

Review

Using artificial intelligence to optimize anti-seizure treatment and EEG-guided decisions in severe brain injury

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ABSTRACT

Electroencephalography (EEG) is invaluable in the management of acute neurological emergencies. Characteristic EEG changes have been identified in diverse neurologic conditions including stroke, trauma, and anoxia, and the increased utilization of continuous EEG (cEEG) has identified potentially harmful activity even in patients without overt clinical signs or neurologic diagnoses. Manual annotation by expert neurophysiologists is a major resource limitation in investigating the prognostic and therapeutic implications of these EEG patterns and in expanding EEG use to a broader set of patients who are likely to benefit. Artificial intelligence (AI) has already demonstrated clinical success in guiding cEEG allocation for patients at risk for seizures, and its potential uses in neurocritical care are expanding alongside improvements in AI itself. We review both current clinical uses of AI for EEG-guided management as well as ongoing research directions in automated seizure and ischemia detection, neurologic prognostication, and guidance of medical and surgical treatment.

Introduction

Continuous electroencephalography (cEEG) is frequently used in the critical care setting for detection of seizures, prognostication, and monitoring ischemia and depth of sedation [1]. Nation-wide epidemiological studies have shown increasing use of cEEG in the critical care setting over the last two decades [2,3]. A recent study examining national trends in cEEG utilization in patients with acute cerebrovascular diseases demonstrated a 364 % increase in cEEG use from 2014 to 2020 [3]. Similar work from the nationwide inpatient sample has shown a greater than 10-fold increase in cEEG use in critical care [2].

The increasing use of cEEG has led to increasing detection of seizures and other epileptiform abnormalities including periodic and rhythmic patterns and the ictal-interictal continuum (IIC) [4,5]. Several studies have demonstrated that the presence and increasing burden of seizures, epileptiform abnormalities, and IIC patterns are associated with secondary brain injury, higher risk for mortality, and worse functional and cognitive outcomes [6–9]. cEEG allows high-resolution monitoring of these patterns in hospitalized patients and has improved the capture of nonconvulsive seizures, highlighting that many of these would have been missed with clinical observation and routine EEG alone [5,10].

Nonconvulsive status epilepticus often manifests solely as altered mental status [11], requires EEG for reliable diagnosis [12,13], and is likely underdiagnosed without prolonged monitoring [14]. cEEG can thus improve seizure detection [15] and is associated with improved inpatient survival [2,3,16], despite patients who receive cEEG likely being sicker.

There continues to be a growing clinical and research interest in the diagnostic and prognostic significance of common EEG patterns seen in the critical care setting along with research efforts to understand optimal EEG-guided anti-seizure treatment strategies. One of the major limitations of cEEG use, both in clinical practice and in research studies, is the time-intensive and laborious nature of raw EEG review. Artificial intelligence (AI) can help address this need by monitoring epileptiform activity, prognosticating outcomes, and guiding treatment strategies. In this narrative review, we highlight the AI-based methods that have been developed to optimize EEG-guided decision making.

Methods

We performed a MEDLINE search for articles on the application of AI in critical care EEG monitoring. Specific emphasis was given to studies directly pertaining to the clinical indications of cEEG monitoring

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including those defined in the American Clinical Neurophysiology society consensus statement for critical monitoring [1]. We additionally discuss current research directions utilizing AI for dataset generation to enable algorithm development and for improved clinical trial design.

Seizure Prediction, Detection and Management

An estimated 20–30 % of critically ill patients on cEEG have seizures [10,17,18], ~90 % of which are subclinical [17]. A prospective study of patients without primary neurologic diagnoses found nonconvulsive seizures in more than 10 % [19]. In addition to seizures, 40–50 % of critically ill patients undergoing cEEG are at risk of having other periodic

and rhythmic patterns [20]. The American Clinical Neurophysiology Society has proposed a standardized nomenclature for common EEG patterns seen in the critical care setting [21]. This nomenclature is now routinely used in clinical practice and in research studies. Fig. 1 shows examples of common EEG patterns using ACNS definitions.

Seizure prediction

Given cEEG is resource-intensive, selecting patients who are likely to benefit from cEEG and determining the duration of monitoring are major challenges in proactive seizure management. Presence of periodic and epileptiform discharges on initial EEG recording are associated with a

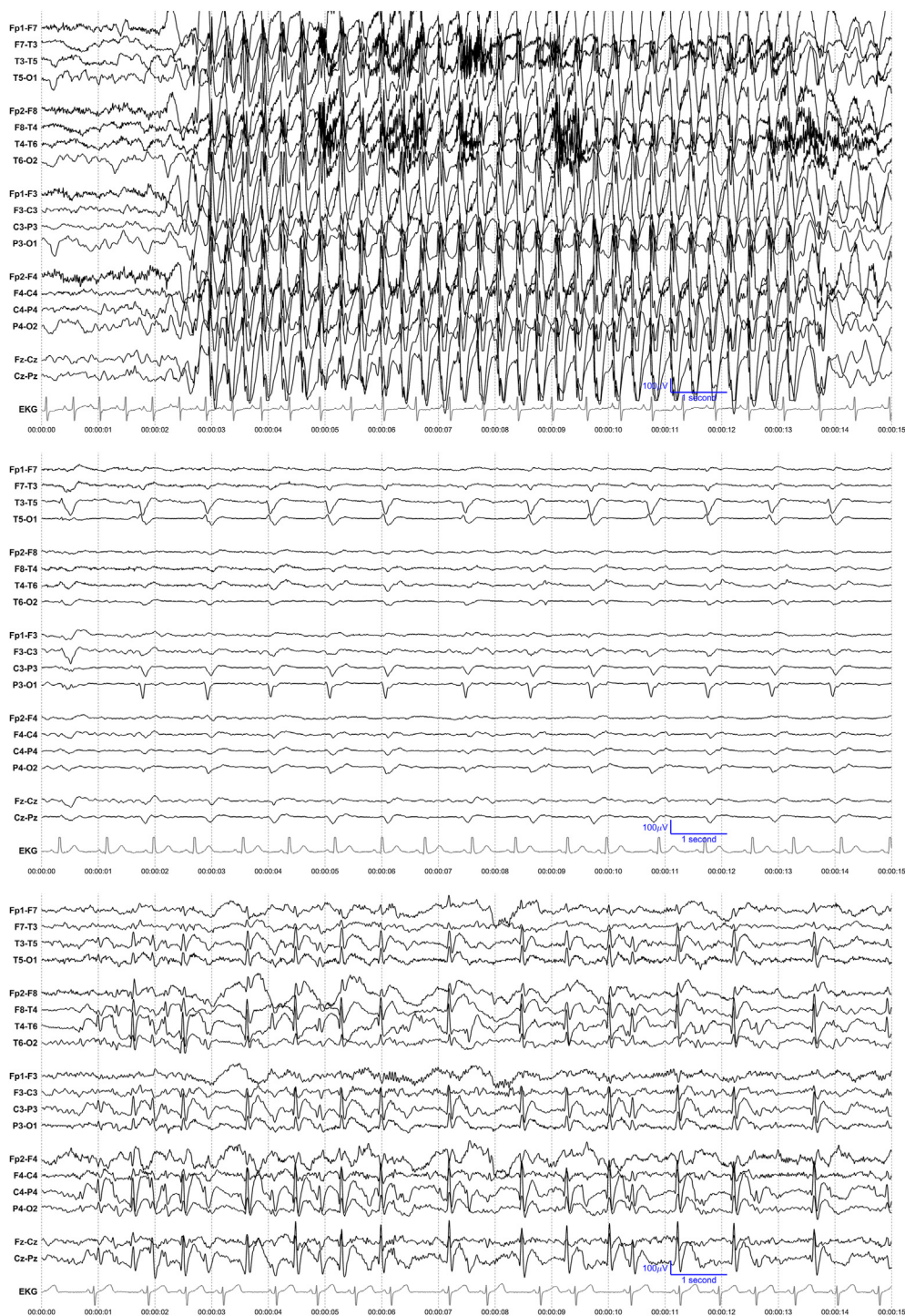
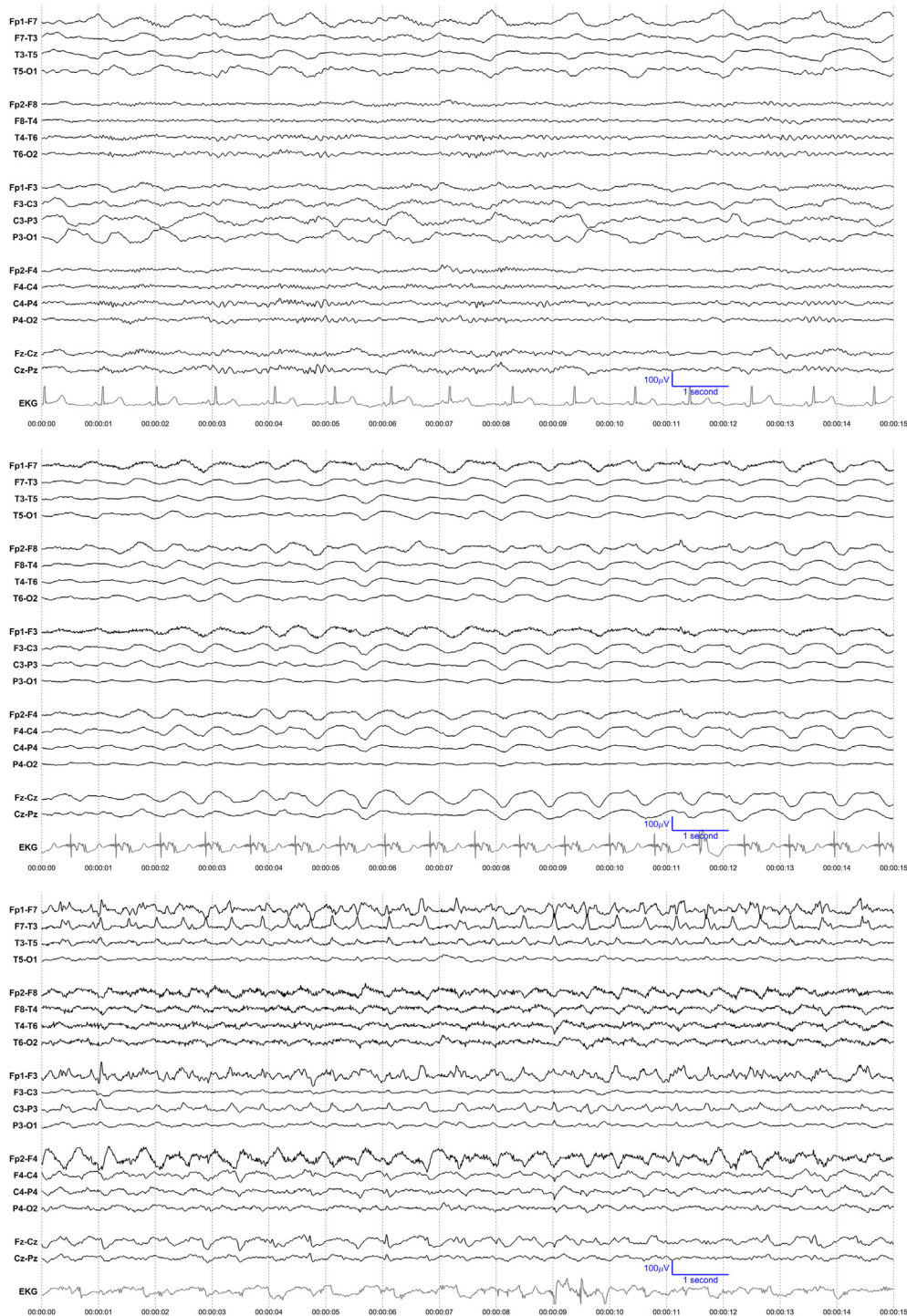


Fig. 1. Common continuous EEG patterns seen in the critical care setting as defined by the American Clinical Neurophysiology Society nomenclature. a) Example of electrographic seizure. b) Example of lateralized periodic discharges. c) Example of generalized periodic discharges. d) Example of lateralized rhythmic delta activity. e) Example of generalized rhythmic delta activity. f) Example of Ictal-Interictal continuum pattern.

Fig. 1. (continued).



higher risk of seizures as demonstrated in diverse cohorts, including central nervous system infections [22], intracerebral hemorrhages [23], and pediatrics [24]. Patients lacking early epileptiform abnormalities have vanishingly decreasing seizure risk [18], and the rate at which risk decreases depends on the presence of epileptiform abnormalities [10].

The 2HELPS2B model was developed to incorporate these early EEG features, along with prior history of seizure, to produce an interpretable seizure risk score [25]. While most clinical risk scores are developed with manual feature selection, 2HELPS2B used a machine learning method designed to optimize risk scores with a small selection of variables [26]. The 2HELPS2B score has been validated on independent patient cohorts and can stratify seizure risk using just 1 h of screening EEG, improving cEEG

allocation [27]. Application of the 2HELPS2B on 1-h rapid response EEG, which includes fewer leads and reduced time-to-application, was found to be noninferior to conventional EEG for seizure prediction [28]. Table 1 shows the components of the 2HELPS2B score, the predicted probabilities of seizure based on the total score, and the corresponding recommended cEEG duration. Fig. 2 shows three examples of the application of the 2HELPS2B score to guide duration of EEG monitoring in clinical practice.

EEG screening and seizure detection using quantitative EEG

Several quantitative EEG (qEEG) tools have been developed that can assist in rapid screening of recordings for seizures and other periodic and

Table 1
Overview of 2HELPS2B score.

Variable	Point Assignment
Brief (ictal) rhythmic discharges	2
Presence of lateralized periodic discharges, lateralized rhythmic delta activity, or bilateral independent periodic discharges	1
Sporadic epileptiform discharges	1
Frequency greater than 2.0–Hz for any periodic or rhythmic pattern	1
Presence of "plus" features (superimposed, rhythmic, sharp, or fast activity)	1
Prior seizure	1

2HELPS2B score	Predicted seizure probability	cEEG recommendation
0	5%	No need for cEEG
1	12%	At least 12hr cEEG
2	27%	At least 24hr cEEG
3	50%	At least 24hr cEEG
4	73%	At least 24hr cEEG
5	88%	At least 24hr cEEG
6+	> 95%	At least 24hr cEEG

cEEG: continuous electroencephalography.

rhythmic patterns [29,30]. Compressed spectral arrays (CSA) are among the mostly commonly used qEEG tools [31]. Seizures, periodic and rhythmic patterns, and background slowing have distinct features on CSAs, and a standardized nomenclature for CSAs has been developed with high sensitivity and inter-rater agreement [32]. Seizures have a classic "solid flame" appearance on CSAs, shown in Fig. 3. The presence of solid flames can have a sensitivity of up to 87.5 % and specificity of 92.5 % for the detection of seizures [32].

Use of CSAs can expedite screening of EEGs. In one study, CSAs identified seizures with sensitivity of 51–67 % and median review time of 6 min and CSA plus raw EEG review identified seizures with sensitivity of 63–68 % and median time 14.5 min, compared to raw EEG review with median time 19 min [31]. Another study found that the mean time to review 24 h of cEEG was 8 min for CSA-guided vs 38 min for conventional review, and 10 min vs. 44 min when there were seizures [33].

Finally, qEEG can enable non-neurophysiologists to screen for seizures, with several studies demonstrating that CSA-based seizure detection was comparable between neurophysiologists and non-neurophysiologists [34,35]. While qEEG and CSAs can expedite seizure screening and detection, they cannot fully replace review of raw EEG and are most often used to aid this process.

Automated annotation and interpretation of EEG

Several AI algorithms have been developed for automated EEG analysis with variable success and degree of human involvement [36–45]. The scalability and reliability of machine learning methods depends on large training datasets annotated by experts, making AI-expedited annotation especially valuable. Unsupervised machine learning methods can be used to pre-cluster seizure, periodic and rhythmic patterns, and burst suppression from prolonged EEG recordings, facilitating more efficient labeling by expert neurophysiologists [46]. Active learning can be used to select which EEG segments are most valuable for humans to annotate for downstream training, enabling rapid annotation of large datasets for deep neural networks that approach expert-level performance [8,47]. Fig. 4 shows an example of a Graphical User Interface used to annotate large EEG datasets. Application of such neural networks to a cohort of neurologic, medical, and surgical patients undergoing cEEG achieved a rate of one annotation per 2 s and revealed that increasing peak epileptiform burden is associated with worse neurologic outcomes across all diagnostic categories [8]. The combination of deep learning and large labeled datasets has enabled AI systems to independently annotate EEGs at least as well as experts [48–50] and to offer interpretable assistance to experts that improves diagnostic accuracy [51]. These tools are a way forward to deal with the resource-intensive and laborious tasks of manual EEG review for clinical care, research studies, and clinical trials.

Seizure management

In the critical care setting, anti-seizure medications (ASMs) are routinely prescribed for seizures and frequently for periodic and rhythmic patterns [8,52–54]. Treatment is often escalated to use of anesthetics, particularly in the setting of status epilepticus [55]. EEG monitoring is used to guide ASM escalation and determine response to anesthetic medications [1,53,56]. Seizure or burst suppression are common treatment targets when using anesthetics for refractory seizures or status epilepticus in critically ill patients [1]. qEEG tools can be used to assess the degree of burst suppression and sedation and to titrate anesthetics accordingly [29]. Similarly, qEEG can be used as a guide in weaning anesthetic sedation. Fig. 5 shows an example of burst suppression in response to escalating doses of anesthetics in a patient with status epilepticus.

Ongoing research is focused on using AI to optimize EEG-guided management. ASMs carry significant risks and narrow therapeutic indexes [57] and have variable pharmacokinetics and pharmacodynamics [58–60]. Guidelines for ASM use in seizure and epilepsy are developed according to population-level analyses [61–63]. While the importance of individualized therapy is well-understood, this is challenging in practice, particularly in critically ill patients who have altered physiology [64]. Furthermore, periodic and rhythmic patterns and electrographic seizures are often aggressively managed despite uncertain benefit [5,65,66].

By learning pharmacokinetic and pharmacodynamic relationships at an individual level, AI methods can perform causal inference to quantify the benefit of ASMs and design personalized treatment strategies, improving outcomes for patients who may have required either more restrictive or more aggressive regimes than the management they received [67]. These pharmacokinetic-pharmacodynamic analyses have additionally identified major limitations in clinical trial design for seizure treatment, highlighting the role of machine learning in informing data-driven trial design for treatment of seizures in the critical care setting [68]. Validated automated EEG annotation systems can significantly increase the feasibility of randomized trials for seizure/status epilepticus management by mitigating the laborious task of manual EEG review for assessment of treatment endpoints. Finally, in patients with medication-refractory epilepsy, AI-augmented methods can utilize interictal EEG features to localize seizure-generating tissue (i.e. the seizure onset zone), thereby informing neurosurgical management [69].

Prognostication in Acute Injury and Neurocritical Care

Prognostication in disorders of consciousness

14–32 % of patients in minimally conscious or vegetative states may have cognitive-motor dissociation (CMD), which is characterized by clinical unresponsiveness with evidence of brain activation on EEG or functional magnetic resonance imaging (fMRI) [70,71]. In a cohort of 104 unresponsive patients [72], digital bedside EEG recordings were obtained following commands for patients to move their hands, and power in predetermined frequency ranges was calculated and used to train a machine learning classifier to detect brain activation [73]. 16 (15 %) had brain activation detected. 50 % of patients with brain activation vs. 26 % of patients without brain activation improved to following commands prior to discharge, and 44 % vs. 14 % had a GOS-E level [74] of ≥ 4 at 12 months. A multi-center study identified responses to commands on EEG and/or fMRI in 25 % of patients without an observable response, with EEG analyses being performed either by comparison of power spectral densities or by a machine learning algorithm [75]. Identification of patients with CMD may in turn influence management, as neurologic prognosis is important in decisions regarding life-sustaining therapy [76,77]. However, application of machine learning algorithms, and the associated resources, including the expertise for performing the test, and interpreting and communicating results may not be available in the clinical setting, particularly in resources

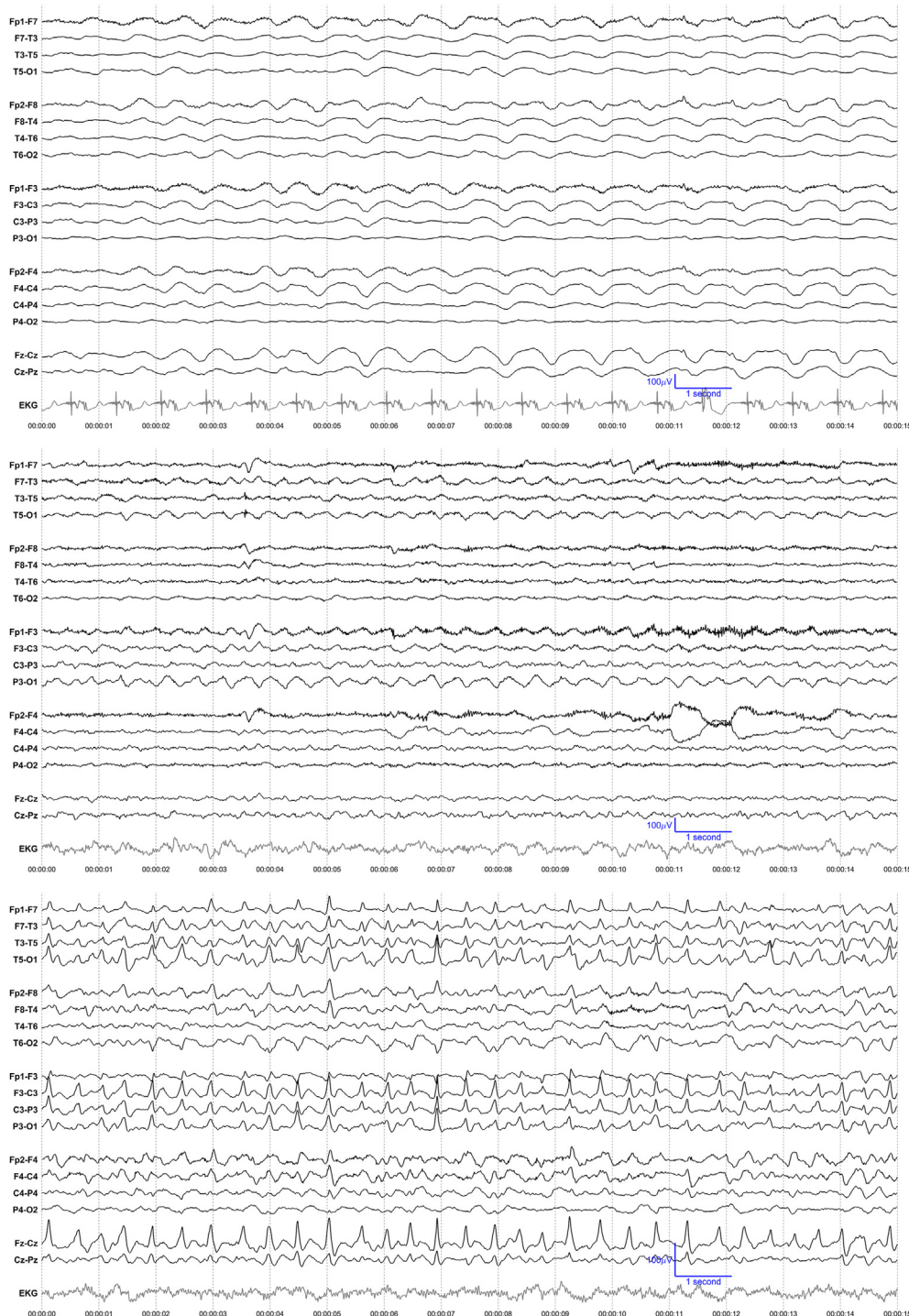


Fig. 2. Application of the 2HELPS2B score. a) Case 1: Patient with urosepsis and altered mental status. EEG demonstrates generalized slowing and generalized rhythmic delta activity. 2HELPS2B score is 0, due to absence of all components listed in the score. The predicted probability of seizures is 5 %, and the recommended length of additional EEG monitoring is 0 h. b) Case 2: Patient with left sided acute subdural hematoma and a generalized seizure on admission to emergency, prior to EEG initiation. EEG demonstrates left lateralized rhythmic delta activity. 2HELPS2B score is 3 for lateralized rhythmic delta activity (1 point), frequency > 2Hz (1 point) and prior seizure (1 point). The predicted probability of seizures is 50 %, and 24 h of cEEG monitoring is recommended. c) Case 3: Patient left MCA stroke and hypoxic respiratory failure. EEG obtained for altered mental status and demonstrates left lateralized periodic discharges. 2HELPS2B score is 2 for LPDs (1 point), frequency > 2Hz (1 point). The predicted probability of seizures is 27 %, and 24 h of cEEG monitoring is recommended.

limited settings. Efforts to develop evidence-based guidelines for identifying patients with CMD have emphasized the importance of standardized approaches in data acquisition and analysis as well as the challenges in interpreting and communicating these results [78].

Prognostication in traumatic brain injury

TBI is a major cause of morbidity and mortality with a rising global burden [79,80]. The long-term consequences of TBI are myriad and include seizure, neurodegenerative, vascular, and psychiatric disorders, suggesting that TBI should be considered a chronic and progressive disease [80,81]. Prognostication of mortality and functional outcomes is a

major challenge in TBI management. Patients with moderate-to-severe TBI, corresponding to an admission Glasgow Coma Scale (GCS) score of ≤ 12 out of 15, experience a broad spectrum of functional recovery that physicians are unable to reliably forecast according to an individual's clinical variables [82]. Mild TBI (GCS score 13 to 15) constitutes over 90 % of TBI [83], but more than 50 % of people with mild TBI experience residual functional impairments one year post-injury [84], and prediction of outcomes for these patients is similarly difficult [85].

TBI is associated with acute, subacute, and chronic EEG changes, even in mild injury [86,87] yet the utility of these changes in managing TBI has been uncertain [88,89]. An early decision in the management of TBI is the selection of patients for imaging with computed tomography (CT)

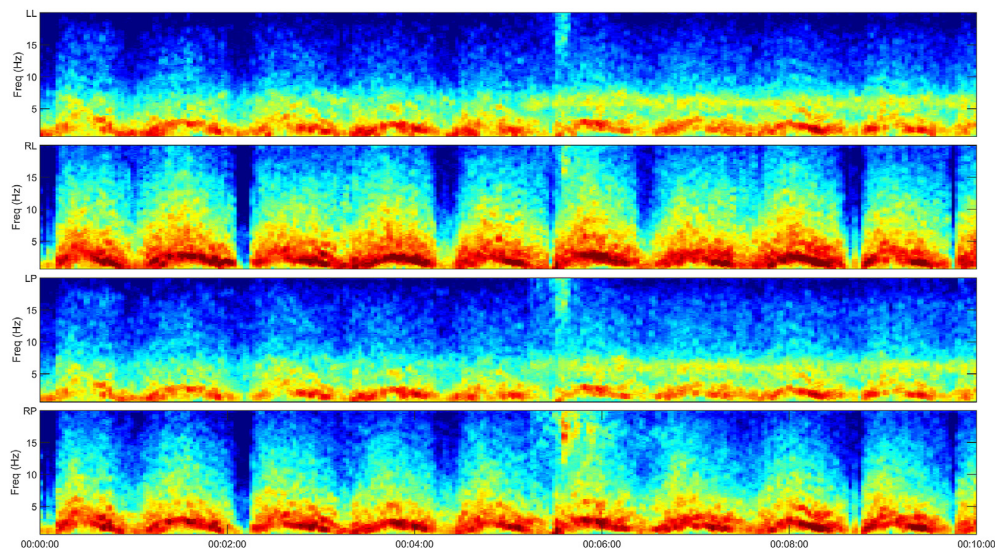


Fig. 3. Example of a Compressed Spectral Array showing recurrent seizures. The seizures have a classic flame shaped appearance.

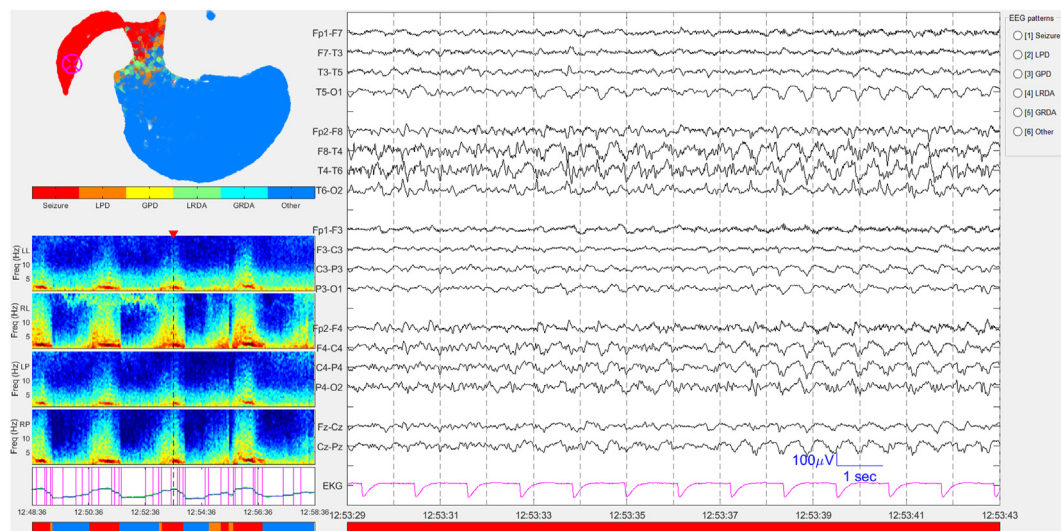


Fig. 4. A Graphical User Interface for semi-automated annotation of EEG.

in the emergency setting. CT can guide decisions regarding hospital admission or surgical intervention but subjects patients to radiation and in most scanned patients identifies no intracranial injury [83]. One study used an automated EEG-based algorithm to predict whether CT would be positive, achieving a negative predictive value of 96 % [90]. Machine learning can further assist with the initial identification of TBI, using qEEG features and demographic variables to classify patients with TBI, stroke, or normal EEGs [91].

Another controversy in acute TBI management is the administration of prophylactic ASMs. Guidelines have recommended early ASMs to mitigate the risk of posttraumatic seizures [92,93], which may present subclinically [94]. The moderate supportive evidence and important side effects of these therapies have called this practice into question [95]. Statistical algorithms have been developed to identify risk factors and prognosis for early posttraumatic seizures [96], and machine learning models using early qEEG features including spectral power, power variance, and peak envelope can identify patients at high risk of developing posttraumatic epilepsy [97]. These recent advancements can improve the long-term management of patients at risk for seizures following TBI as well as protect patients from unnecessary and potentially harmful pharmacologic interventions.

In disorders of consciousness specifically following moderate and severe TBI, machine learning models have also been effective in using early EEG to predict recovery [98] and have shown improved prognostic accuracy when incorporating sixteen EEG features (including power spectral features, brain symmetry index, coherence, Shannon entropy, regularity, aperiodic component, long range temporal correlation, and broken detailed balance) than when using clinical, radiological, and laboratory parameters without EEG [99]. However, current application in clinical practice is often limited by resources and the availability of technology and expertise.

Prognostication in Anoxic brain injury after cardiac arrest

The proportion of individuals surviving cardiac arrest and subsequent coma is increasing, but forecasting neurologic recovery in these patients remains an important challenge [100,101]. A number of clinical variables are linked to neurologic prognosis, including examination, laboratory, and imaging findings [102]. Several risk scores have been developed to predict neurologic outcome using combinations of these variables [103], as well as deep learning models [104,105], but these have not achieved sufficient evidence for reliable use [102].

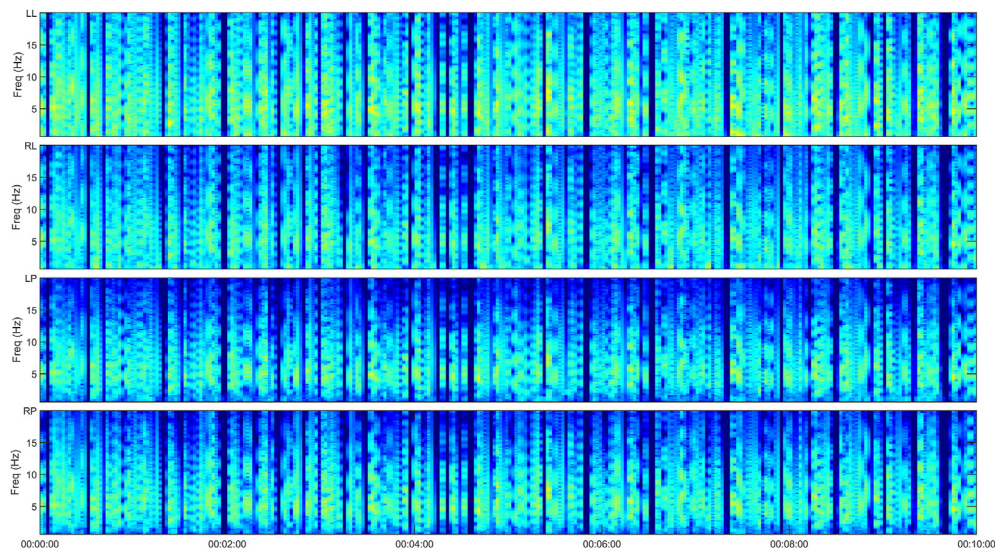


Fig. 5. Compressed Spectral Array demonstrating burst suppression pattern.

EEG monitoring has proven to be a valuable complement to other modalities in these patients, including those treated with targeted temperature management (therapeutic hypothermia) [106–110] and especially when considering EEG reactivity (EEG-R) alongside EEG background pattern [111,112]. More rapid EEG review can be facilitated with an algorithm incorporating serial qEEG measurements [113], and this automated approach improves with the incorporation of a machine learning-based classifier [114] and an expanded set of qEEG features [115]. Sequential analysis of qEEG features additionally underscores the importance of long-term EEG monitoring, as positive trends in neurophysiologic evolution are associated with good prognosis despite malignant features in early EEG [116]. Among machine learning models predicting neurologic outcomes after cardiac arrest, the most commonly-used EEG features include band power, Shannon entropy, and burst-suppression ratio [117].

Deep learning models bypass the need for feature extraction, learning flexibly from EEG and predicting post-arrest outcome more accurately than other machine learning architectures [118] and trained experts [119]. Despite increased model complexity, these systems can extract interpretable patterns that align with those utilized in visual analysis [120]. Furthermore, they enable temporal modeling of EEG dynamics such that the algorithm's prognostic accuracy scales with increased monitoring time [121]. In addition to automated prognostication, deep learning can uncover novel modalities for assessing brain function, such as via auditory stimuli, and create insights into the electrophysiologic characteristics of consciousness [122].

Detection and Management of Delayed Cerebral Ischemia in Subarachnoid Hemorrhage

Subarachnoid hemorrhage (SAH) is a life-threatening cerebrovascular emergency with stable incidence and risk of significant functional impairment in patients who survive [123–125]. Delayed cerebral ischemia (DCI) is a major complication that can present up to two weeks after SAH [126] and triples the odds of a poor outcome [127]. While the majority of surveillance efforts have emphasized the importance of cerebral vasospasm, DCI has a multifactorial etiology and requires a multimodal approach for early diagnosis [126,128,129].

EEG signatures of ischemic injury are well-established, including in SAH [130–132]. Seizures are often a secondary cause of injury in patients following SAH [133,134], and seizure burden in SAH is associated with worse functional and cognitive outcome [135]. Patients without seizures but with EEG background changes are still more prone to functional

impairment [133], such that prophylaxis with ASMs is often considered [136,137] despite limited evidence regarding this practice [138].

Recent work has capitalized on these EEG changes to predict DCI following SAH. cEEG monitoring in patients following SAH revealed that the presence of epileptiform abnormalities is associated with increased risk for DCI [139], and this risk can be stratified according to degree of epileptiform burden and trends in epileptiform activity over time [140]. In a prospective study, early cEEG monitoring identified one additional case of DCI prior to clinical symptoms for every 3–7 patients monitored [141]. However, these analyses required manual EEG review, which is a barrier to widespread implementation of their findings toward DCI prediction. Initial attempts to automate EEG analysis for DCI detection, using signal processing techniques, were unsuccessful [142]. In contrast, a machine learning approach incorporating spatial and temporal EEG features could accurately predict DCI following SAH and identified alpha-delta ratio, percent alpha variability, Shannon entropy, and epileptiform discharge burden as important predictive variables [143]. Further improvement is likely to be attained by AI models integrating other data modalities including clinical demographics and imaging, such as transcranial doppler ultrasound [144].

Anesthetic Dosing and Sedation Management

Anesthetics are commonly used for treatment of refractory status epilepticus, for the management of refractory intracranial pressure, and for ventilatory synchrony in patients with respiratory failure. EEG is indicated for monitoring the depth of sedation for these indications, with sedation frequently titrated to burst suppression [1,55]. Careful management is necessary in these patients as sedative medications and prolonged ventilation carry risk [145]. Although burst suppression is often targeted in nonconvulsive status epilepticus management, there is no data to support that it improves outcomes [146]. At the same time, over-sedation may result in adverse effects [147], making the balance between over- and under-sedation challenging.

To perform EEG-based sedation monitoring, clinicians consider metrics such as number of bursts per minute or percentage of time spent in the suppressed state. Calculation of these parameters is time-consuming and potentially variable between experts. Automated algorithms for calculating the degree and time spent in burst suppression can overcome the challenges of manual EEG review and assist in preventing under and over sedation. Quantitative EEG tools and software can be used in clinical practice to assess burst suppression ratio [148]. Machine learning algorithms have also been developed that first rely on segmentation of EEG

Table 2
Indications for cEEG monitoring and current and future AI applications within each domain.

Indication for EEG monitoring [1]	AI- based approaches in current clinical practice	Future research directions and clinical applications
Diagnosis of non-convulsive seizures and paroxysmal events	2HELPS2B score applied to first hour of EEG for seizure risk prediction [25,27] Quantitative EEG to assist rapid screening of seizures [29–33]	Automated annotation of EEG and seizure risk prediction [36–51] Automated EEG annotation and report generation for bedside providers
Treatment of seizures and status epilepticus	Use of quantitative EEG to assess degree of seizure control and burst suppression [148–149]	Realtime automated EEG annotation and treatment recommendations for patients with seizures Use of automated EEG annotation and automated report generation to increase feasibility of randomized trials of EEG guided treatment of status epilepticus and super-refractory status epilepticus Data-driven simulations to design randomized controlled trials of anti-seizure treatment in critical care
Detection of cerebral ischemia	Use of quantitative EEG, including the alpha to delta ratio and percent alpha variability for early detection of delayed cerebral ischemia in aneurysmal SAH [130–143]	Clinical trials and comparative studies examining the independent impact of quantitative EEG monitoring on outcomes in SAH Automated multimodal alarms for ischemia detection- integrating EEG alarms (e.g., new discharges or change in alpha/delta ratio), bedside cardiovascular monitoring, other forms of neuromonitoring (e.g., brain tissue oxygen)
Monitoring sedation e.g., in treatment of status epilepticus, and treatment of intracranial hypertension	Quantitative EEG monitor depth of burst suppression [148–149]	Automated algorithms for annotation and assessment of burst suppression and degree of suppression
Neuro-prognostication	Detection of cognitive motor dissociation- digital bedside EEG with a machine learning classifier to detect brain activation following commands	Development of standardized approaches in data acquisition and analysis. Addressing resource requirements and challenges in interpreting and communicating results.

CMD: cognitive-motor dissociation; EEG: electroencephalography; SAH: sub-arachnoid hemorrhage.

into bursts and suppressions, which can be performed automatically with relatively simple algorithms at the level of expert annotators [149]. More sophisticated unsupervised machine learning models can achieve this without requiring manual EEG annotations for parameter estimation, enabling robust segmentation for patients whose burst-suppression patterns evolve with time (as may be expected in a long ICU admission) [150]. Other algorithms have been proposed that perform sequential updating as physicians provide new annotations during routine care, thus leveraging artificial and human intelligence simultaneously [151].

Increased use of EEG can improve management of patients with primary acute neurologic diagnoses as well as those at risk of secondary

injury, in part due to the frequency with which harmful activity is observed on EEG without overt clinical signs. However, manual review of EEG requires highly-trained neurophysiologists and is a major resource burden. AI has already begun to address this challenge through the development of 2HELPS2B, an interpretable risk score that is routinely used in clinical care for prediction of seizure risk and optimization of cEEG allocation accordingly. qEEG has additionally enabled more rapid EEG review for seizure screening, neurologic prognostication, and real-time management. In addition to its value in patient care, expedited EEG review is essential for research using EEG-derived endpoints and for the development of more advanced AI systems. Table 2 summarizes the main indications for cEEG monitoring in the critical care setting and some of the key citations in this review, highlighting the role of AI in each of these domains.

The uses of EEG-based AI in severe brain injury are as broad as those of EEG itself. AI can perform automated EEG review and annotation of seizures with deep learning models identifying and classifying seizures and other harmful patterns at least as well as experts. Pharmacokinetic-pharmacodynamic models can help design treatment regimens that are personalized according to each patient's unique characteristics. In patients with drug-resistant epilepsy requiring neurosurgical management, AI can use interictal EEG to map seizure-generating brain tissue without recording any actual seizures. Beyond seizure, AI can improve prognostic accuracy following traumatic brain injury or cardiac arrest. In patients with disorders of consciousness, AI can identify brain activation on EEG that is otherwise covert but corresponds with improved outcomes. Following SAH, AI can help identify patients at risk for DCI before the manifestation of any clinical signs. Finally, in patients requiring anesthetics, AI can guide EEG review to avoid over- or under-sedation.

AI has begun to elucidate the importance of EEG signatures that are found in diverse neurologic disorders but are of uncertain clinical significance, potentially improving our understanding of the neurophysiologic processes underlying both acute and chronic brain injury. Several barriers exist in the widespread adoption of AI for clinical EEG analysis, including the variable availability of prolonged EEG, computing resources, and experienced staff across institutions, as well as the lack of prospective studies elucidating the full impact of AI-augmented approaches on outcomes and cost. There is also the question of generalizability of some of these approaches, due to limitations or biases (e.g., use of single center data or single brain injury type) in the training data used to create the algorithms. While more work is needed to validate these systems before full clinical deployment, AI is already influencing clinical care, and further methodologic advancements and generation of large, high-quality datasets promise to make EEG-guided management more efficient and effective.

Author contributions

All authors contributed to conceptualization and design, acquisition of data, analysis and interpretation of data, and drafting and revising the manuscript. All authors approve of the content of the manuscript.

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Declaration of competing interest

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References

- [1] Herman ST, Abend NS, Bleck TP, Chapman KE, Drislane FW, Emerson RG, et al. Consensus statement on continuous EEG in critically ill adults and children, part I: indications. *J Clin Neurophysiol* 2015;32(2):87–95.
- [2] Hill CE, Blank LJ, Thibault D, Davis KA, Dahodwala N, Litt B, et al. Continuous EEG is associated with favorable hospitalization outcomes for critically ill patients. *Neurology* 2019;92(1):E9–18.
- [3] Amerineni R, Sun H, Fernandes MB, Westover MB, Moura L, Paterno E, et al. Real-world continuous EEG utilization and outcomes in hospitalized patients with acute cerebrovascular diseases. *J Clin Neurophysiol* 2025 Jan 1;42(1):20–7.
- [4] Alkhachroum A, Appavu B, Egawa S, Foreman B, Gaspard N, Gilmore EJ, et al. Electroencephalogram in the intensive care unit: a focused look at acute brain injury. *Intensive Care Med* 2022;48(10):1443–62.
- [5] Zafar SF, Subramaniam T, Osman G, Herlopian A, Struck AF. Electrographic seizures and ictal-interictal continuum (IIC) patterns in critically ill patients. *Epilepsy Behav [Internet]* 2020;106:107037. <https://doi.org/10.1016/j.yebeh.2020.107037>.
- [6] Sivaraju A, Gilmore EJ. Understanding and managing the ictal-interictal continuum in neurocritical care. *Curr Treat Options Neurol* 2016;18(2):8.
- [7] Tabaeizadeh M, Aboul Nour H, Shoukat M, Jin J, Javed F, Kassa S, et al. Burden of epileptiform activity predicts discharge neurologic outcomes in severe acute ischemic stroke. *Neurocritical Care* 2020;32(3):697–706.
- [8] Zafar SF, Rosenthal ES, Jing J, Ge W, Tabaeizadeh M, Nour HA, et al. Automated annotation of epileptiform burden and its association with outcomes. *Ann Neurol* 2021;90(2):300–11.
- [9] Parikh H, Hoffman K, Sun H, Zafar SF, Ge W, Jing J, et al. Effects of epileptiform activity on discharge outcome in critically ill patients in the USA: a retrospective cross-sectional study. *Lancet Digit Heal [Internet]* 2023;5(8):e495–502. [https://doi.org/10.1016/S2589-7500\(23\)00088-2](https://doi.org/10.1016/S2589-7500(23)00088-2).
- [10] Westover MB, Shafi MM, Bianchi MT, Moura LMVR, O'Rourke D, Rosenthal ES, et al. The probability of seizures during EEG monitoring in critically ill adults. *Clin Neurophysiol [Internet]* 2015;126(3):463–71. <https://doi.org/10.1016/j.clinph.2014.05.037>.
- [11] Kubota Y, Nakamoto H, Egawa S, Kawamata T. Continuous EEG monitoring in ICU. *J Intensive Care* 2018;6:39.
- [12] Holtkamp M, Meierkord H. Nonconvulsive status epilepticus: a diagnostic and therapeutic challenge in the intensive care setting. *Ther Adv Neurol Disord* 2011; 4(3):169–81.
- [13] Brophy GM, Bell R, Claassen J, Alldredge B, Bleck TP, Glauser T, et al. Guidelines for the evaluation and management of status epilepticus. *Neurocritical Care* 2012; 17:3–23.
- [14] Sutter R, Rueegg S, Kaplan PW. Epidemiology, diagnosis, and management of nonconvulsive status epilepticus: Opening Pandora's box. *Neurol Clin Pract* 2012; 2(4):275–86.
- [15] Azary S, Caravanas C, Reiner AS, Panageas KS, Dhawan V, Avila EK. Incidence of seizure and associated risk factors in patients in the medical intensive care unit (ICU) at Memorial Sloan Kettering Cancer center (MSK) from 2016–2017. *J Intensive Care Med* 2022;37(10):1312–7.
- [16] Ney JP, Van Der Goes DN, Nuwer MR, Nelson L, Echer MA. Continuous and routine eeg in intensive care. *Neurology* 2013;81(23):2002–8.
- [17] Claassen J, Mayer SA, Kowalski RG, Emerson RG, Hirsch LJ. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. *Neurology* 2004;62(10):1743–8.
- [18] Shafi MM, Brandon Westover M, Cole AJ, Kilbride RD, Hoch DB, Cash SS. Absence of early epileptiform abnormalities predicts lack of seizures on continuous EEG. *Neurology [Internet]* 2012;79(17):1796–801. Available from: www.neurology.org.
- [19] Gilmore EJ, Gaspard N, Choi HA, Cohen E, Burkart KM, Chong DH, et al. Acute brain failure in severe sepsis: a prospective study in the medical intensive care unit utilizing continuous EEG monitoring. *Intensive Care Med* 2015;41(4):686–94.
- [20] Ruiz AR, Vlachs J, Lee JW, Gilmore EJ, Ayer T, Haider HA, et al. Association of periodic and rhythmic electroencephalographic patterns with seizures in critically ill patients. *JAMA Neurol* 2017;74(2):181–8.
- [21] Hirsch LJ, Fong MWK, Leitinger M, Laroche SM, Beniczky S, Abend NS, et al. American clinical Neurophysiology society's standardized critical care EEG Terminology: 2021 Version. *J Clin Neurophysiol* 2021;38(1):1–29.
- [22] Carrera E, Claassen J, Oddo M, Emerson RG, Mayer SA, Hirsch LJ. Continuous electroencephalographic monitoring in critically ill patients with central nervous system infections. *Arch Neurol* 2008;65(12):1612–8.
- [23] Claassen J, Jetté N, Chum F, Green R, Schmidt M, Choi H, et al. Electrographic seizures and periodic discharges after intracerebral hemorrhage. *Neurology* 2007; 69(13):1356–65.
- [24] Jette N, Claassen J, Emerson RG, Hirsch LJ. Frequency and predictors of nonconvulsive seizures during continuous electroencephalographic monitoring in critically ill children. *Arch Neurol* 2006;63(12):1750–5.
- [25] Struck AF, Ustun B, Ruiz AR, Lee JW, LaRoche SM, Hirsch LJ, et al. Association of an electroencephalography-based risk score with seizure probability in hospitalized patients. *JAMA Neurol* 2017;74(12):1419–24.
- [26] Ustun B, Rudin C. Learning optimized risk scores. *J Mach Learn Res* 2019;20:1–75.
- [27] Struck AF, Tabaeizadeh M, Schmitt SE, Ruiz AR, Swisher CB, Subramaniam T, et al. Assessment of the Validity of the 2HELPS2B score for inpatient seizure risk prediction. *JAMA Neurol* 2020;77(4):500–7.
- [28] Kalkach-Aparicio M, Fatima S, Selté A, Sheikh IS, Cormier J, Gallagher K, et al. Seizure assessment and forecasting with efficient rapid-EEG: a retrospective Multicenter Comparative Effectiveness study. *Neurology* 2024;103(2):e209621.
- [29] Hwang J, Cho SM, Ritzl EK. Recent applications of quantitative electroencephalography in adult intensive care units: a comprehensive review, vol. 269. *Journal of Neurology*; 2022. p. 6290–309.
- [30] Sansevere AJ, Hahn CD, Abend NS. Conventional and quantitative EEG in status epilepticus. *Seizure [Internet]* 2019;68:38–45. <https://doi.org/10.1016/j.seizure.2018.09.011>.
- [31] Haider HA, Esteller R, Hahn CD, Westover MB, Halford JJ, Lee JW, et al. Sensitivity of quantitative EEG for seizure identification in the intensive care unit. *Neurology* 2016;87(9):935–44.
- [32] Zafar SF, Amorim E, Williamson CA, Jing J, Gilmore EJ, Haider HA, et al. A standardized nomenclature for spectrogram EEG patterns: inter-rater agreement and correspondence with common intensive care unit EEG patterns. *Clin Neurophysiol [Internet]* 2020;131(9):2298–306. <https://doi.org/10.1016/j.clinph.2020.05.032>.
- [33] Moura LMVR, Shafi MM, Ng M, Pati S, Cash SS, Cole AJ, et al. Spectrogram screening of adult EEGs is sensitive and efficient. *Neurology* 2014;83(1): 56–64.
- [34] Swisher CB, White CR, Mace BE, Dombrowski KE, Husain AM, Kolls BJ, et al. Diagnostic accuracy of electrographic seizure detection by neurophysiologists and non-neurophysiologists in the adult ICU using a Panel of quantitative EEG trends. *J Clin Neurophysiol* 2015;32(4):324–30.
- [35] Amorim E, Williamson CA, Moura LMVR, Shafi MM, Gaspard N, Rosenthal ES, et al. Performance of spectrogram-based seizure identification of adult EEGs by critical care Nurses and neurophysiologists. *J Clin Neurophysiol* 2017;34(4): 359–64.
- [36] Kelly KM, Shiau DS, Kern RT, Chien JH, Yang MCK, Yandora KA, et al. Assessment of a scalp EEG-based automated seizure detection system. *Clin Neurophysiol [Internet]* 2010;121(11):1832–43. <https://doi.org/10.1016/j.clinph.2010.04.016>.
- [37] Herta J, Koren J, Fürbass F, Hartmann M, Kluge T, Baumgartner C, et al. Prospective assessment and validation of rhythmic and periodic pattern detection in NeuroTrend: a new approach for screening continuous EEG in the intensive care unit. *Epilepsy Behav [Internet]* 2015;49:273–9. <https://doi.org/10.1016/j.yebeh.2015.04.064>.
- [38] Fürbass F, Ossenblok P, Hartmann M, Perko H, Skupch AM, Lindinger G, et al. Prospective multi-center study of an automatic online seizure detection system for epilepsy monitoring units. *Clin Neurophysiol* 2015;126(6):1124–31.
- [39] González Otárola KA, Mikhael-Demo Y, Bachman EM, Balaguera P, Schuele S. Automated seizure detection accuracy for ambulatory EEG recordings. *Neurology* 2019;92(14):E1540–6.
- [40] O'Shea A, Lightbody G, Boylan G, Temko A. Neonatal seizure detection from raw multi-channel EEG using a fully convolutional architecture. *Neural Networks [Internet]* 2020;123:12–25. <https://doi.org/10.1016/j.neunet.2019.11.023>.
- [41] Saab K, Dunmon J, Ré C, Rubin D, Lee-Messer C. Weak supervision as an efficient approach for automated seizure detection in electroencephalography. *npj Digit Med [Internet]* 2020;3:59. <https://doi.org/10.1038/s41746-020-0264-0>.
- [42] Bernabei JM, Owoputi O, Small SD, Nyema NT, Dumenyo E, Kim J, et al. A full-stack application for detecting seizures and reducing data during continuous electroencephalogram monitoring. *Crit Care Explor* 2021;3(7):E0476.
- [43] Kamousi B, Karunakaran S, Gururangan K, Markert M, Decker B, Khankhanian P, et al. Monitoring the burden of seizures and highly epileptiform patterns in critical care with a novel machine learning method. *Neurocrit Care [Internet]* 2021;34(3): 908–17. <https://doi.org/10.1007/s12028-020-01120-0>.
- [44] Scheuer ML, Wilson SB, Antony A, Ghearing G, Urban A, Bagić AI. Seizure detection: interreader agreement and detection algorithm assessments using a large dataset. *J Clin Neurophysiol* 2021;38(5):439–47.
- [45] Gomez-Quintana S, O'Shea A, Factor A, Popovici E, Temko A. A method for AI assisted human interpretation of neonatal EEG. *Sci Rep [Internet]* 2022;12:10932. <https://doi.org/10.1038/s41598-022-14894-4>.
- [46] Jing J, Drangremont E, Zafar S, Rosenthal ES, Tabaeizadeh M, Ebrahim S, et al. Rapid annotation of seizures and interictal-ictal continuum EEG patterns. *Proc Annu Int Conf IEEE Eng Med Biol Soc EMBS* 2018:3394–7.
- [47] Ge W, Jing J, An S, Herlopian A, Ng M, Struck AF, et al. Deep active learning for interictal ictal injury continuum EEG patterns. *J Neurosci Methods [Internet]* 2021;351:108966. <https://doi.org/10.1016/j.jneumeth.2020.108966>.
- [48] Jing J, Sun H, Kim JA, Herlopian A, Karakis I, Ng M, et al. Development of expert-level automated detection of epileptiform discharges during electroencephalogram interpretation. *JAMA Neurol* 2020;77(1):103–8.
- [49] Tveit J, Aurlien H, Plis S, Calhoun VD, Tatum WO, Schomer DL, et al. Automated interpretation of clinical electroencephalograms using artificial intelligence. *JAMA Neurol* 2023;80(8):805–12.
- [50] Jing J, Ge W, Hong S, Fernandes MB, Lin Z, Yang C, et al. Development of expert-level classification of seizures and rhythmic and periodic patterns during EEG interpretation. *Neurology* 2023;100(17):E1750–62.
- [51] Barnett AJ, Guo Z, Jing J, Ge W, Kaplan PW, Kong WY, et al. Improving clinician performance in classifying EEG patterns on the ictal–interictal injury continuum using interpretable machine learning. *NEJM AI* 2024;1(6).
- [52] Allen B, Vespa PM. Antiseizure medications in critical care: an update. *Curr Opin Crit Care* 2019;25(2):117–25.
- [53] Abend NS, Dlugos DJ, Hahn CD, Hirsch LJ, Herman ST. Use of EEG monitoring and management of non-convulsive seizures in critically ill patients: a survey of neurologists. *Neurocritical Care* 2010;12(3):382–9.
- [54] Zafar SF, Rosenthal ES, Postma EN, Sanches P, Ayub MA, Rajan S, et al. Antiseizure medication treatment and outcomes in patients with subarachnoid hemorrhage undergoing continuous EEG monitoring. *Neurocritical Care* 2022; 36(3):857–67.

- [55] Oddo M, Crippa IA, Mehta S, Menon D, Payen JF, Taccone FS, et al. Optimizing sedation in patients with acute brain injury. *Crit Care* [Internet] 2016;20:128. <https://doi.org/10.1186/s13054-016-1294-5>.
- [56] Claassen J, Taccone FS, Horn P, Holtkamp M, Stocchetti N, Oddo M. Recommendations on the use of EEG monitoring in critically ill patients: consensus statement from the neurointensive care section of the ESICM. *Intensive Care Med* 2013;39(8):1337–51.
- [57] Perucca E, Beghi E, Dulac O, Shorvon S, Tomson T. Assessing risk to benefit ratio in antiepileptic drug therapy. *Epilepsy Res* 2000;41(2):107–39.
- [58] Wright C, Downing J, Mungall D, Khan O, Williams A, Fonkem E, et al. Clinical pharmacology and pharmacokinetics of levetiracetam. *Front Neurol* 2013;4:192.
- [59] Methaneethorn J. A systematic review of population pharmacokinetics of valproic acid. *Br J Clin Pharmacol* 2018;84(5):816–34.
- [60] Löscher W, Klein P. The pharmacology and clinical efficacy of antiseizure medications: from bromide salts to cenobamate and beyond. *CNS Drugs* [Internet] 2021;35(9):935–63. <https://doi.org/10.1007/s40263-021-00827-8>.
- [61] Kanner AM, Ashman E, Gloss D, Harden C, Bourgeois B, Bautista JF, et al. Practice guideline update summary: efficacy and tolerability of the new antiepileptic drugs I: treatment of new-onset epilepsy: report of the guideline development, dissemination, and implementation subcommittee of the American academy of Neurology 2018;91(2):74–81.
- [62] Kanner AM, Ashman E, Gloss D, Harden C, Bourgeois B, Bautista JF, et al. Practice guideline update summary: efficacy and tolerability of the new antiepileptic drugs II: treatment-resistant epilepsy: report of the guideline development, dissemination, and implementation subcommittee of the American academy of Neurology 2018;91(2):82–90.
- [63] Kanner AM, Bicchi MM. Antiseizure medications for adults with epilepsy: a review. *JAMA* 2022;327(13):1269–81.
- [64] Farrokhi S, Tahsili-Fahadan P, Ritzl EK, Lewin JJ, Mirski MA. Antiepileptic drugs in critically ill patients. *Crit Care* 2018;22:153.
- [65] Rubinos C, Reynolds AS, Claassen J. The ictal–interictal continuum: to treat or not to treat (and how)? *Neurocritical Care* 2018;29(1):3–8.
- [66] Ruijter BJ, Keijzer HM, Tjepkema-Cloostermans MC, Blans MJ, Beishuizen A, Tromp SC, et al. Treating rhythmic and periodic EEG patterns in comatose survivors of cardiac arrest. *N Engl J Med* 2022;386(8):724–34.
- [67] Parikh H, Lanners Q, Akras Z, Zafar SF, Westover MB, Rudin C, et al. Safe and interpretable estimation of optimal treatment regimes. *Proc Mach Learn Res* 2024;238:2134–42.
- [68] Parikh H, Sun H, Amerineni R, Rosenthal ES, Volfovsky A, Rudin C, et al. How many patients do you need? Investigating trial designs for anti-seizure treatment in acute brain injury patients. *Ann Clin Transl Neurol* 2024;11(7):1681–90.
- [69] Varatharajah Y, Berry B, Cimbalkin J, Kremen V, Gompel J Van, Stead M, et al. Integrating artificial intelligence with real-time intracranial EEG monitoring to automate interictal identification of seizure onset zones in focal epilepsy. *J Neural Eng* 2018;15(4):046035.
- [70] Kondziella D, Friberg CK, Frokjaer VG, Fabricius M, Møller K. Preserved consciousness in vegetative and minimal conscious states: systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry* 2016;87(5):485–92.
- [71] Schiff ND. Cognitive motor dissociation following severe brain injuries. *JAMA Neurol* 2015;72(12):1413–5.
- [72] Claassen J, Doyle K, Matory A, Couch C, Burger KM, Velazquez A, et al. Detection of brain activation in unresponsive patients with acute brain injury. *N Engl J Med* 2019;380(26):2497–505.
- [73] Edlow BL, Chatelle C, Spencer CA, Chu CJ, Bodien YG, Connor KLO, et al. Early detection of consciousness in patients with acute severe traumatic brain injury. *Brain* 2017;140(9):2399–414.
- [74] Wilson JTL, Pettigrew LEL, Teasdale GM. Structured interviews for the glasgow outcome scale and the extended glasgow outcome scale: guidelines for their use. *J Neurotrauma* 1998;15(8):573–80.
- [75] Bodien YG, Allanson J, Cardone P, Bonhomme A, Carmona J, Chatelle C, et al. Cognitive motor dissociation in disorders of consciousness. *N Engl J Med* 2024;391(7):598–608.
- [76] Turgeon AF, Lauzier F, Simard JF, Scales DC, Burns KEA, Moore L, et al. Mortality associated with withdrawal of life-sustaining therapy for patients with severe traumatic brain injury: a Canadian multicentre cohort study. *C Can Med Assoc J* 2011;183(14):1581–8.
- [77] Elmer J, Torres C, Aufderheide TP, Austin MA, Callaway CW, Golan E, et al. Association of early withdrawal of life-sustaining therapy for perceived neurological prognosis with mortality after cardiac arrest. *Resuscitation* [Internet] 2016;102:127–35. <https://doi.org/10.1016/j.resuscitation.2016.01.016>. Available from: .
- [78] Bodien YG, Fecchio M, Freeman HJ, Sanders WR, Meydan A, Lawrence PK, et al. Clinical implementation of fMRI and EEG to detect cognitive motor dissociation. *Neurol Clin Pract* [Internet] 2025 Feb;15(1). Available from, <https://www.neurology.org/doi/10.1212/CPJ.0000000000200390>.
- [79] Johnson WD, Griswold DP. Traumatic brain injury: a global challenge. *Lancet Neurol* 2017;16(12):949–50.
- [80] Maas AIR, Menon DK, David Adelson PD, Andelic N, Bell MJ, Belli A, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. *Lancet Neurol* 2017;16(12):987–1048.
- [81] Bramlett HM, Dietrich WD. Long-term consequences of traumatic brain injury: current status of potential mechanisms of injury and neurological outcomes. *J Neurotrauma* 2015;32(23):1834–48.
- [82] McCrea MA, Giacino JT, Barber J, Temkin NR, Nelson LD, Levin HS, et al. Functional outcomes over the first year after moderate to severe traumatic brain injury in the prospective, longitudinal TRACK-TBI study. *JAMA Neurol* 2021;78(8):982–92.
- [83] Maas AIR, Menon DK, Manley GT, Abrams M, Åkerlund C, Andelic N, et al. Traumatic brain injury: progress and challenges in prevention, clinical care, and research. *Lancet Neurol* 2022;21(11):1004–60.
- [84] Nelson LD, Temkin NR, Dikmen S, Barber J, Giacino JT, Yuh E, et al. Recovery after mild traumatic brain injury in patients presenting to us level I trauma centers: a transforming research and clinical knowledge in traumatic brain injury (TRACK-TBI) study. *JAMA Neurol* 2019;76(9):1049–59.
- [85] Mikolić A, Polinder S, Steyerberg EW, Retel Helmrich IRA, Giacino JT, Maas AIR, et al. Prediction of global functional outcome and post-concussive symptoms after mild traumatic brain injury: external validation of prognostic models in the collaborative European NeuroTrauma effectiveness research in traumatic brain injury (CENTER-TBI) study. *J Neurotrauma* 2021;38(2):196–209.
- [86] Ianof JN, Anghinah R. Traumatic brain injury: an EEG point of view. *Dement Neuropsychol* 2017;11(1):3–5.
- [87] Thatcher RW, North DM, Curtin RT, Walker RA, Biver CJ, Gomez JF, et al. An EEG severity index of traumatic brain injury. *J Neurosurg* 2001;13(1):77–87.
- [88] Nuwer MR, Hovda DA, Schrader LM, Vespa PM. Routine and quantitative EEG in mild traumatic brain injury. *Clin Neurophysiol* 2005;116(9):2001–25.
- [89] Haneef Z, Levin HS, Frost JD, Mizrahi EM. Electroencephalography and quantitative electroencephalography in mild traumatic brain injury. *J Neurotrauma* 2013;30(8):653–6.
- [90] Hanley D, Prichep LS, Bazarian J, Huff JS, Naunheim R, Garrett J, et al. Emergency department triage of traumatic head injury using a brain electrical activity biomarker: a multisite prospective observational validation trial. *Acad Emerg Med* 2017;24(5):617–27.
- [91] Vivaldi N, Caiola M, Solarana K, Ye M. Evaluating performance of EEG data-driven machine learning for traumatic brain injury classification. *IEEE Trans Biomed Eng* 2021;68(11):3205–16.
- [92] Chang BS, Lowenstein DH. Practice parameter: antiepileptic drug prophylaxis in severe traumatic brain injury: report of the quality standards subcommittee of the American academy of neurology. *Neurology* 2003;60(1):10–6.
- [93] Torbic H, Fornl AA, Anger KE, Degrado JR, Greenwood BC. Use of antiepileptics for seizure prophylaxis after traumatic brain injury. *Am J Heal Pharm* 2013;70(9):759–66.
- [94] O'Neill BR, Handler MH, Tong S, Chapman KE. Incidence of seizures on continuous EEG monitoring following traumatic brain injury in children. *J Neurosurg Pediatr* 2015;16(2):167–76.
- [95] Wat R, Mammi M, Paredes J, Haines J, Alasmari M, Liew A, et al. The effectiveness of antiepileptic medications as prophylaxis of early seizure in patients with traumatic brain injury compared with placebo or No treatment: a systematic review and meta-analysis. *World Neurosurg* [Internet] 2019;122:433–40. <https://doi.org/10.1016/j.wneu.2018.11.076>.
- [96] Laing J, Gabbe B, Chen Z, Perucca P, Kwan P, O'Brien TJ. Risk factors and prognosis of early posttraumatic seizures in moderate to severe traumatic brain injury. *JAMA Neurol* 2022;79(4):334–41.
- [97] Pease M, Elmer J, Shahabadi AZ, Mallela AN, Ruiz-Rodriguez JF, Sexton D, et al. Predicting posttraumatic epilepsy using admission electroencephalography after severe traumatic brain injury. *Epilepsia* 2023;64(7):1842–52.
- [98] Cleri NA, Saadon JR, Zheng X, Swarna SA, Zhang J, Vagal V, et al. Predicting traumatic brain injury outcomes using a posterior dominant rhythm. *J Neurosurg* 2023;139(6):1523–33.
- [99] Tewarie PKB, Beernink TMJ, Eertman-Meyer CJ, Cornet AD, Beishuizen A, van Putten MJAM, et al. Early EEG monitoring predicts clinical outcome in patients with moderate to severe traumatic brain injury. *NeuroImage Clin* [Internet] 2023;37:103350. <https://doi.org/10.1016/j.nicl.2023.103350>.
- [100] Rossetti AO, Rabinstein AA, Oddo M. Neurological prognostication of outcome in patients in coma after cardiac arrest. *Lancet Neurol* [Internet] 2016;15(6):597–609. [https://doi.org/10.1016/S1474-4422\(16\)00015-6](https://doi.org/10.1016/S1474-4422(16)00015-6).
- [101] Perkins GD, Callaway CW, Hayward K, Neumar RW, Lilja G, Rowland MJ, et al. Brain injury after cardiac arrest. *Lancet* [Internet] 2021;398(10307):1269–78. [https://doi.org/10.1016/S0140-6736\(21\)00953-3](https://doi.org/10.1016/S0140-6736(21)00953-3).
- [102] Rajaje V, Muehlschlegel S, Wartenberg KE, Alexander SA, Busl KM, Chou SHY, et al. Guidelines for neuroprognostication in comatose adult survivors of cardiac arrest. *Neurocrit Care* [Internet] 2023;38(3):533–63. <https://doi.org/10.1007/s12028-023-01688-3>.
- [103] Naik R, Mandal I, Gorog DA. Scoring systems to predict survival or neurological recovery after out-of-hospital cardiac arrest. *Eur Cardiol* 2022;17:e20.
- [104] Kwon J myoung, Jeon KH, Kim HM, Kim MJ, Lim S, Kim KH, et al. Deep-learning-based out-of-hospital cardiac arrest prognostic system to predict clinical outcomes. *Resuscitation* [Internet] 2019;139:84–91. <https://doi.org/10.1016/j.resuscitation.2019.04.007>.
- [105] Johnson J, Björnsson O, Andersson P, Jakobsson A, Cronberg T, Lilja G, et al. Artificial neural networks improve early outcome prediction and risk classification in out-of-hospital cardiac arrest patients admitted to intensive care. *Crit Care* 2020;24:474.
- [106] Rossetti AO, Oddo M, Logroscino G, Kaplan PW. Prognostication after cardiac arrest and hypothermia: a prospective study. *Ann Neurol* 2010;67(3):301–7.
- [107] Cloostermans MC, Van Meulen FB, Eertman CJ, Hom HW, Van Putten MJAM. Continuous electroencephalography monitoring for early prediction of neurological outcome in postanoxic patients after cardiac arrest: a prospective cohort study. *Crit Care Med* 2012;40(10):2867–75.
- [108] Westhall E, Rossetti AO, Van Rootselaar AF, Kjaer TW, Horn J, Ullén S, et al. Standardized EEG interpretation accurately predicts prognosis after cardiac arrest. *Neurology* 2016;86(16):1482–90.
- [109] Youn CS, Callaway CW, Rittenberger JC. Combination of initial neurologic examination, quantitative brain imaging and electroencephalography to predict

- outcome after cardiac arrest. Resuscitation [Internet] 2017;110:120–5. <https://doi.org/10.1016/j.resuscitation.2016.10.024>.
- [110] Rossetti AO, Tovar Quiroga DF, Juan E, Novy J, White RD, Ben-Hamouda N, et al. Electroencephalography predicts poor and good outcomes after cardiac arrest: a two-center study. *Crit Care Med* 2017;45(7):e674–82.
- [111] Admiraal MM, Horn J, Hofmeijer J, Hoedemaekers CWE, Van Kaam CR, Keijzer HM, et al. EEG reactivity testing for prediction of good outcome in patients after cardiac arrest. *Neurology* 2020;95(6):E653–61.
- [112] Admiraal MM, Ramos LA, Delgado Olabarriaga S, Marquering HA, Horn J, van Rootselaar AF. Quantitative analysis of EEG reactivity for neurological prognostication after cardiac arrest. *Clin Neurophysiol* [Internet] 2021;132(9):2240–7. <https://doi.org/10.1016/j.clinph.2021.07.004>.
- [113] Tjepkema-Cloostermans MC, van Meulen FB, Meinsma G, van Putten MJAM. A Cerebral Recovery Index (CRI) for early prognosis in patients after cardiac arrest. *Crit Care* 2013;17(5):R252.
- [114] Tjepkema-Cloostermans MC, Hofmeijer J, Beishuizen A, Hom HW, Blans MJ, Bosch FH, et al. Cerebral recovery index: reliable help for prediction of neurologic outcome after cardiac arrest. *Crit Care Med* 2017;45(8):e789–97.
- [115] Nagaraj SB, Tjepkema-Cloostermans MC, Ruijter BJ, Hofmeijer J, van Putten MJAM. The revised Cerebral Recovery Index improves predictions of neurological outcome after cardiac arrest. *Clin Neurophysiol* [Internet] 2018;129(12):2557–66. <https://doi.org/10.1016/j.clinph.2018.10.004>.
- [116] Amorim E, Zheng WL, Jing J, Ghassemi MM, Lee JW, Wu O, et al. Neurophysiology state dynamics underlying acute neurologic recovery after cardiac arrest. *Neurology* 2023;101(9):E940–52.
- [117] Chen CC, Massey SL, Kirschen MP, Yuan I, Padiyath A, Simpaio AF, et al. Electroencephalogram-based machine learning models to predict neurologic outcome after cardiac arrest: a systematic review. *Resuscitation* 2024;194:110049.
- [118] Pham SDT, Keijzer HM, Ruijter BJ, Seeber AA, Scholten E, Drost G, et al. Outcome prediction of postanoxic coma: a comparison of automated electroencephalography analysis methods. *Neurocrit Care* [Internet] 2022;37(s2):248–58. <https://doi.org/10.1007/s12028-022-01449-8>.
- [119] Tjepkema-Cloostermans MC, da Silva Lourenco C, Ruijter BJ, Tromp SC, Drost G, Kornips FHM, et al. Outcome prediction in postanoxic coma with deep learning. *Crit Care Med* 2019;47(10):1424–32.
- [120] Jonas S, Rossetti AO, Oddo M, Jenni S, Favaro P, Zubler F. EEG-based outcome prediction after cardiac arrest with convolutional neural networks: performance and visualization of discriminative features. *Hum Brain Mapp* 2019;40(16):4606–17.
- [121] Zheng WL, Amorim E, Jing J, Ge W, Hong S, Wu O, et al. Predicting neurological outcome in comatose patients after cardiac arrest with multiscale deep neural networks. *Resuscitation* [Internet] 2021;169:86–94. <https://doi.org/10.1016/j.resuscitation.2021.10.034>.
- [122] Aellen FM, Alnes SL, Loosli F, Rossetti AO, Zubler F, De Lucia M, et al. Auditory stimulation and deep learning predict awakening from coma after cardiac arrest. *Brain* [Internet] 2023;146(2):778–88. <https://doi.org/10.1093/brain/awac340>.
- [123] Van Gijn J, Rinkel GJE. Subarachnoid haemorrhage: diagnosis, causes and management. *Brain* 2001;124(Pt 2):479–78.
- [124] Lovelock CE, Rinkel GJE, Rothwell PM. Time trends in outcome of subarachnoid hemorrhage: population-based study and systematic review. *Neurology* 2010;74(19):1494–501.
- [125] Zacharia BE, Hickman ZL, Grobelny BT, DeRosa P, Kotchetkov I, Ducruet AF, et al. Epidemiology of aneurysmal subarachnoid hemorrhage. *Neurosurg Clin* 2010;21(2):221–33.
- [126] Ikram A, Javaid MA, Ortega-Gutierrez S, Selim M, Kelangi S, Anwar SMH, et al. Delayed cerebral ischemia after subarachnoid hemorrhage. *J Stroke Cerebrovasc Dis* [Internet] 2021;30(11):106064. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.106064>.
- [127] Mees SMD, Kerr RS, Rinkel GJE, Algra A, Molyneux AJ. Occurrence and impact of delayed cerebral ischemia after coiling and after clipping in the International Subarachnoid Aneurysm Trial (ISAT). *J Neurol* 2012;259(4):679–83.
- [128] Diringer MN, Bleck TP, Hemphill JC, Menon D, Shutter L, Vespa P, et al. Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the neurocritical care society's multidisciplinary consensus conference. *Neurocritical Care* 2011;15(2):211–40.
- [129] Dodd WS, Laurent D, Dumont AS, Hasan DM, Jabbour PM, Starke RM, et al. Pathophysiology of delayed cerebral ischemia after subarachnoid hemorrhage: a review. *J Am Heart Assoc* 2021;10(15):e021845.
- [130] Claassen J, Hirsch LJ, Kreiter KT, Du EY, Sander Connolly E, Emerson RG, et al. Quantitative continuous EEG for detecting delayed cerebral ischemia in patients with poor-grade subarachnoid hemorrhage. *Clin Neurophysiol* 2004;115(12):2699–710.
- [131] Gollwitzer S, Groemer T, Rampp S, Hagge M, Olmes D, Huttner HB, et al. Early prediction of delayed cerebral ischemia in subarachnoid hemorrhage based on quantitative EEG: a prospective study in adults. *Clin Neurophysiol* 2015;126(8):1514–23.
- [132] Rots ML, van Putten MJAM, Hoedemaekers CWE, Horn J. Continuous EEG monitoring for early detection of delayed cerebral ischemia in subarachnoid hemorrhage: a pilot study. *Neurocritical Care* 2016;24(2):207–16.
- [133] Claassen J, Perotte A, Albers D, Kleinberg S, Schmidt JM, Tu B, et al. Nonconvulsive seizures after subarachnoid hemorrhage: multimodal detection and outcomes. *Ann Neurol* 2013;74(1):53–64.
- [134] Raper DMS, Starke RM, Komotar RJ, Allan R, Connolly ES. Seizures after aneurysmal subarachnoid hemorrhage: a systematic review of outcomes. *World Neurosurg* [Internet] 2013;79(5–6):682–90. <https://doi.org/10.1016/j.wneu.2012.08.006>.
- [135] De Marchis GM, Pugin D, Meyers E, Velasquez A, Suwatcharakoon S, Park S, et al. Seizure burden in subarachnoid hemorrhage associated with functional and cognitive outcome. *Neurology* 2016;86(3):253–60.
- [136] Kodankandath TV, Farooq S, Wazni W, Cox JA, Southwood C, Rozansky G, et al. Seizure prophylaxis in the immediate post-hemorrhagic period in patients with aneurysmal subarachnoid hemorrhage. *J Vasc Interv Neurol* [Internet] 2017;9(6):1–4. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29445430> <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=P MC5805895>.
- [137] Karamchandani RR, Fletcher JJ, Pandey AS, Rajjee V. Incidence of delayed seizures, delayed cerebral ischemia and poor outcome with the use of levetiracetam versus phenytoin after aneurysmal subarachnoid hemorrhage. *J Clin Neurosci* [Internet] 2014;21(9):1507–13. <https://doi.org/10.1016/j.jocn.2014.03.009>.
- [138] Marigold R, Günther A, Tiwari D, Kwan J. Antiepileptic drugs for the primary and secondary prevention of seizures after stroke. *Cochrane Database Syst Rev* 2013;2013(6):CD008710.
- [139] Kim JA, Rosenthal ES, Biswal S, Zafar S, Shenoy AV, O'Connor KL, et al. Epileptiform abnormalities predict delayed cerebral ischemia in subarachnoid hemorrhage. *Clin Neurophysiol* [Internet] 2017;128(6):1091–9. <https://doi.org/10.1016/j.clinph.2017.01.016>.
- [140] Kim JA, Zheng WL, Elmer J, Jing J, Zafar SF, Ghanta M, et al. High epileptiform discharge burden predicts delayed cerebral ischemia after subarachnoid hemorrhage. *Clin Neurophysiol* [Internet] 2022;141:139–46. <https://doi.org/10.1016/j.clinph.2021.01.022>.
- [141] Rosenthal ES, Biswal S, Zafar SF, O'Connor KL, Bechek S, Shenoy AV, et al. Continuous electroencephalography predicts delayed cerebral ischemia after subarachnoid hemorrhage: a prospective study of diagnostic accuracy. *Ann Neurol* 2018;83(5):958–69.
- [142] Wickering E, Gaspard N, Zafar S, Moura VJ, Biswal S, Bechek S, et al. Automation of classical QEEG trending methods for early detection of delayed cerebral ischemia: more work to do. *J Clin Neurophysiol* 2016;33(3):227–34.
- [143] Zheng WL, Kim JA, Elmer J, Zafar SF, Ghanta M, Moura Junior V, et al. Automated EEG-based prediction of delayed cerebral ischemia after subarachnoid hemorrhage. *Clin Neurophysiol* [Internet] 2022;143:97–106. <https://doi.org/10.1016/j.clinph.2022.08.023>.
- [144] Chen HY, Elmer J, Zafar SF, Ghanta M, Moura Junior V, Rosenthal ES, et al. Combining transcranial Doppler and EEG data to predict delayed cerebral ischemia after subarachnoid hemorrhage. *Neurology* 2022;98(5):E459–69.
- [145] Dale CR, Kannas DA, Fan VS, Daniel SL, Deem S, Yanez ND, et al. Improved analgesia, sedation, and delirium protocol associated with decreased duration of delirium and mechanical ventilation. *Ann Am Thorac Soc* 2014;11(3):367–74.
- [146] Fisch U, Jünger AL, Baumann SM, Semmlack S, De Marchis GM, Hunziker S, et al. Association between induced burst suppression and clinical outcomes in patients with refractory status epilepticus: a 9-year cohort study. *Neurology* 2023;100(19):E1955–66.
- [147] Watson PL, Shintani AK, Tyson R, Pandharipande PP, Pun BT, Ely EW. Presence of electroencephalogram burst suppression in sedated, critically ill patients is associated with increased mortality. *Crit Care Med* 2008;36(12):3171–7.
- [148] Peedicaïl J, Mehdiratta N, Zhu S, Nedjadrul P, Ng MC. Quantitative burst suppression on serial intermittent EEG in refractory status epilepticus. *Clin Neurophysiol Pract* [Internet] 2021;6:275–80. <https://doi.org/10.1016/j.cnp.2021.10.003>.
- [149] Westover MB, Shafi MM, Ching SN, Chemali JJ, Purdon PL, Cash SS, et al. Real-time segmentation of burst suppression patterns in critical care EEG monitoring. *J Neurosci Methods* [Internet] 2013;219(1):131–41. <https://doi.org/10.1016/j.jneumeth.2013.07.003>.
- [150] Narula G, Haeberlin M, Balsiger J, Strässle C, Imbach LL, Keller E. Detection of EEG burst-suppression in neurocritical care patients using an unsupervised machine learning algorithm. *Clin Neurophysiol* [Internet] 2021;132(10):2485–92. <https://doi.org/10.1016/j.clinph.2021.07.018>.
- [151] Zheng WL, Sun H, Akeju O, Westover MB. Adaptive sedation monitoring from EEG in ICU patients with online learning. *IEEE Trans Biomed Eng* 2020;67(6):1696–706.