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Using a brain electrical activity biomarker could aid in the objective identification of mild Traumatic Brain Injury patients

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The overall number of Emergency Departments (ED) visits from 2006 to 2010 reportedly increased by 3.6%, during which time visits for Traumatic Brain Injury (TBI) increased by 29.1% [1]. This sharp increase reflects heightened awareness about TBI, which is expected to drive this number even higher in the future [1]. Further, 95% of all head-injured patients who visit the ED present with mild symptoms [2].

Currently, Computerized Tomography (CT) is the accepted gold standard for identifying acute intracranial injuries in the ED. Although the vast majority of head injured patients receive a CT scan, over 90% are found to be CT negative [3,4]. Standard clinical practice in the ED does not include assessment of functional brain injury or concussion in patients found to be CT−. Early identification of mild TBI/concussion is associated with lower risk of re-injury, reduced morbidity and improved outcomes [5]. The identification of mTBI/concussed patients and their ED discharge referrals could be greatly aided by accurate, objective, quantitative information about brain function status [6].

In a multi-site prospective clinical validation trial, the Brain Function Index (BFI), an EEG-only, objective assessment of the brain function abnormalities resulting from mTBI/concussion, was shown to scale with severity of functional impairment [7,8]. The BFI was derived from EEG features reflective of the current consensus of concussive physiology, (e.g., disruption in "connectivity" related to integrity of fiber tracts), and is scaled as a percentile of a non-head-injured population.

This trial was conducted in 11 US EDs and included 720 patients with GCS 12–15, evaluated within 72 h of sustaining a head injury, with informed consent obtained in all cases [7]. 5–10 min of EEG data was acquired from frontal and frontotemporal locations using the handheld BrainScope One device. The present retrospective analysis focuses on the cohort of this population in the 18–40 age range who were found to be CT−, which is of major relevance to both sports-related concussions and military-related head injuries. There were 296 subjects in this subgroup (54.7% males), with a mean age of 26.6 (sd = 6.1), mean GCS = 14.98 (98% with GCS = 15). The significance of the difference in BFI as a function of presence or absence of functional brain impairment was explored.

In the absence of a gold standard for mTBI/concussion, the presence, number, and severity of acute signs and symptoms as self-reported or observed by an evaluating physician, were used to establish presence (mild or moderate) or absence ("asymptomatic" controls) and severity of clinical functional brain impairment using a rule-based algorithm. These features included: loss of consciousness (LOC), retrograde or Post-Traumatic Amnesia, disorientation, headache, and alteration of mental status (AMS).

Significant differences in BFI percentiles were found comparing asymptomatic controls and mTBI/concussed subjects ($p = 0.045$). The median BFI of the mTBI group (mild combined with moderate) was 8 points lower than that of the asymptomatic controls, corresponding to a relative drop of 23%. Cohen's $d = 0.27$ is considered to be in the "small-to-medium" range. Significant differences in BFI between the controls and the moderate TBI group were also found ($p = 0.012$). The median BFI of the moderate mTBI group was 12 points lower than that of the asymptomatic controls (34% relative drop), with a Cohen's $d = 0.384$, in the upper half of what is considered to be in the "small-to-medium" range. No significant differences were found in the BFI between mild and moderate mTBI groups, nor in the BFI between asymptomatic controls and mild mTBI.

Presence of symptoms that are frequently associated with mTBI/concussion was compared in patients with BFI percentile scores above 50 ($N = 65$) and below 50 ($N = 138$) in the subgroup of subjects that are not classified as likely CT+. Table 1 shows the number of occurrences of such symptoms, including: Loss of Consciousness, severe headache (>3 on a Likert 0–7 scale), Altered Mental Status and Post-Traumatic Amnesia. For each of these symptoms, the relative presence was significantly higher in the "BFI ≤ 50" than in the "BFI > 50" group, which supports that the EEG-based BFI percentile is an index which is strongly associated with typical subjective symptoms of concussion, but has the significant advantages of being a single number/score which is objective and directly reflects perturbations of brain electrical activity associated with functional brain impairment and can be easily integrated into the ED patient care path.

These analyses demonstrate that important information about brain function in CT negative head injured patients can be obtained using a brain electrical activity biomarker derived from EEG signals acquired rapidly on a hand-held, easy to use at the point-of-care, device. Integrated into the assessment process, this biomarker can potentially aid in early, objective identification of mTBI/concussed patients in the busy ED environment, thereby informing discharge referrals and potentially contributing to the reduction of short and long-term consequences associated with delayed identification and intervention.

Disclosure

Dr. Michelson is on the Medical Advisory Board of BrainScope. Dr. Jacquin is an employee of BrainScope. All other authors have nothing to disclose.

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Table 1
Number and percentage of occurrences of typical mTBI/concussion (Loss of consciousness (LOC), severe headache (Likert scale >3), Altered Mental Status, Post-Traumatic Amnesia) in the subjects with "BFI > 50" and "BFI ≤ 50," for subjects not likely CT+.

Number (percent) with symptom	Age 18–40	
	BFI > 50	BFI ≤ 50
Loss of consciousness	7 (23.3%)	23 (76.7%)
Severe headache	27 (38%)	44 (62%)
Altered Mental Status	4 (28.6%)	10 (71.4%)
Post-Traumatic Amnesia	2 (18.2%)	9 (81.8%)

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