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ORIGINAL ARTICLE

Use of brain electrical activity to quantify traumatic brain injury in the emergency department

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Abstract

Primary objective: To validate a QEEG algorithm on traumatic brain injury in an Emergency Department (ED) setting.

Methods and procedures: EEG data were collected from 105 patients with head injury (53 CT+ and 52 CT−) and 50 ED controls. Ten minutes of eyes closed resting EEG was collected from five frontal locations. A discriminant index of the probability of belonging to the TBI CT+ group was computed. Analysis of variance was computed comparing this index across the three patient groups. Using ROC curves, the $p < 0.05$ confidence level was determined to compute sensitivity and specificity for the TBI CT+ population.

Results: CT+ patients had a mean TBI discriminant index of 80.4, CT− patients 38.9 and controls 24.5; $F = 70.2$, $p < 0.0001$. Sensitivity was 92.45% for the CT+ group and specificity was 90.00% for the control group.

Conclusions: The TBI discriminant index appears to be a sensitive index of brain function. It may be used to suggest whether or not a patient presenting with altered mental status requires a CT scan. This index may aid in the triage of such patients in the ED. Such an easy to use, automated system may greatly enhance the clinical utility of EEG in the ED.

Keywords: *Electroencephalogram, traumatic brain injury*

Introduction

The incidence of traumatic brain injury (TBI) in Emergency Departments (EDs) is estimated to be more than 1,250,000 visits per year (not including those who are hospitalized) according to the CDC's most current figures, many of which would be considered in the mild category. An extensive literature review suggests that quantitative electroencephalography (QEEG) is a sensitive indicator of the presence of brain injury after mild head trauma [1]. QEEG variables distinguish normal controls from patients with mild traumatic brain injury (mTBI) [2] and patients with mTBI from those with severe TBI [3]. QEEG has also been shown to be highly sensitive to post-concussion syndrome [4, 5] and to predict recovery of function at 1 year post-injury [6]. EEG discriminant functions were sensitive indicators of brain dysfunction after blast concussion mild head injury [7]. Cao et al. [8] conclude that EEG features are useful for the classification of athletes with residual brain injury subsequent to concussion. However, despite such data, EEG remains an under-utilized tool in the ED, for several reasons: it is not readily available, requires a skilled technician for data acquisition and a professional specialist to interpret the findings.

In this study a limited montage on the frontal scalp locations was used. The proximity of frontal and anterior temporal regions to bony structures and cavities of the skull makes them particularly susceptible to injury, particularly when rotational

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acceleration affects a freely moving head [9, 10]. The frontal and temporal regions are three times more likely to be affected than other cortical regions [11]. Neuropathologic and neuroimaging studies show that frontal regions are the most vulnerable for focal deficits after closed head trauma [12]. Ptito et al. [13] found that the most common post-concussion symptoms were characteristic of frontal and/or temporal lobe dysfunction. Children with moderate TBI were most likely to show diffusion tensor imaging abnormality in inferior frontal, superior frontal and supracollasal regions [14]. This increased susceptibility of the frontal regions to damage after closed head trauma most likely results from direct contusions to this region and the disruption of the extensive connections between this region and other cortical regions [15].

This paper presents an initial evaluation of a hand-held quantitative EEG (QEEG) device (Instrument in development, Brainscope Company, Inc. Bethesda, MD) in development which is designed to be easily utilized in an ED environment by ED staff to rapidly provide information about the seriousness of traumatic head injury in head injured patients presenting with altered mental state. The purpose of the present study was to determine the feasibility of using such a device in the ED and whether an index of brain function, implemented in the hand held device, can be used to distinguish between mTBI patients with a positive CT scan, those traumatic head injury patients with a negative CT scan and ED control patients.

Methods

Subjects

The study population consisted of a sample of 105 consecutive patients who arrived either at Washington University in St Louis, MO, Barnes Hospital or the Bellevue Hospital Center Emergency Department, New York, with complaints of altered mental status (AMS), following a closed head injury and whom met the inclusion/exclusion criteria described below. The control population consisted of 50 consecutive ED patients without complaints of AMS and no indication of head injury.

Inclusion/exclusion criteria

TBI patients. Males and females between the ages of 18–80, who entered the ED with MTBI and had a CT scan of the head planned as part of their evaluation were eligible for the study. Patients were excluded whose clinical condition would not allow placement of the electrodes or were intoxicated or obtunded to the point where they could not sign an informed consent form. In addition, patients with known psychiatric disorder or chronic drug or alcohol abuse, chronic seizure history, mental retardation or who were taking CNS active medication were not eligible for the study.

Control patients. The control group consisted of males and females between the ages of 18–80, who entered the ED under distress with non-head injuries, no AMS and no known direct central nervous system involvement. Since controls were selected based upon consecutive ED admissions this was a very diverse sample that included patients admitted for problems such as orthopaedic-related problems, lacerations/amputations and abrasions, cardiac related problems and complications due to pregnancy. The same exclusion criteria were used as for the TBI group.

From this sample, 53 had positive CT scans (CT+), 52 had negative CT scans (CT−) and 50 were chosen as ED controls. Written informed consent was obtained prior to the time of testing. All patient records were reviewed after emergency room or hospital discharge. All CT scan results were based upon the reports issued by the neuroradiologists at each institution. The majority of the CT+ findings included traumatic brain haemorrhages, brain contusions, traumatic subdural and epidural haematomas. A majority of the CT− patients received a diagnosis of concussion.

Design and procedures

Once a patient was admitted to the ED a technician was contacted and the patient and/or his family gave written informed consent to collect the EEG recording during the period of time prior to his discharge home or admission the hospital for further evaluation. In majority of the cases EEG recordings were made within 24 hours of precipitating event.

EEG acquisition. Patients and controls underwent 10 minutes of eyes closed resting EEG recording on the BrainScope^{TM} device in development. The EEG data were collected using self-adhesive electrodes from frontal electrode sites of the International 10/20 system which included FP1, FP2, AFz[1] (located just anterior to Fz on the forehead, below the hairline), F7 and F8, referenced to linked ears. All electrode impedances were below 5 kΩ. Amplifiers had a bandpass from 0.5–70 Hz (3 dB points). Set-up was accomplished in all cases in less than 5 minutes.

EEG data analysis. The collected EEG data was subjected to artifact rejection by an EEG

Table I. Incidence of clinical symptoms (in percentages) in the patient groups at time of admission to the ED.

Group	*n*	Amnesia	Dizziness/Vertigo Nausea/Vomiting	'Neurological' Symptoms: Numbness/Weakness/ Facial Droop/Dysarthria/ Photophobia/Ataxia	LOC	Headache
CTL	50	0.00%*▼	8.00%*	16.00%	0.00% *▼	6.00%*▼
CT−	52	7.69%	30.77%	9.62%	63.46%	42.31%
CT+	53	7.55%	18.87%	18.87%	71.70%	37.74%

Chi-square results are coded in the table for significance $p < 0.05$ as follows: * CTL vs CT−, ▼ CTL vs CT+. No differences were found between CT− and CT+.

technologist with several years experience processing EEG, with the aid of an artifact algorithm built into the BrainScope device, to remove any biologic and non-biologic contamination, such as that from eye movement or muscle movement. Previous experience has demonstrated that sufficient artifact-free data (60–120 seconds) can be obtained from this 10-minute recording.

The artifact-free EEG data was submitted to Fast Fourier Transform (FFT) to extract QEEG features of absolute and relative (%) power, mean frequency, inter- and intra-hemispheric coherence and symmetry computed for the delta (1.5–3.5 Hz), theta (3.5–7.5 Hz), alpha (7.5–12.5 Hz), beta (12.5–25 Hz) and gamma (30–45 Hz) frequency bands. All quantitative features were log transformed to obtain Gaussianity, age-regressed, and *Z*-transformed relative to age expected normal values. The importance of each of these steps in enhancing the sensitivity and specificity of brain electrical activity has been described in detail elsewhere [16], as are test–re-test reliability [17] and independent replications of the Neurometric normative data of brain electrical activity [18].

This study applies a previously developed QEEG-based discriminant function (Version #1650-2 073109) which discriminated the normal control population ($n = 293$) from patients who had suffered a closed head injury ($n = 189$) in an ED population with high sensitivity and specificity (details of the discriminant methodology used are reported elsewhere [19]. This discriminant algorithm was constructed using split-half populations of normals and TBI patients for training and test (independent validation). Discriminant functions provide the user with a discriminant score that represents the probability of belonging to a specific group. For example, in this study this score represents the probability of having an EEG profile similar to that seen in CT+ patients. Features that contributed most to this discriminant included: relative power increase in slow waves in frontal regions, relative power decrease in alpha 1 and alpha 2 in frontal regions, power asymmetries in theta and total power between lateral and midline frontal regions, incoherence in slow waves between frontopolar regions and decrease in mean frequency of the total spectrum composited across frontal regions. It is important to point out that patient age was taken into account prior to calculation of the brain state discriminant score since all EEG features were age-regressed prior to inclusion in discriminant analyses.

The discriminant score (range 0–100) was used as an index (TBI-DS) of the probability of TBI CT+, where the larger the number, the greater the probability. A three-way analysis of variance (ANOVA) was computed comparing this index across the three patient groups defined as patients with AMS who had CT+ findings, patients with CT− findings and emergency room admission control patients. In addition, using the ROC curve derived from the test group from discriminant construction, the $p < 0.05$ confidence level was identified (50.0) and was also evaluated.

All EEG processing and calculation of the brain state index was accomplished while the technician was blinded to group membership.

Results

Patient populations

Distribution by gender did not differ across the three groups, with each group containing 57% males. The mean age of patients in each group differed, with mean age higher in the CT+ group than those in the CT− group and the controls (CT+ = 61.1 (22–90); CT− = 39.9 (18–84); and controls = 42.0 (23–81) years). It should be noted that such differences in age should not be a factor in this work since all data is age regressed as described above. Table I presents the frequency of occurrence of the major presenting signs and symptoms reported by the control, CT− and CT+ groups. No significant differences were seen between the CT− and CT+ groups with respect to the percentage of subjects reporting amnesia, dizziness, neurological symptoms, loss of consciousness or headaches. However, significant differences were noted between CT− and Controls (CTL) and CT+ and CTL patients, as shown in Table I. It was noted that there were no differences between the three groups with respect to neurological symptoms. The mechanism of injury included assaults, motor vehicle and pedestrian accident, falls and sports-related injury, with the majority of patients tested within 24 hours. The CT+ and CT− patient groups presented with Glasgow coma scores between 12–15.

TBI discriminant score (TBI-DS)

A three-way analysis of variance was computed comparing the TBI-DS index across the three patient groups defined as patients with AMS with CT+ scan findings, patients with AMS with CT− scan findings and emergency room admission control patients. The results of this analysis were highly significant; $F = 70.2$, $p < 0.0001$. CT+ patients had a mean TBI-DC of 80.4, CT− patients a value of 38.9 and control patients a mean index of 24.5. All differences between these three groups were significantly different from each other at the $p < 0.001$ level (Duncan multiple comparisons).

Figure 1 presents mean values and standard error of the means for each patient group. In order to determine the sensitivity and specificity of this TBI-DC, an index score of 50 or greater ($p < 0.05$) was used as the cut-point in determining whether or not an individual within each group should be classified as brain-injured. For the CT+ group, 49 (92.45%) were classified as brain-injured and four (7.55%) as normal ($\chi^2 = 38.2$, $p < 0.0001$). For the CT− group, 18 (34.62%) were classified as brain-injured and 34 (65.38%) as normal brain function ($\chi^2 = 4.9$, $p < 0.03$). For the control group, five were classified as brain-injured (10%) and 45 (90%) as normal brain function ($\chi^2 = 32.0$, $p < 0.0001$). Thus, the sensitivity for CT+ is 92.45% and the specificity for normal controls is 90.00%. The negative predictive value was 91.8% and the positive predictive value was 90.7%.

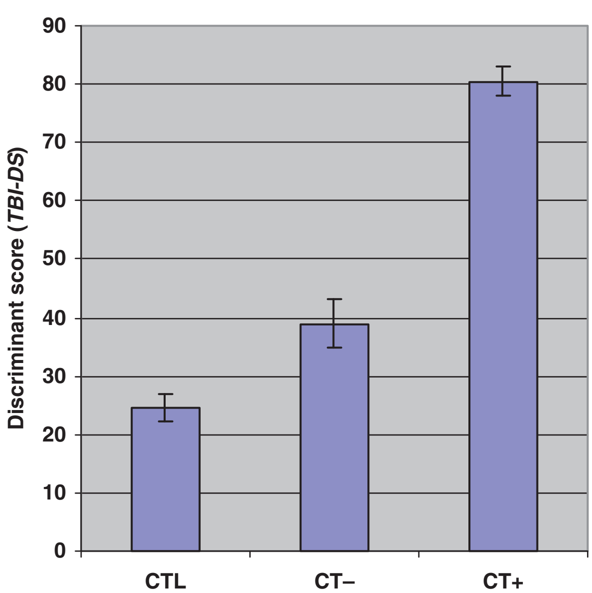

Figure 1. Histogram of the mean discriminant score (*TBI-DS*) in the three patient populations, with standard error of the mean shown on each bar.

Discussion

The costs incurred in the evaluation and treatment of minor head injury has been estimated to be 1.5 billion dollars per year, with up to 20% of patients showing symptoms which persist up to 30 days after injury [20]. Further, an evaluation of 381 MHI patients, all of whom received CT scans, revealed an incidence of 38% positive scans requiring further treatment. Age, mode of injury, loss of consciousness, seizure presence, ENT bleeding and vomiting did not predict positive CT scan, while Glasgow coma score, the presence of focal neurological signs and the presence of a radiographic skull fracture only had moderate predictive power of a CT+ [21]. In the current study, the presence of specific symptoms at the time of admittance to ED including amnesia or LOC did not correlate with the outcome of the CT imaging, suggesting that clinical presentation is not sufficient to make a prediction regarding the presence of abnormalities in brain function, further stressing the need for measures which would lead to more clinical useful triage for CT. In fact, the presence of neurological symptoms such as numbness, tingling and facial droop did not distinguish the three groups. As it turned out, CTL patients often presented with these symptoms, although due to peripheral nervous system involvement. While CT scans are readily available in this country, overuse can be very costly and several recent studies have highlighted the adverse effects of radiation from CT scans [22, 23].

The QEEG derived *TBI-DS* appears to be a sensitive index of brain function that can be utilized in conjunction with other clinical information to determine whether or not a patient presenting with altered mental status has a brain injury that is severe enough to warrant further diagnostic evaluation and treatment. The differences between the CT− and CT+ groups were present despite very similar presenting symptoms when admitted into the emergency room. This index was able to predict which patients presenting with altered mental status were likely to have future CT+ images vs those with CT− images. Further, the finding that the *TBI-DC* was greater for CT− patients than for control patients may indicate that a subset of the CT− patients showed signs of disturbed brain function, possibly representing the effects of concussion. In this sample, 34.62% of the CT scan negative patients had a *TBI-DS* that was greater than 50, suggesting some significant brain dysfunction in this subsample of CT− patients. Bazarian et al. [24] reported that after concussion the presence of a normal CT scan does not rule out the presence of a functional brain injury due to axonal injury. In fact, Slobounov et al. [25] report that derived EEG indices may reveal signs of brain injury in concussed individuals that are often missed by other assessment tools and that these indices may play a role in assessing and monitoring residual brain dysfunction in MHI patients that appear otherwise asymptomatic. This sub-set of CT− patients probably warrants further treatment and counselling about the importance and relevance of post-concussion signs and symptoms. The fact that the mean *TBI-DS* in this sample of CT− patients was approximately half way between that found for CT scan positive and controls may indicate that this index is sensitive not only to the presence or absence of brain dysfunction, but also may index the degree of brain dysfunction as well. This is supported by the work of Thatcher et al. [3] who used an EEG-based discriminant function to classify patients with mild, moderate and severe head trauma. Mild head trauma could be distinguished from severe head trauma with a sensitivity of 95.5% and a specificity of 97.4%. Further, those with moderate head trauma had discriminant scores that were intermediate between those with mild and severe head trauma.

As noted in the Results section, the CT+ patients were older than those in the other groups, most probably reflecting the increased risk of injuries resulting in head trauma in this age group. The resilience of the method to age effects, due to age regression (comparing the patient to age expected normal values), further emphasizes the clinical utility of the method.

The authors are aware of the need for prospective independent replications of this work in larger populations and are currently involved in such a study. If replicated, it can be suggested that the *TBI-DS* can play an important role in the ED setting in determining which patients presenting with altered mental status have a need for further imaging evaluation. The BrainScope device in development used in this study is a potential tool for the reintroduction of the EEG into the ED, especially given the ease of use, speed and automation of the acquisition and analysis of data. Such a tool could be an important addition to the routine techniques employed within the emergency room environment.

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