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A Quantitative Electroencephalographic Index for Stroke Detection in Adults

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Abstract

Purpose: Electroencephalography (EEG) remains underutilized for stroke characterization. We sought to assess the performance of the EEG Correlate Of Injury to the Nervous system (COIN) index, a quantitative metric designed for stroke recognition in children, in discriminating large from small ischemic strokes in adults.

Methods: Retrospective, single-center cohort of adults with acute (within 7 days) ischemic stroke who underwent at least 8 hours of continuous EEG monitoring in hospital. Stroke size was categorized as large or small based on a threshold of 100 mL using the ABC/2 approach. EEG data were processed on MATLAB. COIN was independently calculated from consecutive 4-second EEG epochs. Student t-test and logistic regression were used to assess COIN performance in stroke size discrimination across the entire recording; random forest classification was used to determine COIN performance in limited EEG time windows ranging from 5 to 30 minutes in duration.

Results: Thirty-five patients with mean age 67 (SD \pm 17) years were analyzed with mean 4.5 \pm 1.3 hours of clean EEG per patient. Ten patients had large stroke and 25 had small stroke. Participants with large strokes had larger COIN values than those with small strokes (-53 vs. -16 , $P = 0.0001$). Logistic regression for stroke size classification model showed accuracy 83% \pm 8%, sensitivity 70% \pm 15%, specificity 88% \pm 8%, and area under the receiver operator curve 0.75 \pm 0.10. Random Forest Classification performance was similar using 5 or 30 minutes of EEG data with accuracy 81% to 82%, specificity 91% to 92%, and sensitivity 55% to 58%, respectively.

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Conclusions: COIN differentiated large from small acute ischemic strokes in this single-center cohort. Prospective evaluation in larger multicenter data sets is necessary to determine COIN utility as an aid for bedside detection of large ischemic strokes in contexts where neuroimaging cannot be easily obtained or when neurologic examination is limited by sedation or neuromuscular blockade.

Keywords

Stroke; Quantitative Electroencephalography; COIN index; Neurocritical Care

Arterial ischemic stroke (AIS) affects approximately 800,000 Americans yearly.¹ Delays in the diagnosis of stroke occur in both prehospital and in-hospital settings.^{2,3} Patients with a limited neurologic examination, whether due to depression of consciousness or the use of sedation and neuromuscular blockade, are at greater risk of delayed AIS recognition and interventions.⁴ A key challenge in hyperacute stroke evaluation is the ascertainment of brain tissue volume at risk for infarction, which is an important factor in patient selection for thrombolysis or mechanical thrombectomy.⁵

Electroencephalography (EEG) is a diagnostic procedure that can identify signs of cerebral ischemia, and growing interest exists on identifying patients with stroke due to large vessel occlusion in prehospital and hospital settings.^{6,7} Deployment of point-of-care EEG is hindered by limited availability of trained experts and technologies to continuously monitor and interpret continuous EEG data.^{8,9} Quantitative EEG (QEEG) analysis has the potential to support the development of automated systems of stroke recognition,¹⁰ but limited progress exists in developing algorithms with easily interpretable summaries and visualizations that are accessible to bedside providers without formal EEG interpretation training.

The Correlate Of Injury to the Nervous system (COIN) index is a QEEG asymmetry metric developed for pediatric stroke diagnosis that includes a brain topologic visualization with color changes in focal areas of EEG asymmetry to help non-EEG experts recognize stroke.¹¹ In this study, we leveraged a data set from adult patients with radiographically confirmed acute arterial ischemic stroke who underwent continuous EEG monitoring to determine whether COIN could be used to discriminate large (>100 mL) from smaller (<100 mL) infarcts.

METHODS

Study Population

Retrospective, secondary data analysis of a single-center convenience sample of patients >18 years of age admitted from October 2011 to September 2013 with a diagnosis of acute AIS confirmed with neuroimaging (CT or MRI) who underwent at least 8 hours of continuous EEG monitoring within 7 days of acute stroke diagnosis as part of standard of care and after stroke diagnosis. The work was performed under an IRB approved by the Massachusetts General Hospital IRB with a waiver of informed consent (protocol # 2013P001024). Clinical variables in the pre-existing data set included age, sex, stroke laterality, stroke location,

stroke etiology, history of stroke, NIH Stroke Scale (NIHSS), and stroke volume calculated on CT or MR images using the ABC/2 method.^{12,13} Stroke etiology was categorized using the TOAST classification as “Large Artery Disease,” “Cardioembolic,” “Small Vessel Disease,” “Other,” or “Unknown.”¹⁴ Information about mechanical ventilatory status, use of sedatives, and stroke interventions was not available.

EEG Preprocessing

Continuous EEG was obtained using 19 channels and a 10 to 20 system (Natus, CA). The first 8 h of EEG recording after acute stroke diagnosis was used for analysis. EEG preprocessing was performed on MATLAB (MathWorks, Natick, MA) using Fieldtrip.¹⁵ The EEG was re-referenced to a bipolar montage and split into nonoverlapping 4-second epochs. Epochs with minimal variability (<0.05 uV) or large voltage deflections (>300 uV) were automatically identified and removed using the Fieldtrip Toolbox “ft_artifact_clip” and “ft_artifact_threshold” algorithms.¹⁶ EEG artifact attributable to muscle activity and patient movement was automatically identified using the Fieldtrip Toolbox “ft_artifact_zvalue” artifact recognition algorithm.^{15,17} Each 4-second epoch containing >2.5 seconds of muscle or movement artifact was rejected; epochs containing <2.5 seconds of artifact had the artifactual portion of EEG data removed to allow analysis of the remaining data from the epoch. Band power was calculated using the discrete Fourier transform for each bipolar channel pair.

Qualitative EEG Analysis

Raw EEG data files were converted to European data format (.edf) and loaded into Persyst (Persyst Development Corporation, Solana Beach, CA) for qualitative review by an epileptologist (R.S.) blinded to clinical data and imaging results. Studies were reviewed using a bipolar montage and interpreted for the presence of background abnormalities (generalize slowing, focal slowing, amplitude asymmetry) and epileptiform abnormalities (seizures, rhythmic or periodic patterns, sporadic interictal epileptiform discharges).

COIN Calculation and Visualization

COIN is designed to simultaneously quantify and graphically represent the extent of focal background EEG power suppression so that regions of EEG asymmetry can be easily visualized by a bedside examiner. A COIN value of 0 implies a symmetric background EEG, whereas increasingly negative values indicate the presence of more conspicuous focal power attenuation across one or more bipolar channels. The COIN index and visualizer were originally designed to recognize AIS in children by analyzing spectral power in the theta (5–8 Hz) and alpha (8–12 Hz) power range.

$$r_{ij} = \log_2 \left(\frac{a_{ij}}{\frac{1}{M} \sum_{j=1}^M a_{ij}} \right) \quad (1)$$

$$s_{ij} = \log_2 \left(\frac{a_{ij}}{a_{ik}} \right) \quad (2)$$

$$Q = R^2 \bullet S \quad (3)$$

$$q_{ij} = 0, \text{ where } r_{ij}s_{ij} < 0 \quad (4)$$

In brief, EEG data are passed through a Fast-Fourier Transform to yield a power spectrum matrix A with power bands $i = n, n + 1, \dots, N$ and channels $j = 1, 2, \dots, M$ (where channel k is the contralateral homologue to j). Two matrices R & S of equal dimensions are individually calculated from A (Eqs 1 and 2) and are subsequently passed through an elementwise matrix multiplication $R^2 \bullet S$ to generate the COIN matrix Q (Eq 3). Q is then passed through a gating function to remove instances where r_{ij} and s_{ij} have opposite polarity (Eq 4).

Conceptual overview of COIN: the goal is to identify the presence of an asymmetric loss of power in one or more channels in a bipolar montage. This is done by simultaneously assessing the power in independent 1-Hz bands in each channel relative to the mean of the entire field (Matrix R) and relative to its contralateral homologue (Matrix S). By using the log function of the power ratio, we set a value of “0” to a hypothetical situation where the power is equal across all bands in all channels. The R matrix is squared to indicate the magnitude of asymmetry, which when multiplied against matrix S , the asymmetry signal is augmented in channels where the band power is further from the mean of the field. The gating function then forces the transformation to only accept elements in which R and S are isopolar, that is, that they are either both less or greater than the denominator in their respective power ratios from Equations 1 and 2.

Mean Q values from 8 to 18 Hz within each channel are mapped to corresponding topographic channel locations to generate the visualizer. A summary COIN value C is calculated for each epoch representing the sum of negative mean Q values in each channel (Eq 5). The values for C are smoothed using a 5-minute moving average.

$$C = \sum_{j=1}^M \left(\frac{1}{(18 - 8 + 1)} \sum_{i=8}^{18} q_{ij} \right) \text{ for all } \left(\sum_{i=8}^{18} q_{ij} \right) < 0. \quad (5)$$

Values below -20 in children suggest the presence of focal suppression as is typically observed with large volume stroke.¹¹ For this study, we adjusted COIN to analyze a higher power range (8–18 Hz), because adults have a higher frequency admixture than children and this range has been used to monitor for cerebral ischemia in adults.⁸ Continuous COIN values were independently calculated in every 4-second epoch of artifact-rejected EEG data to generate a COIN time series with 4-second resolution that was used for statistical analysis.

Rendered videos of COIN visualization (a graphic of a head that shows color changes in areas of focal EEG suppression) were reviewed (M.C.) to find representative visualizations to compare with available neuroimaging. Median hemispheric COIN values were calculated for left and right hemispheres and compared to determine concordance with infarct on neuroimaging. A difference greater than two points between hemispheres was used to determine laterality of maximal hemispheric COIN. Hemispheric COIN was considered concordant to neuroimaging if the greater COIN value was ipsilateral to radiographic infarct, and discordant if contralateral to radiographic infarct. COIN was considered indeterminate if no apparent asymmetry was noted in COIN or neuroimaging.

Statistical Analysis

Patients were divided into large versus small stroke volume groups based on a threshold of 100 mL. We used a cutoff of 100 mL to reflect the volume of perfusion lesion in the DEFUSE-3 trial, which reported a median perfusion lesion between 114 and 116 among randomized subjects.¹⁸ Clinical variables within the two groups were compared for statistical significance using two-tailed t-test for continuous variables and Pearson χ^2 for categorical variables. Performance of COIN for large and small stroke volume discrimination was evaluated in two steps. First, we sought to determine the optimal COIN cutoff using logistic regression for the entire 8 hours of EEG available for each patient. Then, we used a random forest classifier to evaluate how COIN's performance changes with increasing EEG time windows. For this time-varying window analysis, we randomly sampled EEG epochs from the entire EEG recordings with duration of 5–30 minutes.

For the COIN cutoff analysis, patients were separated in large or small stroke volume groups. The median COIN value was calculated across all 4-second epochs in the 8-hour recordings and used as an individual data point for statistical analysis. We used two-tailed t-tests to compare COIN distribution between groups and logistic regression to assess diagnostic performance. The Youden J Statistic (sensitivity + specificity -1) was calculated as a function of COIN cutoffs to determine optimal COIN values to maximize sensitivity and specificity. Analysis was performed on MATLAB 2021b using the Statistics Toolbox. The calculated optimal COIN cutoff value was used to categorize large and small stroke as COIN-positive or COIN-negative, and these categorizations were used to calculate the odds ratio (OR) of large stroke with COIN-positivity. The Mantel–Haenszel method was used to adjust the OR based on the presence of stroke history. Linear regression was used to evaluate whether there is an association separately between raw or binary COIN results and NIHSS.

For the varying time window analysis, mean continuous COIN values were extracted from 200 randomly sampled EEG clips with “t” length time windows. This process was repeated

in incremental 1-minute “t” intervals from 5 to 30 minutes—that is, 200 five-minute long clips per patient, then 200 six-minute long clips, and repeated until we obtained 200 thirty-minute clips per patient. The summary COIN value for each clip was expressed as percentages of time spent with COIN values between -5 and -125 , similarly to our analysis in pediatric stroke.¹¹ These 200% values were pooled for each patient. A random forest classifier model (scikit-learn, Python [version 3.9.1])¹⁹ was used to determine COIN accuracy, sensitivity, specificity, and area under the receiver operator curve (AUROC) in discriminating large from small stroke volumes for each “t” length time window. We used the 10-fold cross-validation method, whereby patients were divided into 10 balanced folds with similar number of patients with large and small strokes. In each fold, 90% of the data were used for training and 10% for testing, with no overlap between training and testing sets. Average performance metrics and related standard errors of the mean across the 10-folds were calculated. This process was iteratively repeated for increasing “t” from 5 to 30 minutes in 1-minute intervals.

RESULTS

Clinical Characteristics and Ancillary Findings

Thirty-five patients with acute stroke were analyzed with mean (SD) age 67 years (17), 49% women, and NIHSS 14 (7). Infarct volume was 100 mL in 10 patients (50% women) and <100 mL in 25 patients (48% women). Seven patients (three with acute stroke >100 mL and four with acute stroke <100 mL) had a history of remote stroke. There was no significant difference in age, NIHSS, stroke laterality, circulation, or etiology by TOAST score between the two stroke volume groups. Patients with infarct volume 100 mL were more likely to have generalized slowing ($P = 0.004$) on qualitative EEG analyses, with no difference in the presence of epileptiform abnormalities between groups (Table 1). After algorithmic identification and removal of suprathreshold, no-variability, muscle-associated, and movement-associated artifact, the proportion of data left over for analysis from each patient’s EEG was a mean of 0.60 (SD 0.11) with infarct volume 100 mL and 0.62 (SD 0.10) in infarct volume <100 mL ($P = 0.62$).

COIN Analysis and Visualization

A sample comparison of raw EEG, the COIN matrix “Q”, Topographic COIN visualization, summary COIN trend, and Fast-Fourier Transform spectrographic data is shown in Fig. 1. Across all patients, the average (SD) of median COIN values across the 8-hour EEG recording was -53.1 (13) for large strokes and -15.7 (1.2) for small strokes ($P = 0.0001$). Maximal hemispheric COIN values were concordant with neuroimaging in all 10 (100%) large strokes, while laterality was concordant in 12 (48%), discordant in 4 (16%), and indeterminate in 9 (36%) small strokes (Table 1). Comparison of representative neuroimages and COIN visualization are shown in Fig. 2.

Logistic regression using the median COIN value from all EEG data per patient had an AUROC of 0.88 (95% confidence interval 0.59–0.98) in discriminating large from small stroke. A COIN cutoff value of -20 resulted in the maximal Youden J statistic of 0.74 with

corresponding sensitivity of 90%, specificity of 84%, and accuracy of 86%. Specificity of 100% was seen at a COIN cutoff of -28 , with corresponding sensitivity of 60% (Fig. 3).

In unadjusted analysis, COIN below -20 had greater odds of large stroke (crude OR 36.0, 95% CI 3.7–354.3, $P < 0.001$) and after adjustment for history of stroke (OR 44.0, 95% CI 3.6–538.8, $P < 0.001$). Neither raw COIN values ($P = 0.10$) nor COIN values below -20 status ($P = 0.24$) were associated with NIHSS when assessed using linear regression.

Time Window Analysis

A random forest classifier model was used to assess COIN's performance in discriminating large and small strokes on randomly selected time windows. When using the 8 hours of recording per patient, test characteristics were accuracy $83\% \pm 8\%$, sensitivity $70\% \pm 15\%$, specificity $88\% \pm 8\%$, and AUROC 0.75 ± 0.10 . The optimal COIN cutoff values and test characteristics did not vary substantially when different time windows were used. Test performance across 200 EEG epoch samples with window size duration from 5 to 30 minutes was accuracy 81% to 82%, sensitivity 55% to 58%, specificity 91% to 92%, and AUROC 0.73 to 0.75. The optimal COIN cutoff values were mean -23 (SD 3) with a 5-minute time window to -22 (SD 2) with a 30-minute time window. Individually calculated test characteristics and COIN cutoff values in each time window are shown in Fig. 4.

DISCUSSION

This study demonstrates that the quantitative EEG metric COIN can discriminate large and small strokes in adults (core infarct volume threshold of 100 mL). A cutoff value of -20 provided the highest accuracy, mirroring our findings in a pediatric cohort.¹¹ The use of discrete cutoff values and visualizations to inform brain function asymmetry in patients at risk or with suspicion for stroke may support the development of intuitive diagnostic tools for prehospital and inpatient providers without formal training in EEG interpretation. The results of our time window analysis indicate that recording periods as short as a 5 minutes in duration may be sufficient for assessing stroke volume, which may be of particular relevance in large vessel occlusion stroke screening.

The use of EEG as an adjunct to stroke diagnosis in the prehospital and inpatient setting is of growing interest in AIS management.^{20–23} Our group previously compared COIN with other established markers of brain ischemia and asymmetry such as the alpha–delta power ratio and the brain symmetry index in a pediatric case–control study.¹¹ Therein, we found that COIN had similar test characteristics to the BSI, with the added benefit of identifying the focality of power suppression. BSI does not provide localization data, and its output cannot be used to generate a topographical display.^{24,25} The ADR has been shown to be useful for dynamic detection and trending of cerebral ischemia in subarachnoid hemorrhage.^{8,26} However, the ADR is not routinely used for acute stroke screening because it requires a priori knowledge of the area of brain at risk for stroke. In addition, pseudonormalization of the ADR can occur with loss of delta power in infarcted brain, effecting its diagnostic sensitivity in severe stroke. A small pilot study reported a significant ability of ADR to discriminate acute strokes >20 mL in volume from those <20 mL in volume without reporting sensitivity or specificity.²⁷

The establishment of COIN as a numeric EEG index that facilitates a threshold-based stroke-risk assessment may allow providers to recognize stroke with increasing clinical suspicion because COIN becomes more negative. Although a value of -20 optimized the combined sensitivity and specificity for AIS in this study, a value of -28 showed 100% specificity; values below this would be strongly suggestive of a focal cortical process that—in the appropriate clinical context—would suggest the presence of a large stroke. Moreover, the COIN matrix provides a rich source of quantitative EEG data that could be incorporated into machine learning algorithms for the differentiation between focal electrographic changes.

COIN values below -20 were most consistently seen with AIS in the anterior circulation, which were also the only strokes in this data set with volume >100 mL. Conventional surface EEG recordings capture cortical surface activity from brain tissue predominantly supplied by the anterior circulation, potentially explaining why this population would develop focal power suppression captured by COIN. The focus of this analysis was large territorial strokes. Further studies with larger sample sizes are needed to determine the performance of COIN for deep gray, white matter, and lacunar strokes, and intracranial hemorrhage,²⁸ TBI, and other intracranial lesions. AIS in the posterior circulation—and especially in the brainstem—would be less likely to manifest abnormal COIN signals because there is less cortical representation and the territory of injured brain tends to be smaller. COIN could thus assist in localization of stroke territory for patients without a clearly defined stroke syndrome; the similar NIHSS scores between the large and small stroke groups suggest that COIN may provide additional diagnostic value when paired with the neurologic examination.

This study is limited because it is a secondary analysis of a retrospective data set obtained to understand EEG predictors of patient outcome after stroke, rather than biomarkers of stroke presence and volume. The absence of a control arm without AIS is also a limitation. The data set did not include information on the relative timing of acute stroke onset, imaging, and start of the EEG recording, which would clarify how the COIN signal evolves over time after stroke. Data on angiographic findings were not available, thus precluding our ability to determine the utility of COIN in diagnosis of large vessel occlusive stroke. We suspect COIN will be more reliable in patients with less EEG noise and artifact. As such, it may prove to be useful in patients who are intubated and sedated, because of the relative lack of patient movement and muscle contamination. Future study will endeavor to build a framework of how COIN might fit into the early diagnosis and management workflow for AIS within distinct clinical contexts.

COIN between 0 and -20 is of uncertain value in adults. COIN is predicated on the presence of focal voltage attenuation and explicitly relies on asymmetry between channels to generate a negative COIN signal. This study does not address the use of COIN to differentiate AIS from other cerebral pathology such as hemorrhagic stroke, seizures, or malignancy—all of which may influence the COIN signal. Future assessment of COIN will need to focus on its diagnostic value in various clinical contexts.

Our qualitative review of the raw EEG found that all 10 patients with large stroke had generalized slowing, but only 4 had focal slowing or voltage asymmetry identified by human visual inspection. We hypothesize that generalized slowing may obscure the recognition of more subtle focal slowing assessment by clinicians, and that use of COIN may increase sensitivity of focal asymmetry evaluation. Future studies will need to focus on assessing COIN implementation in specific clinical contexts such as acute stroke presentation in the emergency department, during high-stroke risk procedures, or in the intensive care unit.

COIN is a quantitative QEEG index that may aid in the differentiation of large from small strokes in adults. Prospective evaluation in larger multicenter cohorts is required to determine COIN's utility as a diagnostic aid in arterial ischemic stroke diagnosis and management in different care delivery contexts.

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REFERENCES

1. Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statisticsd2020 update: a report from the American Heart Association. *Circulation* 2020;141:e139–e596. [PubMed: 31992061]
2. Shivaraju A, Yu C, Kattan MW, Xie H, Shroff AR, Vidovich MI. Temporal trends in percutaneous coronary intervention–associated acute cerebrovascular accident (from the 1998 to 2008 nationwide inpatient sample database). *Am J Cardiol* 2014;114:206–213. [PubMed: 24952927]
3. Aleu A, Hussain MVS, Lin R, et al. Endovascular therapy for cardiac catheterization associated strokes. *J Neuroimaging* 2011;21:247–250. [PubMed: 21281378]
4. Cummings S, Kasner SE, Mullen M, et al. Delays in the identification and assessment of in-hospital stroke patients. *J Stroke Cerebrovasc Dis* 2022;31:106327. [PubMed: 35123276]
5. De Havenon A, Zhou LW, Koo AB, et al. Endovascular treatment of acute ischemic stroke after cardiac interventions in the United States. *JAMA Neurol* 2024;81:264–272. [PubMed: 38285452]
6. Blume WT, Ferguson GG, McNeill DK. Significance of EEG changes at carotid endarterectomy. *Stroke* 1986;17:891–897. [PubMed: 3764960]
7. Kamitaki BK, Tu B, Wong S, Mendiratta A, Choi H. Quantitative EEG changes correlate with post-clamp ischemia during carotid endarterectomy. *J Clin Neurophysiol* 2021;38:213–220. [PubMed: 32044839]
8. Foreman B, Claassen J. Quantitative EEG for the detection of brain ischemia. *Crit Care* 2012;16:216. [PubMed: 22429809]
9. Alkhachroum A, Appavu B, Egawa S, et al. Electroencephalogram in the intensive care unit: a focused look at acute brain injury. *Intensive Care Med* 2022;48:1443–1462. [PubMed: 35997792]

10. Zheng WL, Kim JA, Elmer J, et al. Automated EEG-based prediction of delayed cerebral ischemia after subarachnoid hemorrhage. *Clin Neurophysiol* 2022;143:97–106. [PubMed: 36182752]
11. Caffarelli M, Karukonda V, Aghaeeval M, et al. A quantitative EEG index for the recognition of arterial ischemic stroke in children. *Clin Neurophysiol* 2023;156:113–124. [PubMed: 37918222]
12. Pantano P, Caramia F, Bozzao L, Dieler C, Von Kummer R. Delayed increase in infarct volume after cerebral ischemia: correlations with thrombolytic treatment and clinical outcome. *Stroke* 1999;30:502–507. [PubMed: 10066843]
13. Sims JR, Gharai LR, Schaefer PW, et al. ABC/2 for rapid clinical estimate of infarct, perfusion, and mismatch volumes. *Neurology* 2009;72:2104–2110. [PubMed: 19528517]
14. Adams HP, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993;24:35–41. [PubMed: 7678184]
15. Oostenveld R, Fries P, Maris E, Schoffelen JM. FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Comput Intell Neurosci* 2011;2011:156869. [PubMed: 21253357]
16. Oostenveld R Fieldtrip Toolbox: introduction on dealing with artifacts. Available at: www.fieldtriptoolbox.org/tutorial/artifacts/. Accessed March 11, 2024.
17. Oostenveld R Fieldtrip Toolbox: automatic artifact rejection. Available at: www.fieldtriptoolbox.org/tutorial/automatic_artifact_rejection/. Accessed March 11, 2024.
18. Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med* 2018;378:708–718. [PubMed: 29364767]
19. Pedregosa F, Varoquaux G, Gramfort A, et al. Scikit-learn: machine learning in Python. *J Mach Learn Res* 2011;12:2825–2830.
20. Gottlibe M, Rosen O, Weller B, et al. Stroke identification using a portable EEG device: a pilot study. *Neurophysiol Clin* 2020;50:21–25. [PubMed: 32014371]
21. Van Stigt MN, Groenendijk EA, Van Meenen LCC, et al. Prehospital detection of large vessel occlusion stroke with EEG: results of the ELECTRA-STROKE study. *Neurology* 2023;101:e2522–e2532. [PubMed: 37848336]
22. Thirumala PD, Ahmad AI, Roy PP, et al. Predictive value of multi-modality intraoperative neurophysiological monitoring during cardiac surgery. *J Clin Neurophysiol* 2023;40:180–186. [PubMed: 34510090]
23. van Meenen LCC, van Stigt MN, Siegers A, et al. Detection of large vessel occlusion stroke in the prehospital setting: electroencephalography as a potential triage instrument. *Stroke* 2021;52:e347–e355. [PubMed: 33940955]
24. Vanputten M Extended BSI for continuous EEG monitoring in carotid endarterectomy. *Clin Neurophysiol* 2006;117:2661–2666. [PubMed: 17029954]
25. Wilkinson CM, Burrell JI, Kuziek JWP, Thirunavukkarasu S, Buck BH, Mathewson KE. Predicting stroke severity with a 3-min recording from the Muse portable EEG system for rapid diagnosis of stroke. *Sci Rep* 2020;10:18465. [PubMed: 33116187]
26. Claassen J, Hirsch LJ, Kreiter KT, et al. Quantitative continuous EEG for detecting delayed cerebral ischemia in patients with poor-grade subarachnoid hemorrhage. *Clin Neurophysiol* 2004;115:2699–2710. [PubMed: 15546778]
27. Shreve L, Kaur A, Vo C, et al. Electroencephalography measures are useful for identifying large acute ischemic stroke in the emergency department. *J Stroke Cerebrovasc Dis* 2019;28:2280–2286. [PubMed: 31174955]
28. Tanna R, Amorim E, Caffarelli M. A bedside screening tool for acute intracranial hemorrhages in intubated children using continuous quantitative electroencephalography monitoring. *J Pediatr Epilepsy* 2024;s-0044-1788052

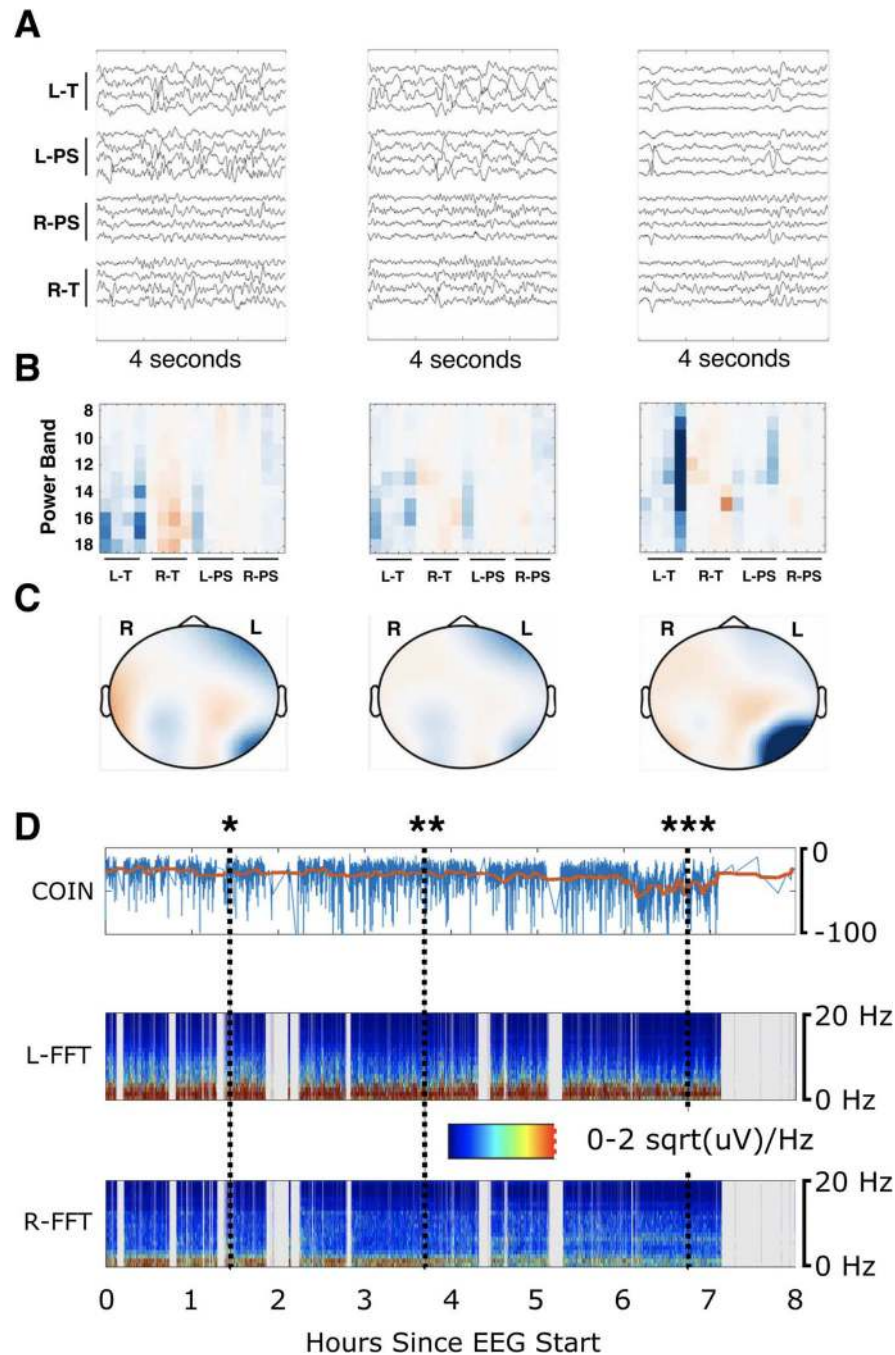
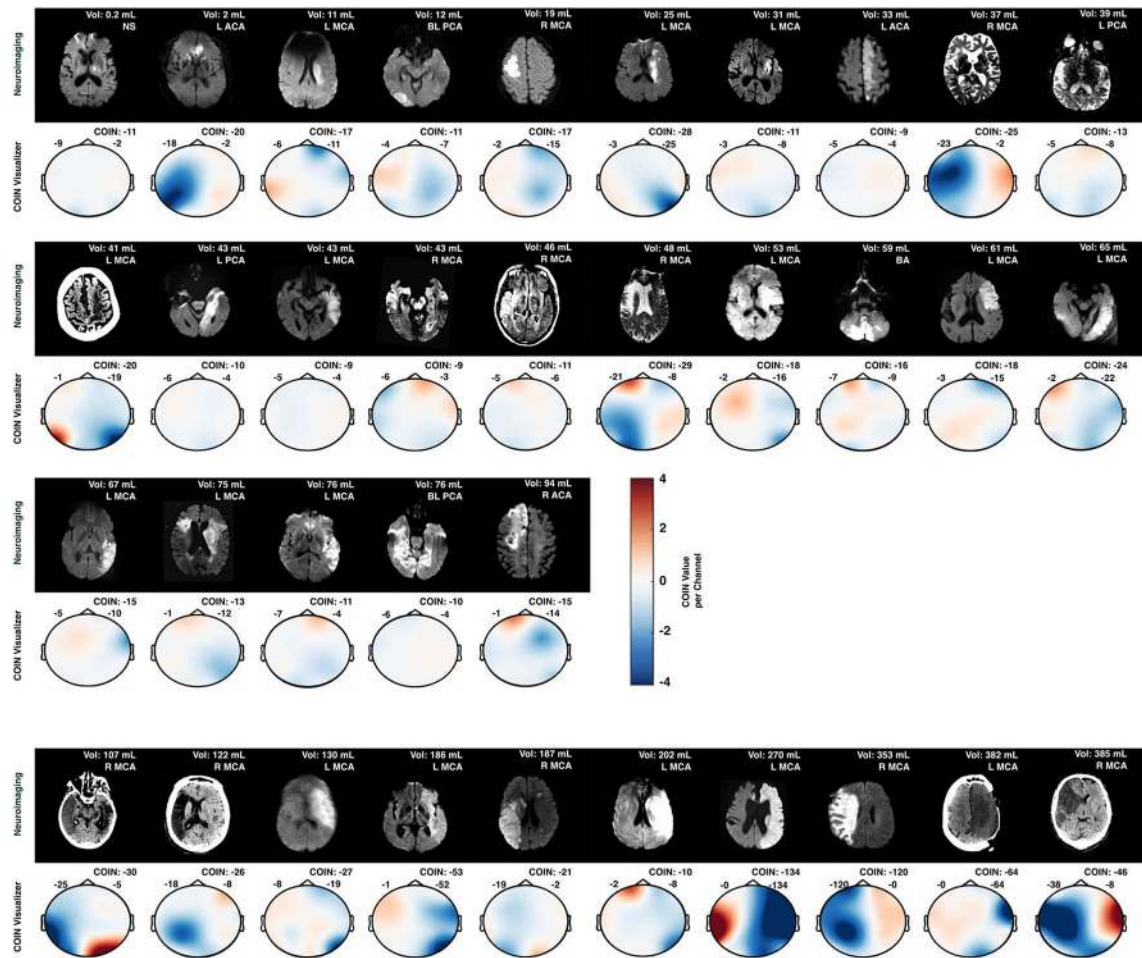


FIG. 1. Comparison of raw EEG in a standard bipolar montage (A), COIN matrix "Q" (B), COIN topographic visualization (C), and COIN and FFT trend (D) for 8 hours of EEG data in a sample patient (see Figure 2, volume 130 mL). Three separate 4-second epochs are selected from the study to demonstrate evolution of the COIN signal calculated from raw EEG. Missing data from COIN and FFT segments represent algorithmically artifact-rejected data. COIN, Correlate Of Injury to the Nervous system; FFT, Fast-Fourier Transform; L, left; PS, parasagittal; R, right; T, temporal.

**FIG. 2.**

Comparison of COIN visualization with neuroimaging for individual study subjects ordered in ascending infarct volume. First three rows show subjects with core infarct volume <100 mL and fourth row shows subjects with core infarct volume >100 mL. Median COIN value is shown for each subject, with left and right hemispheric values on either side of each topographic visualizer. ACA, anterior cerebral artery; BA, basilar artery; BL, bilateral; COIN, Correlate Of Injury to the Nervous system; L, left; MCA, middle cerebral artery; NS, not specified; PCA, posterior cerebral artery; R, right; Vol, volume.

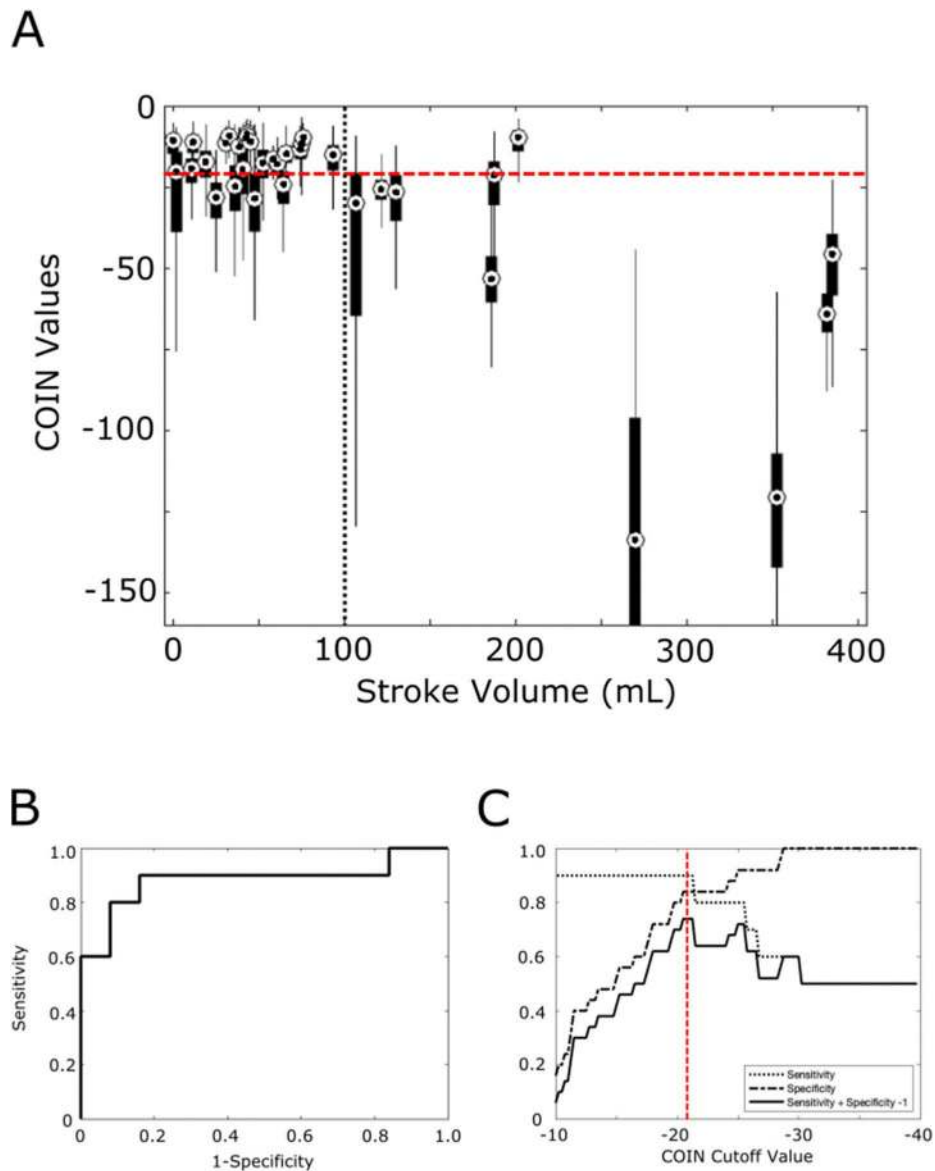


FIG. 3. COIN values from all study subjects with results of logistic regression. **A**, Median and quartile COIN values from 8-hour recordings plotted against core infarct volume. **B**, Receiver operator characteristic curve obtained using median values from individual subjects comparing volume <100 mL with >100 mL. **C**, Sensitivity, specificity, and Youden J statistic as functions of COIN cutoff value. Dashed red line = COIN of -21, black dotted line = stroke volume 100 mL. COIN, Correlate Of Injury to the Nervous system.

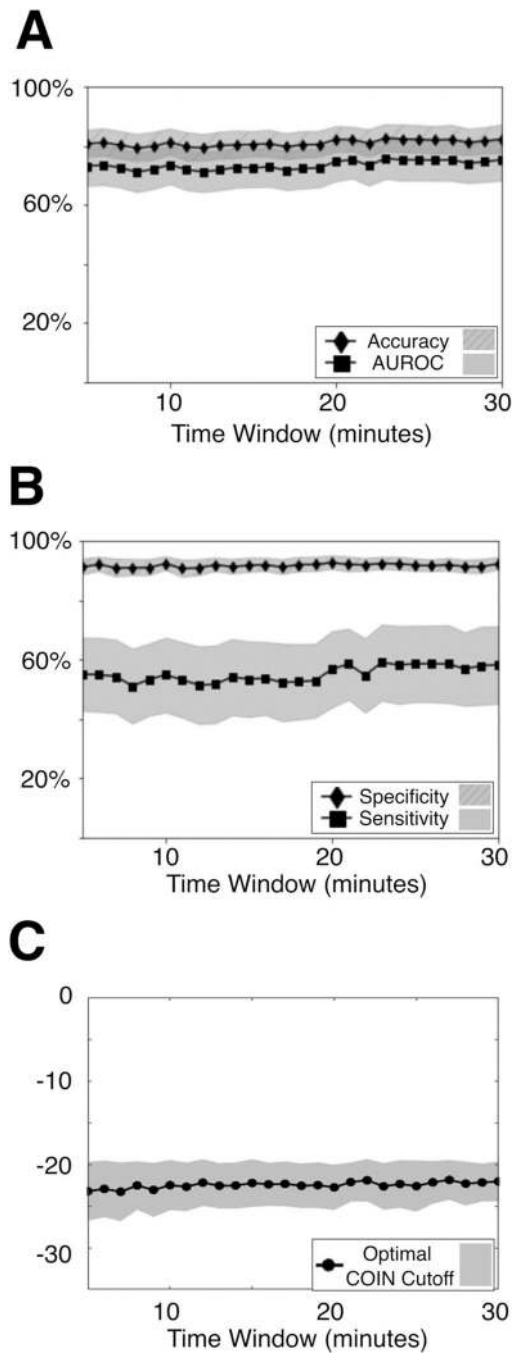


FIG. 4. Results of time window analysis optimized for accuracy showing stable accuracy and area under the receiver operator characteristic (A), sensitivity and specificity (B), and optimal COIN cutoff values with segments from 5 to 30 minutes in recording length.

TABLE 1.

Comparison of Clinical, Neuroimaging, Qualitative EEG, and COIN-based Variables Between Patients With stroke 100 mL and <100 mL

	Stroke Vol.		<i>P</i>
	>100 mL	<100 mL	
	<i>n</i> = 10	<i>n</i> = 25	
Age, years (SD)	62 (15)	69 (18)	0.25
Female sex (%)	5 (50%)	12 (48%)	0.91
Mean NIHSS (SD)	16.1 (5.5)	12.9 (6.8)	0.24
Mean stroke volume, mL (SD)	233 (108)	44 (24)	<0.001
Stroke laterality, <i>n</i> (%)			
Left	5 (50%)	16 (64%)	0.45
Right	4 (40%)	4 (16%)	0.13
Bilateral	1 (10%)	2 (8%)	0.85
Not specified	0 (0%)	3 (12%)	0.25
Stroke circulation, <i>n</i> (%)			
Anterior	10 (100%)	19 (76%)	0.09
Posterior	0 (0%)	5 (20%)	0.13
Not specified	0 (0%)	1 (4%)	0.52
Stroke etiology (TOAST), <i>n</i> (%)			
1: Large artery disease	6 (60%)	8 (32%)	0.13
2: Cardioembolic	4 (40%)	13 (52%)	0.52
3: Small vessel	0 (0%)	0 (0%)	—
4: Other etiology	0 (0%)	2 (8%)	0.36
5: Undetermined etiology	0 (0%)	2 (8%)	0.36
Background EEG abnormalities, any	10 (100%)	17 (68%)	0.04
Generalized slowing	10 (100%)	14 (56%)	0.01
Focal slowing	1 (10%)	4 (16%)	0.64
Amplitude asymmetry >2:1	3 (30%)	2 (8%)	0.09
Epileptiform EEG abnormalities, any	3 (30%)	6 (24%)	0.71
Seizure	1 (10%)	0 (0%)	0.11
Rhythmicity	2 (20%)	4 (16%)	0.78
Spikes	2 (20%)	2 (8%)	0.31
Mean duration of clean EEG data, hours (SD)	4.4 (1.1)	4.5 (1.3)	0.73
Mean proportion of cleaned EEG data available for analysis (SD)	0.60 (0.11)	0.62 (0.10)	0.62
Mean of median COIN value (SE)	-53.1 (13)	-15.7 (1.2)	0.0001
COIN and neuroimaging comparison			
Concordant	10 (100%)	12 (48%)	0.004
Discordant	0 (0%)	4 (16%)	0.18
Indeterminate	0 (0%)	9 (36%)	0.03

P-value <0.05 is considered significant.

COIN, Correlate Of Injury to the Nervous system; SE, standard error; Vol, volume.

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