Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

ORIGINAL CONTRIBUTION

Identification of Acute Stroke Using Quantified Brain Electrical Activity

Edward A. Michelson, MD, Daniel Hanley, MD, Robert Chabot, PhD, and Leslie S. Prichep, PhD

Abstract

Objectives: Acute stroke is a leading cause of brain injury and death and requires rapid and accurate diagnosis. Noncontrast head computed tomography (CT) is the first line for diagnosis in the emergency department (ED). Complicating rapid triage are presenting conditions that clinically mimic stroke. There is an extensive literature reporting clinical utility of brain electrical activity in early diagnosis and management of acute stroke. However, existing technologies do not lend themselves to easily acquired rapid evaluation. This investigation used an independently derived classifier algorithm for the identification of traumatic structural brain injury based on brain electrical activity recorded from a reduced frontal montage to explore the potential clinical utility of such an approach in acute stroke assessment.

Methods: Adult patients (age 18 to 95 years) presenting with stroke-like and/or altered mental status symptoms were recruited from urban academic EDs as part of a large research study evaluating the clinical utility of quantitative brain electrical activity in acutely brain-injured patients. All patients from the parent study who had confirmed strokes, and a control group of stroke mimics (those with final ED diagnoses of migraine or syncope), were selected for this study. All stroke patients underwent head CT scans. Some patients with negative CTs had further imaging with magnetic resonance imaging (MRI). Ten minutes of electroencephalographic data were acquired on a hand-held device in development, from five frontal electrodes. Data analyses were done offline. A Structural Brain Injury Index (SBII) was derived using an independently developed binary discriminant classification algorithm whose input was specified features of brain electrical activity. The SBII was previously found to have high accuracy in the identification of traumatic brain-injured patients who were found to have brain injury on CT (CT+). This algorithm was applied to patients in this study and used to classify patients as CT+ or not CT+. Performance was assessed using sensitivity, specificity, and negative and positive predictive values (NPV, PPV).

Results: Forty-eight stroke patients (31 ischemic and 17 hemorrhagic) and 135 stroke mimic controls were included. Within the ischemic population, approximately half were CT– but later confirmed for stroke with MRI (CT–/MRI+). Sensitivity to stroke was 91.7%, specificity 50.4% (to stroke mimic), NPV 94.4%, and PPV 39.6%. Eighty percent of the CT–/MRI+ ischemic strokes were correctly identified at the time of the CT– scan.

Conclusions: Despite a small population and the use of a classifier without the benefit of training on a stroke population, these data suggest that a rapidly acquired, easy-to-use system to assess brain electrical activity at the time of evaluation of acute stroke could be a valuable adjunct to current clinical practice.

ACADEMIC EMERGENCY MEDICINE 2015;22:67–72 © 2014 by the Society for Academic Emergency Medicine

From the Department Emergency Medicine, University Hospitals Case Medical Center (EAM), Cleveland, OH; the Division of Brain Injury Outcomes, Johns Hopkins University School of Medicine (DH), Baltimore, MD; and Quantitative Neurophysiological Brain Research Laboratories, Department of Psychiatry, New York University School of Medicine (RC, LSP), New York, NY.

Received May 30, 2014; revision received July 28, 2014 and August 3, 2014; accepted August 4, 2014.

Data acquisition for this study was supported by research grants from BrainScope Co., Inc., to the clinical sites. Dr. Michelson was a principal investigator at one of the clinical data acquisition sites at the time of this study. Dr. Prichep serves as a consultant to BrainScope Co., Inc., and holds potential financial interest through patented technology licensed by BrainScope from NYU School of Medicine. Drs. Hanley and Michelson sit on the Medical Advisory Board of BrainScope Co., Inc. Dr. Chabot was a paid consultant to BrainScope. BrainScope had no role in the conduct of the studies, analysis of the data, or preparation of manuscripts. Strict adherence to ethical concerns was followed and all subjects signed written informed consent forms for participation in the study.

Supervising Editor: Joshua Goldstein, MD, PhD.

Address for correspondence and reprints: Leslie S. Prichep, PhD; e-mail: Leslie.prichep@nyumc.org.

doi: 10.1111/acem.12561
ISSN 1069-6563
PII ISSN 1069-6563583

Acute stroke is a leading cause of brain injury and death and must be rapidly and accurately diagnosed to minimize the effect of its consequences both upon the individual and upon subsequent demands placed on our health care system. Rapid and accurate stroke diagnosis is important to guide treatment selection, especially because most current treatments are time-dependent and must be administered within the first 3 to 6 hours after symptom appearance to be maximally effective. Current acute stroke diagnosis relies on history and physical examination. Noncontrast head computed tomography (CT) is the first-line, most commonly used imaging modality in the workup of acute stroke in the emergency department (ED). However, CT results are less than 100% sensitive to ischemic stroke, especially within the first day or two after symptom appearance. Recent studies of the sensitivity and specificity of CT in acute ischemic stroke found levels of sensitivity that ranged from 12.5% to 92.2%, depending on the site and size of the brain lesion.[1] Most studies do not have appropriate control groups and thus levels of specificity are not available. Further, sensitivity and specificity of findings have been shown to be related to the expertise and experience of the radiologist interpreting the CT results, with inter-rater reliability varying from 0.46 to 0.58 for noncontrast CT.[2] There are numerous conditions that when first evaluated in the ED clinically mimic acute stroke, with estimated rates of occurrence falling between 6.5 and 31% of patients presenting with possible acute strokes.[3,4] Stroke mimics can use valuable ED resources to rule out stroke and needlessly expose such patients to CT radiation and testing cost.

An extensive literature exists demonstrating that electrophysiological measures of brain function derived from the electroencephalogram (EEG) have high clinical utility in early diagnosis, outcome prediction, and management of acute ischemic stroke.[5,6] Electrophysiological abnormalities reflecting functional changes may emerge earlier than structural changes and may better detect changes in neuronal function that precede structural changes in acute stroke[7,8] Prior electrophysiological studies were based on monitoring brain electrical activity using the 19 conventional electrode recording locations that are time-consuming and not available in most EDs, making this modality impractical for acute diagnosis and decision-making. Initial screening and triage of stroke patients in the ED would need to be done using a reduced electrode montage that could be rapidly applied, not requiring electroencephalogram (EEG) technologist participation and with rapid feedback to the clinician. Using an independently derived classifier algorithm based on brain electrical activity for the identification of structural brain injury (recorded from a reduced frontal montage using a hand-held device), the objective of this investigation was to explore the potential clinical utility of such technology in the triage of suspected acute stroke.

METHODS

Study Design

This was a retrospective study of adult patients between the ages of 18 and 95 years, presenting to the ED with stroke-like symptoms. All hospital institutional review boards approved the study. Patients signed informed written consent to participate in the study or, in a few cases, consent was obtained by proxy.

Study Setting and Population

Study sites included Bellevue Hospital Center (New York, NY), University Hospitals Case Medical Center (Cleveland, OH), William Beaumont Medical Center (Royal Oak, MI), and Washington University Medical Center (St Louis, MO). All study patients met the following inclusion and exclusion criteria: male and female patients between the ages of 18 and 95 years, who entered the ED with symptoms including altered mental status and/or symptoms suggestive of stroke (e.g., weakness, headache, dizziness), and who had Glasgow Coma Scale (GCS) scores > 8 were eligible for study. Only those with final diagnosis of stroke, migraine, or syncope were evaluated in the current study. Patients were excluded if clinical conditions would not allow placement of the electrodes, or if they were obtunded and therefore unable to provide informed consent, and no proxy was available to provide consent. In addition, patients with known psychiatric disorders or chronic drug or alcohol dependence disorders or history of chronic seizure or who were given or already taking central nervous system active medications were excluded. These exclusions were included to minimize possible confounding factors in this study.

Study Protocol

Decisions to order head CT scans were based on clinicians' suspicions of structural brain injury, hemorrhage, or stroke. Each study candidate received a limited montage EEG as part of participation in a multisite research study evaluating the clinical utility of quantitative brain electrical activity in acutely brain-injured patients in the ED. The patients in our study were all of those patients who had clinical diagnoses of stroke, migraine, or syncope (used as controls) in the larger study. Clinicians had no access to results of the quantitative EEGs obtained during the study. Hence, the diagnosis of stroke in all cases was made by standard clinical practice and not using study data.

EEG Data Acquisition. Each patient underwent acquisition of ten minutes of eyes-closed resting EEG recording acquired on a hand-held device in development (BrainScope Co., Inc.). The EEG recordings were made from frontal electrode sites of the expanded International 10–20 placement system using self-adhesive electrodes pasted on the forehead and referenced to linked ears. Electrode sites included FP1, FP2, AFz (located just anterior to Fz on the forehead, below the hairline), F7, and F8. All electrode impedances were below 10 kΩ. Amplifiers had a bandpass from 0.3 to 250 Hz (3 dB points). EEG recordings were made as close to the time of ED arrival and to CT scan as possible, without interfering with the clinical evaluation.

CT Scans. The decision on who received a CT scan was determined as part of the clinical evaluation of the treating emergency physician (EP). All imaging diagno-

ses were taken from final reports issued by the radiologist/neuroradiologists at each institution. Based on these readings, the study population was divided into two groups based upon their final clinical diagnoses. Group 1 included stroke patients whose etiologies were either ischemic or hemorrhagic in nature. Group 2 included patients whose final diagnoses were syncope or migraine (stroke mimics), although they had presented with altered mental status and/or stroke-like symptoms.

Data Analysis

All data processing and analysis was done offline. EEG data were subjected to artifact rejection algorithms to remove any biologic and nonbiologic contamination, such as that from eye movement or muscle movement. Previous experience has demonstrated that sufficient artifact-free data (60 to 120 seconds) can be obtained from this 10-minute recording (85% in less than 5 minutes). Features needed for input to a previously specified and validated (on an independent population of CT+ traumatic brain injury [TBI] patients) classifier algorithm were then automatically extracted from the artifact-free data.

The classification algorithm used in this study was reported to have high sensitivity and specificity for distinguishing acutely brain-injured patients with structural (CT+) brain damage.[9,10] Such classifier functions consist of a weighted combination of the specified features that maximally separate the groups of interest. These features include those that reflect changes in the characteristics of the frequency spectra as well as those reflecting disruptions in connectivity between recording locations. Details of the derivation of the classification algorithms are described elsewhere.[11,12] The EEGs from the stroke patients in this study were not part of the database used to develop the classification algorithm.

In this study, the previously specified selected features from each patient's brain electrical activity were submitted to the classifier algorithm without any information about the patient's diagnosis or clinical status, and a binary classification, a Structural Brain Injury Index (SBII), was obtained. Patient age was taken into account prior to calculation of the SBII, so all features input to the algorithm are first age-regressed.[13] The classifier is a linear discriminant function, the output of which is a binary indicator of belonging to one of the two categories, probable CT+ or not CT+. The classification is made using a previously defined threshold for a point on the receiver operating characteristic (ROC) curve from the classifier development population, above which classification as CT+ is made. All further results were derived from contingency tables of true positives, false positives, true negatives, and false negatives used to calculate sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV), to describe classification accuracy. It is noted that all EEGs were visually reviewed by an expert EEG technologist for quality of the recording. Where appropriate, demographic differences between groups were tested using two-group t-tests for the significance of differences.

RESULTS

The study included 48 stroke patients, with a mean age of 64.5 years (range = 33.0 to 92.2 years, SD ± 14.3 years). There were 31 ischemic (20 males, 11 females) and 17 hemorrhagic (nine males, eight females) strokes in this group. There were 15 patients in the ischemic stroke group (48%) whose initial acute CT results were negative but who underwent subsequent magnetic resonance imaging (MRI) scans because of continued clinical concerns, and the MRIs confirmed the diagnoses of stroke (ISC CT–/MRI+). The ischemic stroke patients who were CT+ on initial evaluation will be referred to as ISC CT+. The stroke mimic control group included 135 patients, with a mean age of 43.7 years (range = 18 to 81.7 years, SD ± 18.1 years). There were 72 migraine (22 males, 50 females) and 63 syncope (30 males, 33 females) patients in this group. There was a significant difference between the mean ages of the strokes and mimics ($t = -8.18$, $p < 0.0001$), with the stroke group being older, as expected.

Clinical Symptoms at Presentation

All stroke and stroke mimic patients presented to the ED with stroke-like symptoms. In some patients this included focal neurological signs and/or altered mental status. Table 1 shows the most common presenting symptoms as the percentage of the whole group in which they were reported.

As can be seen in Table 1, the most prevalent symptom in the stroke patients was peripheral weakness and dysarthria. In the stroke mimic patients, the most commonly reported symptoms were dizziness and headache, which were also common in the stroke group.

CT Findings

Computed tomography scans were ordered for all of the patients with clinical suspicion of acute stroke, and for 72% (52 of 72) of the migraine patients and 44% (28 of 63) of the syncope patients, as part of the clinical evaluations conducted by the EPs. The mean length of time from the onset of stroke symptoms to ED presentation and CT scan varied greatly. Time was divided into ≤8 hours, >8 hours, and unknown. Table 2 shows the distribution of time from onset of symptoms to ED for all groups. The CT+ stroke group and the stroke mimics were distributed similarly; however, the CT–/MRI+ stroke group were more likely to have been seen earlier, with 60% in 8 hours or sooner. Because these were all ischemic strokes, it may suggest the initial CT– findings, since such strokes are known to be CT– in the early stages. The range reported was from <2 to >72 hours. The mean length of time between the CT scan and the EEG data acquisition was 4.1 hours (with CT coming second in most cases).

Classification Using the SBII

The mean (±SD) length of time between admittance to the ED and the EEG data acquisition was 3.48 (±4.1) hours, with 95.7% occurring in less than 8 hours and all in less than 24 hours. The contingency table for performance and the accuracy of classification as CT+ for the

Table 1
Most Common Presenting Symptoms for Patients in the Stroke and Mimic Groups, Given as Percentage of the Group Who Reported the Symptom

Symptom	% Stroke CT+ (*n*/33)	% Stroke CT–/MRI+ (*n*/15)	% Mimic (*n*/135)
Peripheral weakness	48.5 (16/33)	60.0 (9/15)	3.0 (4/135)
Ataxia	9.1 (3/33)	0.0 (0/15)	3.0 (4/135)
Dizziness	27.3 (12/33)	20.0 (3/15)	34.8 (47/135)
Facial droop	24.2 (13/33)	26.7 (4/15)	2.2 (3/135)
Headache	27.3 (12/33)	13.3 (2/15)	58.5 (79/135)
Dysarthria	42.4 (17/33)	20.0 (3/15)	2.2 (3/135)
Nausea/vomiting	18.2 (7/33)	6.7 (1/15)	23.0 (31/135)
Numbness	15.2 (7/33)	13.3 (2/15)	3.7 (5/135)
Photophobia	3.0 (1/33)	0 (0/15)	8.9 (12/135)
Disorientation/confusion	12.1 (5/33)	6.7 (1/15)	3.0 (4/135)

A patient may have reported multiple symptoms.
CT+ = stroke patients who were CT+ on initial evaluation; CT–/MRI+ = patients whose initial acute CT results were negative but who underwent subsequent MRI scans because of continued clinical concerns and the MRIs confirmed stroke.
CT = computed tomography; MRI = magnetic resonance imaging.

Table 2
Estimated Time From Onset of Symptoms to ED Evaluation by Group, Shown as Percentage of the Group

Time From Onset of Symptoms	% Stroke CT+ (*n*/33)	% Stroke CT–/MRI+ (*n*/15)	% Stroke Mimic (*n*/135)
≤8 Hours	33.3 (11/33)	60.0 (9/15)	34.8 (47/135)
>8 Hours	48.5 (16/33)	26.7 (4/15)	42.2 (57/135)
Unknown	18.2 (6/33)	13.3 (2/15)	23.0 (31/135)

CT+ = stroke patients who were CT+ on initial evaluation; CT–/MRI+ = patients whose initial acute CT results were negative but who underwent subsequent MRI scans because of continued clinical concerns and the MRIs confirmed stroke.
CT = computed tomography; MRI = magnetic resonance imaging.

stroke population is shown in the upper panel of Table 3. The bottom panel of Table 3 shows sensitivity separately for each of the stroke groups. Sensitivity was found to be 91.7% (95% confidence interval [CI] = 80.5% to 96.7%) in the stroke group, with accuracy in identification of both ischemic (all) and hemorrhagic stroke being >90%. In terms of all ischemic strokes, the sensitivity to those that were CT+ upon initial evaluation was 100% (16/16); the sensitivity to those ischemic strokes that were CT– but MRI+ was also high, at 80% (12/15). Specificity was calculated for the stroke mimic controls and was found to be 50.4% (95% CI = 43.0% to 58.7%), with accuracy in identification of migraine as CT– being higher than that for syncope (55.6% and 44.4%, respectively). NPV was 94.4% (95% CI = 85.7% to 98.2%), and PPV was 39.6 (95% CI = 30.6% to 49.4%).

Location of Strokes. The regions in which the strokes were located were widespread and included strokes in the pons; basal ganglia; thalamus; cerebellum; frontal, central, and parietal cortex; and ventricles. Table 4 shows the locations of all strokes correctly identified using the classifier, as the percentage by group. It is noted that the three ischemic strokes missed (false negatives) were in the cerebellum, pons, and central regions, and the hemorrhagic case missed was in the thalamus. While the locations of false-negative cases include those most remote from the recording electrodes, other cases in these same regions were correctly identified.

Table 3
Classification Results for the Structural Brain Injury Index Are Shown in the Top Panel as a Function of Clinical Diagnosis (Sensitivity/Specificity) and by Type of Stroke in the Bottom Panel

		Classification Result	
	N	Stroke	"Not" Stroke
Clinical diagnosis			
Stroke confirmed	48	91.7% (44/48)	8.3% (4/48)
Stroke mimics	135	49.6% (67/135)	50.4% (68/135)
Type of stroke		Sensitivity (%)	
Ischemic (All)	31	90.3	
ISC (CT+)	16	100.0	
ISC (CT–/MRI+)	15	80.0	
Hemorrhagic	17	94.1	
Total (all strokes)	48	91.7	

The bottom panel shows sensitivity divided by the type of stroke.
ISC CT+ = ischemic stroke patients who were CT+ on initial evaluation; ISC CT–/MRI+ = patients whose initial acute CT results were negative but who underwent subsequent MRI scans because of continued clinical concerns, and the MRIs confirmed stroke.

DISCUSSION

An algorithm based on brain electrical activity derived from an independent population (TBI patients) to detect structural brain injury appears to be a sensitive indicator of the presence of stroke in ED patients. In addition

Table 4
Stoke Locations Summarized by Percentage of the Group for Those Cases That Were Correctly Called Stroke by the Classifier Function in Each Location

Location	% HEM (*n*/17)	% ISC CT+ (*n*/16)	% ISC CT–/MRI+ (*n*/15)
Basal ganglia	11.8 (2/17)	18.8 (3/16)	13.3 (2/15)
Central	0.0 (0/17)	6.3 (1/16)	13.3 (2/15)
Cerebellum	0.0 (0/17)	0.0 (0/16)	13.3 (2/15)
Frontal (F)/F-Temporal/F-Parietal	29.4 (5/17)	12.5 (2/16)	6.7 (1/15)
Parietal/occipital	23.5 (4/17)	12.5 (2/16)	0.0 (0/15)
Pons	0.0 (0/17)	12.5 (2/16)	20.0 (3/15)
Thalamus	17.6 (3/17)	18.8 (3/16)	6.7 (1/15)
Other	11.8 (2/17)	6.3 (1/16)	26.7 (4/15)
Unknown	5.9 (1/17)	12.5 (2/16)	0.0 (0/15)

HEM = hemorrhagic stroke; ISC CT+ = ischemic stroke patients who were CT+ on initial evaluation; ISC CT–/MRI+ = patients whose initial acute CT results were negative but who underwent subsequent MRI scans because of continued clinical concerns, and the MRIs confirmed stroke.

to high sensitivity (91.7%), an NPV of 94.4% was found. Considering the high risk of false negatives in this population, the very high NPV supports potential clinical utility. This finding held for both ischemic and hemorrhagic strokes and for those whose acute stage CT scans were negative but subsequent MRIs were positive. The high level of sensitivity is accompanied by specificity of 50.4%. Specificity should be considered in the context of the fact that 75% of the migraine controls were scanned by standard clinical practice. These data suggest that an index based on quantitative features of brain electrical activity performs with high accuracy in the identification of primary vascular mediated brain injury due to ischemia or cerebral hemorrhage.

The performance of the index in the subpopulation of acute stroke patients whose CT scans in the ED were considered normal, but later MRIs confirmed the stroke diagnosis, is important to consider. This group was correctly identified 80% of the time by the structural injury classification algorithm. Changes in brain electrical activity result from disruptions in normal neuronal function and interactions among brain regions. It has been reported in the literature that ischemic strokes are often CT– within the first 24 hours.[1] The fact that the CT–/MRI+ group studied had the highest percentage (60%) of cases seen ≤8 hours suggests that the negative CT finding was not unexpected. However, the algorithm used in this study correctly identified 80% of these cases as positive at the time the CT was negative. Although limited by the small number of patients, these data support the idea that such disturbances can precede evidence of structural injury and may explain why CT and MRI findings are less than perfect when obtained in the acute phase after brain insult.[14,15]

This SBII, based on brain electrical activity recorded from a limited montage of five leads over the frontopolar, midline frontal, and fronto-temporal regions, was sensitive to stroke that was often localized in other cortical regions, including those remote to these electrode sites (e.g., parietal cortex) and those deep in the brain (e.g., pons, basal ganglia, and cerebellum). Although the false-negative cases were from the more remote regions, true positives were also located in these remote regions, suggesting that the frontal recording montage is not a limiting factor. Recent neuroimaging studies of stroke patients have focused on neural networks across brain regions and how these are affected by localized strokes. In one such paper it was concluded that network disturbances after stroke occur not only in the localized region of the stroke, but also extend to remote regions over both the affected and the unaffected cerebral hemispheres.[16] The increased susceptibility of the frontal regions to damage after closed head injury most likely results from direct contusions to this region and the disruption of the extensive connections between this region and other cortical regions.[17] Similarly, the sensitivity of TBI algorithm to stroke may also result from disruptions of the neuronal pathway connections between the frontal region and those regions of structurally damaged brain. These changes in brain electrical conduction and activity, which manifest as signs and symptoms of stroke, are amenable to measurement and analysis by this technology.

Stroke is a time-critical diagnosis. Stroke carries some of the same time concerns as ST-segment elevation myocardial infarction (STEMI) for interventions that can lessen long-term disability. In STEMI diagnosis, based on symptoms and/or risk factors, patients can be screened with a 12-lead electrocardiogram that can then result in correct identification and direction of patients to the catheterization laboratory for earlier angioplasty and revascularization. A similar rapid, noninvasive test to screen for acute stroke is lacking. Such a tool, with appropriate sensitivity and specificity, might in the future be deployed to help identify patients suffering from stroke so they can be directed to stroke centers primarily for treatment and to help guide therapy for earlier intervention.

LIMITATIONS

Based on these results, more work is warranted on a larger population of patients presenting with signs and symptoms consistent with acute stroke. Such future study would be aimed at deriving an optimized brain electrical activity algorithm based on stroke cases, likely to result in improved performance and higher specificity values, which would further improve clinical utility.

Many patients in this population may have suffered prior diagnosed or unrecognized transient ischemic attacks or strokes, leaving them with abnormal new baseline EEGs. The ability of the classification algorithm to distinguish acute versus old strokes will be important if used for triage and treatment decisions. Hence, a control group of patients with prior strokes but no new acute symptoms will be needed.

The decision to use the CT readings of the local site radiologist or neuroradiologists, rather than an independent adjudication panel, was based on the desire to best reflect the current clinical care and was considered to be a conservative approach (as it adds variance); however, in future studies independent neuroradiologist adjudication might be considered. Another concern is that this population likely also includes many patients taking neuroactive pharmaceuticals that could alter the EEG. Further study of these populations is needed. In addition, sensitivity and specificity will both need to be proven sufficiently high to help direct treatment decisions potentially in advance of, or in the absence of, imaging. CT scans are commonly available in most EDs. MRI is much more time-consuming and much less available rapidly at many EDs where patients will present.

CONCLUSIONS

The ability of an index derived from quantitative brain electrical activity to assist in the triage of stroke patients and to help to identify computed tomography–normal patients who are having ischemic brain events may decrease the time for making important treatment decisions. Despite a small population and the use of a classifier without the benefit of training on a stroke population, these findings suggest that a rapidly acquired, easy-to-use system to assess brain electrical activity at the time of evaluation of acute stroke has the potential to be a valuable adjunct to current clinical practice.

The authors acknowledge the contributions of those who made this research possible, including the primary investigators and research technicians at all the clinical sites and the patients who volunteered. This research was supported in part by BrainScope Co., Inc., Bethesda, MD, who granted expenses related to data acquisition.

References

1. Brazzelli M, Sandercock PA, Chappell FM, et al. Magnetic resonance imaging versus computed tomography for detection of acute vascular lesions in patients presenting with stroke symptoms. Cochrane Datab Sys Rev 2009;7:1–56.
2. Scharf J, Brockmann MA, Daffertshofer M, et al. Improvement of sensitivity and interrater reliability to detect acute stroke by dynamic perfusion computed tomography and computed tomography angiography. J Comput Assist Tomogr 2006;30:105–10.
3. Forster A, Griebe M, Wolf ME, Szabo K, Hennerici MG, Kern R. How to identify stroke mimics in patients eligible for intravenous thrombolysis? J Neurol 2012;259:1347–53.
4. Reid JM, Currie Y, Baird T. Non-stroke admissions to a hyperacute stroke unit. Scott Med J 2012;57: 209–11.
5. Finnigan S, van Putten MJAM. EEG in ischaemic stroke: quantitative EEG can uniquely inform (sub-) acute prognoses and clinical management. Clin Neurophysiol 2013;124:10–9.
6. Jordan KG. Emergency EEG and continuous EEG monitoring in acute ischemic stroke. J Clin Neurophysiol 2004;21:341–52.
7. Claassen J, Hirsch LJ, Kreiter KT, et al. Quantitative continuous EEG for detecting delayed cerebral ischemia in patints with poor-grade subarachnoid hemorrhage. Clin Neurophysiol 2004;115:2699–710.
8. Machado C, Cuspineda E, Valdes P, et al. Assessing acute middle cerebral artery ischemic stroke by quantitative electric tomography. Clin EEG Neurosc 2004;35:116–24.
9. Hanley DF, Chabot RJ, Mould WA, et al. Use of brain electrical activity for the identification of hematomas in mild traumatic brain injury. J Neurotrauma 2013;30:2051–6.
10. O'Neil B, Naunheim RS, Prichep LS, Chabot RJ. Can quantitative brain electrical activity aid in the initial screening of mild traumatic brain injured patients. West J Emerg Med 2012;13:394–400.
11. Prichep LS, Jacquin A, Filipenko J, et al. Classification of traumatic brain injury severity using informed data reduction in a series of binary classification algorithms. IEEE Trans Neural Syst Rehab Engin 2012;20:806–22.
12. Prichep LS, Dastidar SG, Jacquin A, et al. Classification algorithms for the identification of structural injury in TBI using brain electrical activity. Comput Biol Med 2014;53C:125–33.
13. John ER, Prichep LS, Friedman J, Easton P. Neurometrics: computer-assisted differential diagnosis of brain dysfunctions. Science 1988;293:162–9.
14. Rajajee V, Kidwell C, Starkman S, et al. Diagnosis of lacunar infarcts within 6 hours of onset by clinical and CT criteria versus MRI. J Neuroimag 2008;18:66–72.
15. Totaro P, Toni D, Durastanti L, et al. Diffusion-weighted MRI in patients with non-diagnostic CT in the post-acute phase of cerebral ischemia. Eur Neurol 2010;63:94–100.
16. Rehme AK, Grefkes C. Cerebral network disorders after stroke: evidence from imaging-based connectivity analyses of active and resting brain states in humans. J Physiol 2013;591:17–31.
17. Malloy PF, Aloia M. Frontal lobe dysfunction in traumatic brain injury. Sem Clin Neuropsych 1998;3:186–94.