidence interval 2.4–35.8), whereas, for motor phenomena, the study did not reach statistical significance ($p = 0.058$) (Table 3).

Impact on Treatment

Of the 159 patients included in this study, 50 underwent ASM changes after cEEG studies. These included ASM initiation or dosage increases in 29 patients and ASM discontinuation or dosage reduction in 21 patients. As stratified by EEG findings, among patients with Y − EEGs ($n = 113$), ASMs were discontinued in 16 patients and initiated in 1 patient (Table 4, Fig. 2). A total of 16 patients had epileptiform interictal discharges on cEEG, among whom 11 patients started a new ASM or their existing ASM dosage was increased. Seizures were captured in 17 patients, all of whom underwent ASM dosage escalation (Table 4, Fig. 2). Among 13 patients who had habitual nonepileptic events, 5 patients discontinued ASM and ASM remained the same in the remaining 8 patients (Table 4, Fig. 2). In total, cEEG findings led to ASM changes in 49 patients (31%). One patient with a nondiagnostic cEEG study was also started on an ASM. For this patient, the ASM initiation was owing to clinical considerations rather than cEEG findings, and therefore the patient was not included in the group of cEEG-guided ASM changes.

Discussion

Paroxysmal events occur frequently in hospitalized patients and may be due to seizures or seizure mimics. Discerning the nature of paroxysmal events can be challenging based solely on clinical history. Epileptic or

Table 4 Summary of cEEG findings and impact on ASMs treatment

Parameter	Discontinuation or reduction	No change of dosage	Initiation or increase	ASM change, n/d (%)	Total
Y − EEG	16	96	1	16/113 (14)	113
Y + EEG					
Interictal discharges	0	5	11	11/16 (69)	16
Ictal discharges	0	0	17	17/17 (100)	17
Nonepileptic events	5	8	0	5/13 (38)	13
Total	21	109	29	49/159 (31)	159

ASM, antiseizure medication, EEG, electroencephalogram, Y − , negative diagnostic yield, Y + , positive diagnostic yield

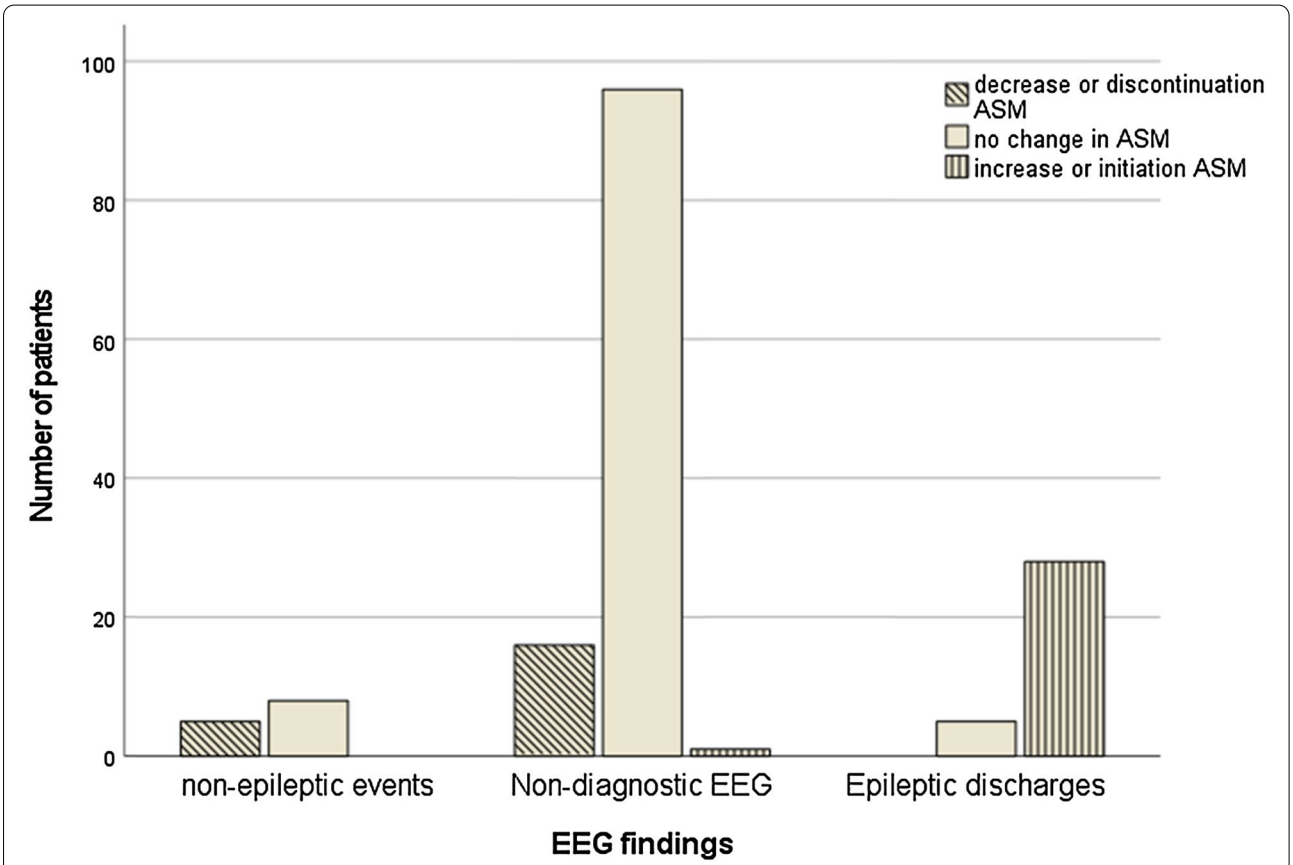

Fig. 2 ASM changes stratified by cEEG findings. ASM, antiseizure medication, cEEG, continuous electroencephalogram

nonepileptic events may have very similar clinical manifestations. Common seizure symptoms are often nonspecific [7]. For example, myoclonus could be epileptic or nonepileptic, and gaze deviation can be observed in patients with epilepsy or in other conditions affecting the frontal eye field. In addition, the diagnostic reliability by direct observation of events often varies depending on the expertise of observers. Furthermore, events are often witnessed by family members or by hospital staff other than a neurologist, which makes the diagnosis even more difficult, as the diagnostic accuracy for paroxysmal events is lower when described by witnesses than when directly observed by a neurologist [8]. Because of those challenges, an EEG study is often crucial for the accurate diagnosis. In this study, we investigated the yield of cEEG in patients in the ICU with paroxysmal events and evaluated the impact of cEEG on treatment decision making.

Clinical Indication for cEEG Studies

The paroxysmal events were dichotomized into the presence or absence of motor phenomena in this study. We found abnormal movements to be a common indication for cEEG monitoring in our study (123 of 159), which indicates a high prevalence of repetitive movements (of either epileptic or nonepileptic nature) in critically ill patients [9]. In a study that analyzed 53 video-captured movements in an ICU, 14 were epileptic and the remaining 38 were nonepileptic, including tremulous movements, jerks, and semipurposeful movements [10]. In addition, abnormal motor movements are likely to prompt further investigations such as cEEG monitoring. Although convulsive seizures are easily recognized, NCSs are often unnoticed, even by medical professionals [11]. Indeed, the diagnostic delay was ten times longer for patients with nonmotor seizures compared with those with seizures with motor manifestations [11].

In our study, gaze deviation was the second most common reason for cEEG monitoring. Abnormal gaze deviation is frequently seen in seizures involving the contralateral frontal eye field. On the other hand, ipsilateral gaze deviation is often seen in destructive brain lesions, such as ischemic strokes [12]. Similarly, speech change is a well-known phenomenon in seizures and stroke, and it often indicates that seizure onset or ischemic brain injury is in the dominant hemisphere [13]. An EEG study is invaluable to further investigate those events and identify the etiology.

Use of cEEG and Predictor of Outcome

The yield of EEG monitoring is inherently related to the indication. In our study, we defined a study as Y + if epileptiform discharges (interictal or ictal) or habitual events were captured, as such findings often help differentiate epileptic from nonepileptic events. In this cohort, the periodic discharges and other rhythmic discharges were indicative of hyperexcitability and underlying epileptogenic foci instead of sedative effects. For example, patients with lateralized periodic discharges also had brain structural changes (intracranial hemorrhage, subdural hematoma, etc.) in the corresponding brain region. We found that the yield of cEEG in paroxysmal events was 29% (46 of 159) in patients in the ICU. This result is in line with a study that investigated epileptic seizures in patients undergoing cEEG monitoring [14]. In previous ICU studies that included the indication of AMS, a higher yield of cEEG (approximately 60%) was revealed when study outcome included the epileptiform discharges and/or nonepileptic events [3, 15]. Although the higher yield in those studies was possibly due to the detection of a large number of NCSs in patients with AMS [1, 3, 15], our study excluded patients undergoing cEEG for AMS evaluation.

In nonurgent clinical settings, paroxysmal events are often evaluated in the epilepsy monitoring unit (EMU) or by ambulatory EEG (aEEG) studies, and the yield was in the range of 55–85% [16–22]. Compared with the EMU or aEEG studies, the relatively lower diagnostic yield in our study is possibly due to the different patient population. Patients with intractable epilepsy are more likely to be referred for EMU monitoring, and those patients are more likely to have abnormal EEG findings [17]. In addition, seizure provocation strategies, such as ASM tapering and sleep deprivation, are frequently used in EMU, and those procedures likely further contribute to the high diagnostic yield. An aEEG is usually ordered for various purposes, such as event characterization, determination of seizure frequency, and capturing epileptiform discharges [18]. Overall, patients with relatively frequent events are more likely to undergo aEEG evaluations. Additionally, only patients with a known history of epilepsy are referred to determine the seizure frequency. Those factors could explain the relatively higher yield in ambulatory studies.

In previous studies of patients in the ICU with various indications of cEEG, seizure predictors included history of epilepsy, coma, and age [1, 23]. A linear increase in seizure incidence with declining mental status was also reported [23]. Seizure predictors in the EMU or ambulatory EEG studies were different, including age, number of ASMs, abnormal brain magnetic resonance imaging, and focal deficits on neurological examination [20, 24–26]. In our study, a history of epilepsy was the only predictive factor identified. In contrast with the EMU study, the presence of focal neurological deficits or imaging abnormalities was not associated with increased diagnostic yield. The difference could be due to various reasons, including the fact that nonepileptic mimics (e.g., tremors, posturing, gaze, or speech changes) are known to occur in individuals with acute brain insults with abnormal imaging or neurological findings. Therefore, the seizure detection ratio might be reduced in critically ill patients. In addition, cEEG could be requested for other reasons in the ICU, for example, early detection of vasospasm, which may also reduce the diagnostic yield of detecting seizure.

Impact on Treatment

Continuous electroencephalogram monitoring had a direct impact on treatment by informing decision making, and ASM adjustments were seen in observational and prospective studies [27–29]. Among those with ASM adjustments, most patients (80–90%) had ASM initiation or dosage escalation. This was due to the high rate

of detection of NCSs while investigating AMS in the ICU [27–29].

Escalation of ASM treatment was also seen in 11 of 16 patients with interictal epileptiform discharges. For the other five patients with interictal discharges, ASM remained the same. For those five patients, the abnormal finding of interictal discharges supported the diagnosis of seizure but did not directly affect the treatment. On the other hand, the presence of ictal discharges led to ASM dosage escalation in all patients. This indicates that seizures are treated more aggressively than interictal findings. In this study, among patients who underwent medication adjustment, we found more patients with ASM discontinuation or dosage reduction (21 of 49, 43%) than previous studies (approximately 10–20%) [27, 28].

In this cohort, 13 patients had habitual events that proved to be nonepileptic. Four patients were not on ASM treatment prior to the cEEG. For these patients, the paroxysmal events prompted cEEG monitoring but were not sufficient to initiate ASM. The cEEG further confirmed the diagnosis of nonepileptic events, although it did not directly change the management. Among the remaining nine patients who started ASMs after paroxysmal events, ASMs were discontinued in five patients after habitual nonepileptic events were captured. This highlights the impact of cEEG on the management of paroxysmal events. Significant risks are associated with misdiagnosing epilepsy, including the side effect of ASMs, and adverse social effects, such as driving restrictions. Reversing the diagnosis of epilepsy can be challenging in clinical practice [30]. Prompt cEEG studies are valuable to avoid unnecessary treatment and improve health care resource use [31].

Interestingly, ASMs were discontinued in 14% (16 of 113) patients with nondiagnostic cEEG studies. Although the absence of epileptiform discharges does not rule out the possibility of seizures, the likelihood of epileptic seizures is reduced with a nondiagnostic cEEG. Therefore, a nondiagnostic cEEG recording may still significantly affect clinical impressions and have a direct impact on clinical decision making. On the other hand, ASM dosage increase was observed in one patient with a nondiagnostic cEEG, which highlights the importance of other clinical information besides cEEG.

Limitations

Our study has several limitations. These include its retrospective design and the small sample size. Additionally, we assessed the use of cEEG through ASM changes. However, cEEG may influence clinical decision making in other ways. For example, focal slowing may prompt additional brain imaging. On the other hand, ASM changes may not be solely dependent on the EEG findings. Other clinical information, such as patient history, could also play a role in these clinical decisions. Moreover, whether cEEG influences the overall clinical outcome was not assessed in this study.

Conclusions

In conclusion, cEEG provides a relatively good yield rate in the evaluation of paroxysmal events in the ICU. A history of epilepsy is associated with a higher diagnostic yield. The presence of epileptiform discharges or habitual events often leads to direct ASM adjustment. Even a nondiagnostic EEG study could have a direct impact on ASM treatments.

Author Contributions

Dr. Chen: design and implementation of the research, data analysis, and article writing. Drs. Atallah and Pauldurai: data collection. Dr. Becker: result discussion and article writing. Dr. Koubeissi: study design and article writing. The final manuscript was approved by all authors.

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Conflicts of Interest

The authors have no financial, consultant, or institutional conflicts of interest related to this study to declare.

Ethical approval/informed consent

We confirm adherence to ethical guidelines and indicate ethical approvals (institutional review board) and the use of informed consent, as appropriate. This study was approved by the George Washington University Institutional Review Board.

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