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Continuous versus Routine Electroencephalography in the Intensive Care Unit: A Review of Current Evidence

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Keywords

Electroencephalography · Prognosis · Seizures · Status epilepticus

Abstract

Background: Electroencephalography (EEG) has long been used to detect seizures in patients with disorders of consciousness. In recent years, there has been a drastically increased adoption of continuous EEG (cEEG) in the intensive care units (ICUs). Given the resources necessary to record and interpret cEEG, this is still not available in every center and widespread recommendations to use continuous instead of routine EEG (typically lasting 20 min) are still a matter of some debate. Considering recent literature and personal experience, this review offers a rationale and practical advice to address this question. ***Summary:*** Despite the development of increasingly performant imaging techniques and several validated biomarkers, EEG remains central to clinicians in the intensive care unit and has been experiencing expanding popularity for at least 2 decades. Not only does EEG allow seizure or status epilepticus detection, which in the ICU often present without clinical movements, but it is also paramount for the prognostic evaluation of comatose patients, especially after cardiac arrest, and for detecting delayed ischemia after subarachnoid hemorrhage. At the end of the last Century, improvements of technical and digital aspects regarding recording and storage of EEG tracings have progressively led to the era of cEEG and automated quantitative analysis. ***Key Messages:*** As compared to repeated rEEG, cEEG in comatose patients does not seem to improve clinical prognosis to a relevant extent, despite allowing a more performant of detection ictal events and consequent therapeutic modifications. The choice between cEEG and rEEG must therefore always be patient-tailored.

Introduction

Disorders of consciousness (DOC) represent one of the most frequent admission reasons to intensive care units (ICUs). Caregivers often initially face a sort of “black box” when the patient is connected to several monitoring systems to provide insight into physiological and pathological parameters but is clinically unresponsive. For the caregiving team, this represents a frequently encountered, challenging scenario in terms of prognostication. The electroencephalogram (EEG) is one of the most frequently applied diagnostic tools in the ICU, as it has been used for more than 70 years [1–4]. Its advantages are the noninvasiveness of the procedure, the broad availability of recording devices, and the nearly unrestricted possibility to apply it to patients (contraindications are virtually restricted to

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extensive open scalp scars). Finally, the optimal time resolution as compared to neuroimaging or biological markers is peculiar to EEG.

Historically, EEGs have been performed as routine studies (rEEG) typically lasting 20–30 min. Roughly 2 decades ago, increasing progress in terms of digital processing and storage has opened the possibility of prolonged, continuous recordings (cEEG) lasting from several hours to even some weeks. The trend of applying cEEG in ICU patients has been markedly expanding over the years, initially driven by a few specialized centers mostly in North America [5–7]. In parallel, quantitative, automated analysis of the traces (qEEG) has become increasingly widespread.

While, as compared to rEEG, cEEG clearly enhances the sensitivity toward detection of seizures and status epilepticus (SE), this procedure is more expensive in terms of personnel and technical resources. In an era where "more" in terms of investment and costs is often uncritically considered to mean "more" in terms of results and benefits for the patient, reasonable questions may arise concerning the correctness of the abovementioned equation. This review aims to offer a critical assessment of the trade-off between cEEG and rEEG and a practical guide for settings where resources are not unlimited.

Methods

To collect data for this narrative review, we ran a PubMed query using different combinations of the following search items: "EEG," "continuous EEG," "intensive care unit," "seizures," "status epilepticus," and "non convulsive" between 2000 and April 2023, restricted to English language articles. After screening titles and abstracts, articles considered more relevant were retained, avoiding redundant information. For a short historical perspective, previous articles were cited in accordance with the authors' experience and judgment regarding relevance to the present review. Since this work is a review, no ethical approval was requested. As the illustrative case does not contain any identifiable information, we did not request next of kin consent for publication.

Results

Some Definitions

The term "epileptic seizure" refers to a transitory objective and/or subjective clinical change elicited by paroxysmal neuronal discharges, as a result of a disturbance in the electrical activity of the cortex [8]. The associated symptoms and signs are directly linked to the affected areas of the brain, being focal or diffuse (generalized). In a syndromic approach, epilepsy is defined as the occurrence of at least one seizure that is not provoked by a reversible condition, such as, for example, alcohol withdrawal. Additionally, there must be a significant risk of experiencing seizure recurrence of at least 60% over the next 10 years; assessed through medical history and clinical examination, EEG, and brain imaging. This definition underscores that epilepsy involves the occurrence of unprovoked seizures and a substantial likelihood of future seizure episodes [9].

SE occurs when a seizure lasts for an unusually prolonged time lapse, as the consequence of dysfunctional mechanisms subtending seizure stop, or pathophysiological cascades prolonging seizure duration. The threshold beyond which a seizure is highly unlikely to stop by itself is set at 5 min for generalized and 10 min for focal seizures [10]. In order to prevent potential complications in terms of morbidity and mortality, rapid stepwise treatment institution is recommended, usually starting with a benzodiazepine, followed by intravenous anti-seizure drugs and subsequently, if needed, general anesthetics; details can be found elsewhere [11, 12].

EEG in the ICU

EEG, particularly cEEG, is broadly recommended to detect seizures/SE and assess their prognosis in this clinical environment [13, 14]. Furthermore, qEEG may detect delayed ischemia in patients with subarachnoid hemorrhage (SAH) several hours earlier than clinical assessments or ultrasound [15]. EEG is also widely used for epileptological and prognostic reasons in other scenarios, such as the emergency room, in hospital wards, as well as, of course, in outpatients. A detailed description beyond the ICU lies outside the aim of the review; the interested reader is referred to existing excellent reviews on these topics [16–19]. The same applies to the use of EEG in patients undergoing rehabilitation after an acute brain injury causing DOC following their treatment in the ICU, which has been covered elsewhere [20–22].

Seizures and SE, also termed ictal events, are common occurrences in DOC patients in the ICU. Their prevalence depends on the underlying conditions, ranging between 1 and 2% (acute ischemic stroke) to 30–40% (severe traumatic brain injury, central nervous system infections, or hypoxic-ischemic encephalopathy [HIE]) [23]. Importantly, the vast majority (roughly 90%) of these ictal features occur without any clinical counterpart, hence the terms of "non-convulsive" or "subclinical" seizures or SE [23, 24]. To the contrary, about three-quarters of patients showing abnormal movements in the ICU do not have seizure or SE, but other conditions, such as motor stereotyped movements, shivering (relatively

Table 1. Overview of the most frequent EEG indications in the intensive care unit stratified by underlying conditions

Underlying condition	Main EEG indication	Common findings
Clinical SE/seizures	Seizure/SE detection	• IIC • Seizures/SE
Suspected non-convulsive SE/Seizures	Seizure/SE detection	• Encephalopathy • IIC • Seizures/SE
Hypoxic-ischemic brain Injury	Prognostication seizure detection	• Diffuse encephalopathy • Background (dis-)continuity and reactivity • Epileptiform transients including IIC
Traumatic brain Injury	Seizure detection	• (Focal) encephalopathy • IIC • Seizures/SE
Subarachnoid hemorrhage	Seizure detection delayed ischemia detection	• (Focal) encephalopathy • Dynamic focal alteration of electrogenesis • IIC • Seizures/SE
Stroke (hemorrhagic or ischemic)	Seizure detection	• (Focal) encephalopathy • IIC • Seizures/SE
Infectious/metabolic/toxic encephalopathy	Seizure detection quantification of encephalopathy	• Diffuse encephalopathy • Seizure/SE

IIC, ictal-interictal continuum features; cEEG, continuous EEG; rEEG, routine EEG; SE, status epilepticus.

frequently observed when general anesthetics are weaned off), subcortical myoclonus, or corticospinal clonus [25, 26].

The logical consequence is to systematically couple video-recordings to the EEG to optimize diagnosis [13, 27]. Additionally, as background EEG reactivity has been shown to inform on prognosis in DOC patients with HIE and beyond [28–30], it is recommended to routinely perform standardized auditory and nociceptive stimulations [31, 32]; this illustrates the importance for the EEG interpreter to consider the whole clinical picture, not relying solely on the electrical signals. Newly developed tools have been recently introduced to allow clinicians to use simplified EEG montages in emergency settings and ICU, offering the possibility to record cerebral activity without the need for an EEG technician, and can be applied to the scalp in as fast as 5 min, and easing the interpretation process by providing automated alerts to unskilled caregivers [33, 34]. Although further validation and clarification of costs issues are needed before a widespread use, such tools may certainly facilitate access to EEG, potentially reducing hospital stays and costs in patients with suspected nonconvulsive ictal events [35]. Table 1 summarizes EEG indications and findings in ICU patients.

EEG Interpretation

Given the variety of features that can be found on EEG recordings in the ICU, we clearly and strongly recommend a standardized approach to its interpretation. The updated American Clinical Neurophysiology Society (ACNS) guidelines [36] provide a comprehensive frame to describe ICU-EEGs. They offer detailed guidance to assess the electrical background (including dominant frequency, and its continuity), epileptiform transients (spikes, spike, and waves, sharp waves), rhythmic or periodic patterns of the so-called ictal-interictal continuum (IIC; e.g., lateralized or generalized periodic discharges, lateralized rhythmic delta activity), and criteria to diagnose nonconvulsive SE [37]. These ACNS criteria have been validated [38] and are increasingly implemented, e.g., to describe the EEG for prognostic purposes in HIE patients [39–41]. The concomitant use of automated qEEG softwares, which allow displaying on the same screen amplitude-integrated traces,

Table 2. 2HELPS2B score adapted from [54]

2H	GRDA, LRDA, BIPD, LPDs, or GPDs with a frequency >2 Hz	1 point
E	Epileptiform discharges	1 point
L	LPD, LRDA or BIPDs	1 point
P	Plus modifiers (superimposed rhythmic, sharp, or fast activity)	1 point
S	Seizures (acute or remote prior seizures)	1 point
2B	BIRDs	2 points

BIPD, Bilateral Independent Periodid Discharges; BIRDS, Brief Potentially Ictal Rhythmic Discharges; GPDs, Generalized Periodic Discharges; GRDA, Generalized Rythmic Delta Activity; LPDs, Lateral Periodic Discharges; LRDA, Lateralized Rythmic Delta Activity. Seizure/SE risk: 3% for 0 points, 12% for 1 point, 34% for 2 points, 52% for 3 points, 71% for 4 points, 84% for 5 points, and 92% for 6 points.

rhythmicity, and frequency-power spectrograms, seizure and spike detections, as well as other features (such as alpha/delta ratios), show constantly improving performances [42, 43]. If used correctly, they reduce considerably the time spent for EEG interpretation; the gain has been estimated by a factor of around two-thirds [44]. However, in our [45] and others [42] experience, a steady access to rough EEG curves is mandatory to allow detection of the many artifacts that can arise in an ICU environment, as well as false-negative qEEG alarms. This implies that the reader should have some training and experience in interpreting raw EEG data, as exclusive reliance on qEEG is often suboptimal [46, 47] and may lead to incorrect treatment decisions.

Does cEEG Improve Prognosis?

As compared to rEEG, cEEG requires more recording machines (as one device only allows recording on one single patient, while in the case of rEEG, several subjects may be subsequentially recorded with the same machine), implying using more reusable and nonreusable material such as electrodes and caps, and, given the increased number of recordings, more personnel to interpret the traces and storage facilities. It has been demonstrated, at least in the USA, that what precedes translates into higher costs [5], but, again in the USA, the higher reimbursement fees received from insurances, as compared to rEEG, outweigh the costs and allow running neuro-ICU units with more than a dozen cEEG performed at the same time (personal communications with several colleagues). These pitfalls may be counterbalanced by the clinical impact: several guidelines stress the importance of cEEG in patients under refractory SE treatment, in order to titrate general anesthetics and antiseizure medication, which could hardly be done relying only on rEEG [11, 13, 48]. While this indication for cEEG is widely accepted, things become less clear for patients in other clinical conditions.

Several independent analyses have outlined that seizures/SE density over time correlates with worsening clinical prognosis in adults [49] and children [50, 51]. However, association does not imply causality. Twenty years ago, a seminal study showed that a recording time of at least 48 h is necessary to detect 90–95% of seizures/SE in the ICU [24]. Other investigators subsequently attempted to refine this observation: it has been found that the first 20–30 min (corresponding to a rEEG) are paramount. Indeed, the lack of epileptiform transients or IIC patterns, during this timeframe, lowers the risk of subsequent ictal events below 5% [52]. More recently, the 2HELPS2B score has been proposed and validated to stratify the risk of subsequent seizure occurrence in ICU patients undergoing EEG (Table 2) [53, 54]. It includes elements of the IIC and the history of recent seizures/SE occurrence. Independently, the Time-dependent electro-clinical Risk Stratification for electrographic Seizures (TERSE) algorithm, which has been also validated, considering consciousness level, seizure/SE occurrence, and IIC patterns, may inform on the optimal EEG duration [55, 56]; a strict application of this algorithm has been described to reduce cEEG recording time by roughly two-thirds.

In the ICU, the use of cEEG is exponentially increasing, especially in relatively selected North American centers, and has been correlated with increased detection of seizures/SE [57], and treatment modifications [58, 59]. In addition, improved clinical outcome, particularly reduced mortality, has been reported in two large retrospective observational studies based on health insurance discharge diagnoses [5, 60]. These studies' design raises the possibility of information and possibly selection biases, which would not be adjustable with multivariable statistical approaches. Also, these results contrast with some retrospective single-center assessments, which did

Table 3. Summary of the results from the CERTA trial (for details, see main text)

Item	Findings regarding cEEG versus rEEG
Mortality	Comparable, also in patients with HIE
Functional outcome	Comparable, also in patients with HIE
Reimbursement (costs)	Comparable*
Seizures/SE detection	Higher sensitivity of cEEG
Epileptiform discharges, IIC	Higher sensitivity of cEEG
Treatment modifications following EEG	More frequent after cEEG
Generalized rhythmic delta activity	Higher sensitivity of cEEG
Spindles activity	Higher sensitivity of cEEG
Background frequency	Comparable
Background continuity	Comparable
Background reactivity	Comparable

IIC, ictal-interictal continuum features; cEEG, continuous EEG; HIE, hypoxic-ischemic encephalopathy; SE, status epilepticus. *Applies to a diagnosis-related group reimbursement system.

not show any correlation between clinical improvement and cEEG [58, 61]. At that point, while it seems clear that cEEG allows a more accurate detection of ictal events and thus a more frequent adaptation of therapeutic procedures, the question regarding the impact on patients' prognosis was still unanswered.

A Randomized Trial

The Continuous EEG Randomized Trial in Adults (CERTA, NCT03129438) represents the first attempt to assess the impact of cEEG on patients' outcome; it was carried out in four large Swiss centers. Patients with Glasgow Coma Scale ≤11 or Full Outline of Unresponsiveness ≤12 [62], needing an EEG for their clinical management, were prospectively recruited. Subjects with seizures/SE in the preceding days were excluded to allow cEEG for SE treatment monitoring (as stated above, representing a widely accepted cEEG indication that was not at stake for the study), as well as those in palliative care situations, or needing major surgery within 24 h. Participants were randomized 1:1 to cEEG over 30–48 h or rEEG (repeated within the same timeframe). EEG interpretation was standardized across centers [63], using the ACNS guidelines of that time [64]. Three-hundred and sixty-five patients were analyzed for mortality at 6 months, the primary outcome, which turned out to be nearly identical across the two interventional groups (48.9% in cEEG, 48.4% in rEEG, relative risk of 1.02, 95% confidence interval 0.83–1.26) [65]. Given the sample size, which was tailored on the mortality difference described in a previous study [60], it is still possible that a small absolute difference in mortality of the magnitude of about 5% (especially in patients without HIE) could remain undetected; to verify this, a trial recruiting an about 15 times bigger cohort would be needed [65]. The findings were more varied regarding secondary outcomes measures. Functional outcome, assessed with Cerebral Performance Categories and the modified Rankin Scale, was also comparable [65]. However, cEEG led more frequently to treatment changes and allowed a higher detection of IIC features (69% vs. 56%) and of ictal events (seizures/SE: 16 vs. 4%). Of note, this cEEG seizure/SE detection rate was nearly identical to a retrospective analysis from North America [66], thus supporting a reasonable generalizability of the results. Patients' outcome was not influenced by the delay between hospital admission and the EEG recording start [67]. Table 3 summarizes the main findings of this trial.

Further analysis of the CERTA dataset shed an interesting and partly new light regarding the role of cEEG versus rEEG in ICU patients, beyond the aforementioned outcomes. Of relevance, in a diagnosis-related group reimbursement system (which is common to many European countries, but also beyond) cEEG does not significantly generate more costs [68], unlike in the USA [5], and thus does not represent any financial incentive. Considering prognostic EEG features, cEEG allows, in comparison to rEEG, a significant increased detection not only of ictal events but also of generalized rhythmic delta [69] and sleep spindles [70], which are both related to favorable prognosis. On the other hand, EEG background frequency, continuity, and reactivity (if performed during the recording) are readily assessable in rEEG [69]. Finally, detailed assessment of patients with HIE, representing more than one-quarter of the studied cohort, confirmed that clinical outcome was independent of EEG type also in this relevant subgroup

Table 4. Proposed pragmatic approach to EEG recording length in the intensive care unit according to different scenarios (1st line), based on clinical findings and the 2HELPS2B score (1, 2)

	1. Recent but resolved seizure/SE	2. Ongoing SE	3. Unexplained DOC	4. Risk of delayed cerebral ischemia (SAH)	5. HIE
Start with	rEEG	cEEG	rEEG	cEEG (with qEEG)	rEEG repeat after 24–48 h
If 2HELPS2B <2, no seizure/SE	Repeat rEEG after 24–48 h if patient not alert (→3.)	Stop after 3–6 h	Repeat rEEG after 24–48 h	Continue cEEG for up to 10–14 days	Repeat rEEG after 24–48 h
If 2HELPS2B ≥2, seizure or SE	Treat and convert to cEEG for 24–48 h	Adapt treatment, continue cEEG for 24–48 h	Treat and convert to cEEG for 24–48 h	Treat and continue cEEG for 10–14 days	Treat; convert to cEEG (for 24–28 h) only if multimodal assessment compatible with favorable prognosis

cEEG, continuous EEG; rEEG, routine EEG; qEEG, quantitative EEG; DOC, disorder of consciousness; HIE, hypoxic-ischemic encephalopathy; SAH, subarachnoid hemorrhage; SE, status epilepticus.

[71]. These data support a valid prognostic use of EEG background in comatose HIE patients [29, 30, 72, 73], assessed over a relatively short time, in a repeated manner.

Illustrative Case

A patient in his 60th man was admitted to the ICU after a severe middle cerebral artery stroke with M1 occlusion. He was treated with iv thrombolysis followed by thrombectomy. The following day, the patient's state of consciousness worsened (FOUR score 6/16) requiring intubation. A CT scan showed a large hemorrhagic transformation. Subsequently, he underwent rEEG, which showed a nonconvulsive seizure on the right temporal region, lasting 40 s. The EEG was then converted to cEEG, showing 2 additional similar nonconvulsive seizures occurring 20 min apart, after 4 h. After the second seizure, he was loaded with 60 mg/kg intravenous levetiracetam followed by 750 mg bid, with no subsequent seizure over the following 36 hours.

The patient died a few weeks thereafter, without ever regaining consciousness (and without seizure relapse on subsequent EEGs), following multi-organ failure. This case illustrates that the underlying lesions played a major prognostic role as compared to the ictal activity detected on cEEG.

Conclusion

Considering the currently available evidence, as compared to repeated rEEG, the use of cEEG in comatose patients does not seem to improve by itself their clinical prognosis in a meaningful magnitude, despite allowing a more performant detection of seizures/SE, epileptiform, and IIC features, and consequent therapeutic modifications. This appears at first glance surprising, contradicting the equation "more is more." It may, however, be at least partly explained by the prominent prognostic role of the underlying patients' biological background, including etiology, comorbidities, and perhaps even medication side effects [74]. Several clinical examples illustrate this thought, such as in the case of repetitive, rhythmic epileptiform discharges detected on top of a suppressed EEG background in a non-sedated comatose patient after traumatic brain injury that may disappear after administration of anti-seizure medications and even general anesthetics; the clinical fate of the patient will nevertheless mostly depend on the extent of the underlying structural brain damage. As expressed in our illustrative case, we would like to emphasize the importance of always and systematically integrate EEG findings (being from cEEG or rEEG) together with the clinical context. We decidedly discourage an "aseptic" neurophysiological interpretation forgetting other prognostic modalities, including as a minimum neurological examination, neuroimaging findings, and laboratory parameters.

Continuous EEG is linked to increased requirements in terms of personnel and material; it is convincingly demonstrated that it does allow better detection of several prognostic features, ictal events (seizures/SE), and that it is related to an increased number of treatment modifications. However, at least in patients without preceding ictal events, cEEG does not seem to offer a clearly measurable effect on prognosis. One should recognize that the current evidence is not optimal, given the relatively limited number of patients enrolled in a single randomized controlled trial; also, relevant long-term outcomes such as the risk to develop epilepsy [75] have not been adequately investigated. Larger, prospective, comparative studies are required to refine current knowledge. However, regarding the clinical impact of cEEG versus repeated rEEG, two arms of about 2500 patients each should be planned, ideally excluding those with HIE (having a peculiar clinical trajectory and globally high mortality). In our experience, this targeted sample would represent a major challenge regarding feasibility and study funding.

For the time being, we propose in Table 4 a pragmatic approach to orient on EEG recording length in centers lacking unlimited access to cEEG, oriented on clinical findings and the 2HELPS2B score [53, 54](Table 2). We recommend pragmatically using the threshold of ≥2 points to consider the patient at considerable risk of seizure occurrence (34%). Of course, the TERSE score, providing an electro-clinical risk stratification of ictal events based on the presence of coma, history of epilepsy, or clinical seizures prior to EEG [55, 56] can further orient on EEG recording length. The choice between cEEG and rEEG must in any case be patient tailored. Indeed, several other clinical parameters, particularly etiology, exert a stronger impact on prognosis than the EEG findings.

A final consideration applies to patients with HIE: conversion of rEEG to cEEG seems reasonable after detecting IIC features or SE only in patients with concomitant multimodal assessment forecasting a possible favorable prognosis, such as early return of a continuous EEG background and reactivity, a late appearance of epileptiform features, return of brainstem reflexes, present cortical response of median nerve somatosensory evoked potentials, lack of markedly elevated biological markers, and of widespread lesions on brain imaging [29, 76–79]. In fact, a systematic, aggressive and prolonged treatment regardless of this multimodal prognostic assessment is probably futile, as recently outlined in a randomized trial [80].

Conflict of Interest Statement

The authors have no conflict of interest to declare.

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Author Contributions

H.F.: performed literature review, drafted the work, approved the final version to be published, agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. A.O.R.: contributed to the conception of the work and the analysis of data, drafted the work, approved the final version to be published, agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. I.B.: substantial contribution to the conception and design article, revised the manuscript critically for important intellectual content, approved the final version to be published, agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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