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Measuring brain electrical activity to track recovery from sport-related concussion

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Abstract

Primary objective: To follow recovery from concussion in a sample of athletes using an electroencephalographic (EEG) index of quantitative brain activity developed previously on an independent Emergency Department (ED) sample of head-injured subjects with traumatic brain injury.

Methods and procedures: EEG recordings from five frontal electrode sites were obtained on 59 injured athletes and 31 controls at the time of injury and at 8 and 45 days afterward. All subjects also completed standardized clinical assessment of post-concussion symptoms, postural stability and cognitive functioning at injury and 8 and 45 days post-injury.

Results: Abnormalities in clinical assessment measures were observed in injured subjects only at time of injury. Statistical analysis of brain electrical activity measures with the ED-based algorithm revealed significant differences between injured athletes vs controls at the time of injury and at day 8. Measures from the two groups did not differ on day 45.

Conclusions: This study demonstrated that an algorithm of brain electrical activity developed on an independent sample of ED subjects with head injury is sensitive to the effects of sport-related concussion. Using this algorithm, abnormal features of brain electrical activity were detected in athletes with concussion at the time of injury and persisted beyond the point of recovery on clinical measures.

Keywords: *Electroencephalography, traumatic brain injury, concussion, athletes*

Introduction

Determining clinically sound approaches to assessment and treatment of concussion in athletes has been a primary focus of sport medicine clinicians and researchers over the past two decades. Findings from recent studies using standardized clinical assessment measures have advanced knowledge on the *clinical* recovery of sports concussion [1]. Several prospective studies have consistently demonstrated that the vast majority of athletes achieve a complete recovery of symptoms, cognitive dysfunction and other impairments within a period of 7–10 days following injury [2–4]. These findings are consistent with results obtained from animal studies demonstrating that concussion is the result of a temporary and reversible alteration in brain functioning [5]. It remains unclear, however, whether the time course in animal brain injury models is equivalent to the course of physiological recovery in humans affected by concussion. Clinically, recent research on the natural course of recovery from concussion has influenced management of sport-related head

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injuries and return to play protocols at all levels of competition [6].

Findings obtained from a number of sources have now demonstrated alterations in brain functions extending beyond the point at which full clinical recovery has been observed. Results from recent studies utilizing advanced neuroimaging techniques suggest that abnormalities in brain functioning can be detected beyond the point at which individuals achieve a complete recovery in symptoms and cognitive functioning [7–9]. Other studies, using magnetic resonance spectroscopy (MRS), have demonstrated abnormalities in cerebral energy metabolism extending beyond the typical period of recovery [10]. Studies using quantitative electroencephalography (QEEG) have also demonstrated a number of functional brain abnormalities in subjects following concussion [11–15].

Normal controls have been discriminated from individuals with mild traumatic brain injury (MTBI) with QEEG methods in previous studies with a reported 96.2% sensitivity and 90.5% specificity [13]. Alterations in brain function of individuals with MTBI were reported using wavelet features of the EEG, which increased when second concussive events occurred [14]. QEEG features have also been used in multivariate classifier functions to discriminate between individuals with MTBI from those with more severe levels of traumatic brain injury (TBI), with a reported 95% sensitivity and specificity of 97% [12]. MTBI resulted in a decreased alpha/theta ratio with the degree of this ratio 0–10 days post-injury correlated with recovery of function at 1-year post-injury [15].

Recent studies have examined the feasibility of use and validity of a hand-held QEEG device (Instrument in development, Brainscope Company, Inc., Bethesda, MD, www.brainscope.com) in both Emergency Department (ED) and sports samples [17, 18]. Findings from the ED setting have demonstrated the utility of using a QEEG-based discriminant function for identifying brain dysfunction in patients presenting with altered mental status following MTBI and the use of such measures for distinguishing between controls, head injured ED patients who are CT positive and those who are CT negative [19]. Findings from the sports setting indicate that this instrument can also be used effectively to record QEEG data from athlete samples, providing further evidence of electrophysiological changes following concussion extending beyond the typical window of clinical recovery [18].

Determining the course of physiological recovery and whether there exists an extended window of brain vulnerability after concussion has significant implications for the clinical management of sports concussion and for advancing knowledge of TBI in general. The purpose of this investigation is to extend previously reported findings in a larger sample and to explore the utility of an index based on changes in brain electrical activity to identify longitudinal changes in brain functioning in a sample of athletes at the time of concussion and up to 45 days afterward.

Methods

Subjects

Male football players from eight high schools and two colleges in the greater Milwaukee, Wisconsin area were enrolled in the study prior to the 2008 and 2009 football seasons. Over the two seasons, 823 player seasons were under investigation. A total of 59 players sustaining a concussion (7.17% of player seasons) were studied at the time of injury and at various time points post-injury. A comparative sample of 31 non-injured athletes matched to injured group on the basis of age, years of education, cumulative grade point average and baseline performance on concussion assessment measures were selected as a control group. This sample of control subjects were 'yoked' to individual athletes based on the best fit to the aforementioned matching variables. This was performed manually by investigators searching the electronic database for the closest control match for each injured athlete based on the combined matching variable set. The research team has refined this approach while conducting studies of sport-related concussion over the past 15 years. The control subjects were administered a protocol that was identical to the injury group at the time of injury and at the time of the same follow-up periods. Control subjects were excluded if there was any reported history of concussion, learning disability, attention deficit hyperactivity disorder, other developmental disorder or current use of psychotropic medications. There were no differences between the injured and control groups in terms of height, weight, years of education, estimated intelligence and grade point average.

This study was approved by the Institutional Review Board for protection of human research subjects at the host institutions of the principal investigators. Written informed consent was obtained from all injured and control participants (or parent/guardian of minors) and each subject voluntarily elected to participate in the study.

Design and procedures

Injured subjects were identified for this study by professional staff members (e.g. certified athletic trainers) located on the sideline during an athletic

Table I. Study protocol and clinical outcome measures.

Acute injury	Day 8* post-injury	Day 45* post-injury
CSI	CSI	CSI
SAC	SAC	SAC
BESS	BESS	BESS
BrainScope	BrainScope	BrainScope
ANAM	ANAM	ANAM

CSI, Concussion Symptom Inventory; SAC, Standardized Assessment of Concussion; BESS, Balance Error Scoring System; ANAM, Automated Neuropsychological Assessment Metrics.
*Study protocol allowed for ±1 day for Day 8 assessment point and ±5 days for Day 45 assessment point.

contest or practice. For inclusion as an injured subject in this study, *concussion* was defined as an injury resulting from a blow to the head causing an alteration in mental status and one or more of the following symptoms prescribed by the American Academy of Neurology (AAN) Guideline for Management of Sports Concussion: headache, nausea, vomiting, dizziness/balance problems, fatigue, trouble sleeping, drowsiness, sensitivity to light or noise, blurred vision, difficulty remembering or difficulty concentrating [20, 21]. Loss of consciousness (LOC), post-traumatic amnesia (PTA) (e.g. inability to recall exiting the field, aspects of the examination, etc.) and retrograde amnesia (RGA) (e.g. inability to recall aspects of the play or events prior to injury, score of the game, etc.) and other acute injury characteristics were also documented immediately after each injury.

All injured players completed a brief battery of sideline tests assessing symptom reporting, cognitive functioning and postural stability. The sideline tests were administered at the time of injury and at 8 and 45 days post-injury. The 8-day post-injury time point was chosen on the basis of previous research demonstrating that this is the period when 95% of injured athletes demonstrate recovery on clinical measures [2]. This time period also serves as a natural time point for studies on football players that typically compete in games on a weekly schedule. The 45-day time point was chosen as a period of long-term follow-up. Team personnel contacted the local investigators (MM, MRP) and briefed them on details of injury characteristics and the early course of recovery. The local investigators then arranged for the follow-up protocol of the player with concussion and their respective control subject. Additional testing, performed on the day of injury, as well as on post-injury days 8 and 45, included a computerized neuropsychological testing battery and electrophysiological testing. Day 8 post-injury was used since most studies report that signs and symptoms of concussion resolve within 7–10 days post-injury. The protocol matrix and listing of clinical outcome measures administered at each assessment point is presented in Table I. Examiners were not blinded to the player's group assignment (injured vs control) at the time of evaluation as these data were collected in the context of direct clinical care delivery. All examiners were trained to perform these evaluations and quality control guidelines were followed rigidly.

Clinical outcome measures

All of the main outcome measures used in this study have been used extensively in head injury research and studies on the effects of sport-related concussion, including the:

- *Concussion Symptom Inventory (CSI)* [22]. The CSI is a brief screening measure assessing the presence and severity of 12 common post-concussion symptoms. A Likert-type scale is used to assess symptom severity (range 0–6 per item). Total score range is 0–72 for the full CSI; higher scores on the CSI indicate more severe symptoms reported. Previous research has shown that symptom inventories detect abnormalities in nearly 90% of injured athletes at the time of injury while less than 5% demonstrate abnormalities by 7 days, as used in this study [23].
- *Standardized Assessment of Concussion (SAC)* [2, 24]. The SAC is a brief cognitive screening tool that has been used extensively to assess the cognitive effects of concussion. It includes brief sub-tests of orientation, immediate memory, concentration and delayed recall. Total score range on the SAC is 0–30; lower scores on the SAC indicate poorer cognitive performance. Sensitivity rates for this instrument are 80% at the time of injury and 2% at 7-days [23].
- *Balance Error Scoring System (BESS*) [2, 25, 26]. The BESS is a brief clinical measure of postural stability. It assesses balance during six separate trials, including three stances (single-leg, double-leg and tandem) on two surfaces (firm and foam). Standardized errors are summed for each trial. Score range for each BESS trial is 0–10 (0–60 for total BESS score); higher scores on the BESS indicate poorer performance. Over 30% of injured athletes exhibit abnormalities on the BESS at the time of injury while less than 10% exhibit abnormalities at the 7-days [23].
- *Automated Neuropsychological Assessment Metrics (ANAM)* [27–30]. ANAM is a computerized neuropsychological test battery that includes measures of cognitive processing speed, reaction time and visual memory. Measures of accuracy and speed are recorded, which combine to form a composite throughput score. For each sub-test, a lower throughput score indicates

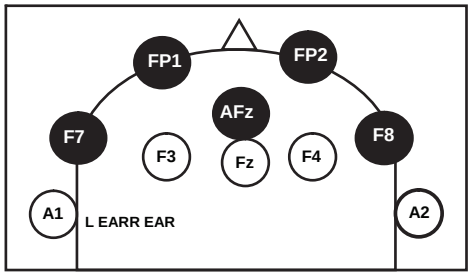

Figure 1 Schematic diagram of regions on the frontal scalp where electrodes are placed for EEG recording (black circles). This schematic is viewed as if looking down at the top of the head, with right side on right and nose up; odd numbers indicating left hemisphere and even numbers indicating right. These locations include the two lateral frontal electrodes, F7 and F8, two frontopolar electrode sites, FP1 and FP2, and AFz, a location slightly anterior to the conventional location of the frontal midline electrode (Fz). All sites are according to the expanded International 10/20 placement system.

poorer performance. These variables have been shown to be sensitive to the effects of concussion at the time of injury.

Electrophysiological testing

Both injured subjects and healthy controls underwent 10 minutes of eyes closed resting electroencephalographic (EEG) recording acquired on the BrainScope clinical research prototype device (www.brainscope.com). Data were sampled at 8 kHz, 24 bits, decimated to 1 kHz and then to 100 Hz for analysis. The EEG recordings were made from frontal electrode sites of the International 10/20 system using self-adhesive electrodes pasted on the forehead and referenced to linked ears. The frontal electrode sites included FP1, FP2, AFz (located just anterior to Fz on the forehead, below the hairline), F7 and F8. Figure 1 is a schematic of the locations of these electrode sites on the forehead. All electrode impedances were below 10 kΩ. Amplifiers had a bandpass from 0.5–70 Hz (3 dB points). Electrode placement in all cases was completed in less than 5 minutes. The EEG data were subjected to artifact rejection by an artifact algorithm built into the Brainscope device (part of previous FDA cleared BrainScope ZOOM 100-DC), to remove any biologic and non-biologic contamination, such as that from eye movement or muscle movement and artifact-free data further subjected to visual inspection by a trained EEG technologist to confirm data quality. The EEG technicians were blinded to whether or not the individual was a member of the injured or control group. Previous experience has demonstrated that sufficient artifact-free data (60–120 seconds) can be obtained from this 10-minute recording.

Quantitative analysis of brain electrical activity. In all cases, the first 1–2 minutes of artifact-free EEG data were used. These data were then submitted for quantitative analyses off-line, using power spectral analysis and Fast Fourier Transform (FFT). For all monopolar and bipolar electrode derivations, absolute and relative (%) power, mean frequency, inter- and intra-hemispheric coherence and symmetry were 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 and for the total spectrum. In addition, non-linear features of 'complexity' of the electrical signal (reflected in fractal measures) and measures of 'connectivity' (relationships between regions, as reflected in mutual information and entropy), were also extracted [31].

Using standard neurometric methods, all quantitative features were log transformed to obtain Gaussianity, age-regressed and *Z*-transformed relative to age expected normal values. Details of this methodology are described elsewhere [32, 33].

This study applies an independently developed QEEG discriminant function, which was derived to maximally separate a normal control population ($n = 255$) from patients who had suffered a TBI/concussion (TBI; $n = 358$) in an ED population with high sensitivity and specificity [17]. This binary discriminant classification algorithm was constructed using iterative methods and cross-validation (leave-one-out and 10-fold [34]) based on features extracted from all patients in the algorithm development database. The algorithm consists of a weighted combination of selected linear and non-linear features of brain electrical activity, which mathematically describe the profile of TBI as distinguished from normal brain activity. The result is expressed as a discriminant score (MTBI-DS) or index (ranging from 0–100). Features that contributed most to the discriminant applied in this study included: relative power increase in slow waves (delta and theta frequency bands) 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, decrease in mean frequency of the total spectrum composited across frontal regions and abnormalities in other measures of connectivity (including mutual information and entropy).

A discriminant TBI-index was obtained by the application of the independently optimized function to each subject in the study and relates to the probability that the patient belongs to the group of patients with disturbances to brain function. It is important to point out that patient age was taken into account prior to calculation of the TBI-Index

Table II. Concussion group and control group results on CSI, SAC and BESS.

	CSI*				SAC				BESS			
	Injured		Control		Injured		Control		Injured		Control	
	M	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD
TOI	20.14	13.56	2.13	3.36	25.56	3.31	27.90	1.60	17.61	11.02	17.65	6.58
Day 8	2.20	6.10	2.63	3.40	27.91	1.91	27.97	1.54	12.21	6.48	16.97	7.57
Day 45	1.18	2.83	3.78	10.64	27.94	2.14	28.11	1.93	11.29	5.60	15.33	6.83

TOI, Time of Injury.
*t-test, $p < 0.05$.

since all EEG features were age-regressed prior to inclusion in discriminant analyses [35].

Statistical analysis

Independent sample *T*-tests were calculated to compare the injured and control groups on the main clinical outcome measures of symptoms (CSI), postural stability (BESS) and cognitive functioning (SAC, ANAM) at each post-injury assessment point. Raw scores were used for the CSI, BESS and SAC for statistical comparison between groups, as is the intended use for each measure.

In the case of ANAM, a throughput score was calculated for each ANAM sub-test and submitted for statistical comparison between groups at each assessment point. The throughput score is derived from the number of correct responses observed on a particular task divided by the cumulative reaction time for both correct and incorrect responses. Throughput scores have been reported as a robust performance measure in previous studies utilizing ANAM, including studies on the cognitive effects of sport-related concussion [29].

The electrophysiological results were evaluated using the MTBI-DS index as the dependent variable. Independent *t*-tests, corrected for unequal *n*'s, were used to compare the control and concussed groups at the time of injury and at days 8 and 45. One-way repeated measures ANOVAs with three levels were computed separately for the control and concussed groups to examine changes between the data collected at the time of injury (initial evaluation for the control group) and at days 8 and 45 after the initial evaluation.

Results

Clinical recovery

Data presented in Table II indicate that injured subjects reported more severe post-concussion symptoms than controls on the CSI at the time of injury. There were no statistically significant differences in symptom reporting at post-injury days 8 or 45. No significant differences were observed between injured and control subjects on the BESS at the time of injury. Control subjects exhibited an unexpected higher number of errors on the BESS at days 8 and 45. The injured group obtained significantly lower scores on the SAC on day of injury, but not beyond that assessment point (see Table II). Lower mean scores were also observed on five of the six ANAM variables at the time of injury (see Table III), but not at any of the subsequent time points.

Electrophysiological recovery

Figure 2 shows the MTBI-DS for the concussed and control groups at time of injury, day 8 and day 45. The *y*-axis on this graph is based on the continuous score obtained and should be interpreted in relation to the cut-off value of 65, the point above which represented the 95% confidence level in prior work [19].

T-tests, corrected for unequal *n*'s, were calculated comparing the control and concussed groups at the time of injury and at days 8 and 45. The MTBI-DS was greater in the concussed group than the control group on the day of injury ($t = 3.75$, $p = 0.0004$) and on day 8 ($t = 2.76$, $p = 0.008$). The two groups did not differ on day 45 ($t = 1.49$, $p = 0.15$).

To examine the course of recovery, a one-way repeated measure ANOVA with three levels was computed comparing the injured group at injury and on day 8 and day 45 after injury. This *F*-ratio was significant ($F = 3.2$; $p = 0.046$). Duncan multiple comparisons showed that the MTBI-DS values at the time of injury and at day 8 were statistically equivalent, whereas the MTBI-DS at injury was significantly greater than 45 days post-injury. A similar ANOVA comparing the control group's initial TBI-DS with those obtained at day 8 and day 45 was not significant ($F = 0.5$; $p = 0.67$),

Table III. ANAM test tesults for concussion group and control group at time of injury and at day 8 and 45 post-injury.

	Time of injury				Day 8				Day 45			
	Injured		Control		Injured		Control		Injured		Control	
	M	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD
ANAM CDD	46.50	17.54	52.11	11.12	51.93	13.08	52.89	12.65	51.04	12.99	48.42	11.96
ANAM CDS	51.41	14.97*	57.71	8.61	57.98	12.20	60.75	9.84	58.50	11.27	58.77	10.23
ANAM M2S	33.20	14.62*	39.16	8.22	37.17	12.27	40.82	12.12	36.42	13.55	40.11	11.54
ANAM MTH	19.98	6.24*	24.04	5.13	20.81	6.78	23.60	8.22	22.89	7.17	25.30	6.40
ANAM SRT	161.3	40.40*	192.1	16.35	188.24	22.74	195.61	19.15	192.9	22.82	193.5	19.59
ANAM SR2	158.1	44.10*	186.9	26.28	184.80	24.47	189.30	31.79	184.9	23.46	188.4	22.11

*Significant difference, $p < .05$.
ANAM abbreviations for specific tasks: CDS, Coding Substitution Learning; CDD, Coding Substitution Delayed; SRT, Simple Reaction Time; SR2, Simple Reaction Time (second administration); MTH, Mathematical Processing; M2S, Matching to Sample. All ANAM data reported is based on throughput scores.

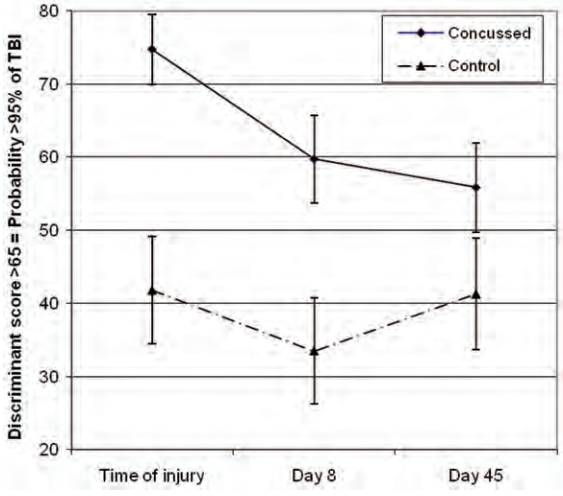

Figure 2 Group average discriminant score for concussed population (solid line, diamonds) and controls (dashed line, triangles) for time of injury, day 8 and day 45. It is noted that discriminant scores >65 have a >95% probability of MTBI. Standard error bars are shown for each data point.

indicating no group changes over time in this sample.

Discussion

This study extends results recently published [18] in a small sample of concussed athletes who showed abnormal features of brain electrical activity at injury and persisting beyond the point of observed clinical symptomatic recovery. This larger sample of athletes extends the prior descriptive results to the application of an algorithm developed on an independent sample of MTBI subjects in an ED setting [17] to test its sensitivity to the effects of sport-related concussion. The probability of brain dysfunction as determined using this algorithm reflected significant abnormalities at the time of injury and evidence of persistence for at least 8 days after sport-related concussion. These abnormalities in brain electrical activity were present beyond the point at which athletes had achieved a full recovery on clinical measures of post-concussion symptoms, cognitive functioning and postural stability and beyond the point at which there were no differences from controls on a computerized neuropsychological test battery.

The findings of lengthier recovery time after sport-related concussion are consistent with results from recent studies that have applied advanced technologies to investigate the time course of *physiological* recovery following concussion. While earlier prospective studies using conventional clinical measures have consistently demonstrated that the overwhelming majority of athletes achieve a complete clinical recovery in symptoms, cognitive dysfunction and other functional impairments within the first week after injury, more recent findings using advanced imaging techniques suggest that the duration of physiological recovery after concussion may extend longer than the observed period of clinical recovery [7–10].

While the difference between the control and concussed group on the MTBI-DS index of brain dysfunction group at 45 days post-injury did not reach statistical significance ($p = .15$) the mean score of the concussed group was 58 and for the control group it was 41. This may indicate that at least some of the concussed subjects may continue to exhibit an alteration of brain functioning at that time point several weeks post-injury. It is possible that these individuals would be more likely to report post-concussive-like symptoms and/or show an increased susceptibility to a subsequent concussion for a more extended period beyond the typical 7–10 day recovery period commonly reported in studies of

sport-related concussion [1]. Future studies in a larger population will allow more systematic study of the heterogeneity of brain function at Day 45 and at time-points of up to 90 days after injury.

The current brain imaging literature supports the hypothesis that concussive head injury results in changes in 'connectivity' between brain regions and reversible axonal and neuronal dysfunction [36]. The MTBI-DS used in the present study utilizes 'phase synchrony' between brain regions as one of the variables incorporated within this EEG based algorithm of brain dysfunction. EEG measures such as phase synchrony have been demonstrated to be highly correlated with findings of disrupted functional connectivity between brain regions as measured by diffusion weighted imaging (DTI) after concussion. Interestingly, the most significant contributors to these DTI results were found in one such study by examining images from cross-lateral-frontal regions [37]. This suggests that the MTBI-DS, which is based upon frontal and frontal-lateral recordings, may be uniquely sensitive to concussive type injury and may reflect such 'connectivity' changes in brain function. These findings may open the way to more sensitive evaluation of concussive injury than those previously available.

The findings from this study and those from earlier studies applying advanced electrophysiological techniques indicate that abnormalities in brain function can be detected beyond the point at which individuals achieve a complete clinical recovery in symptoms and cognitive functioning after sport related concussion. Further, the ease of use of such an algorithm based on a short sample of brain electrical activity from a limited montage on the forehead has significant implications for clinical management of concussion in athletes. Further research at increased intervals of follow-up is necessary to investigate whether sport-related concussion is associated with longer-term alterations in brain electrical activity and to determine the true natural history and time course of physiological recovery after concussion. To that end, ongoing research now incorporates in intermediate assessment point at 15 days post-injury.

These findings add to an evidence-based approach to clinical management of athletes affected by sport-related concussion by further informing understanding of the window of cerebral vulnerability following concussion, during which athletes may still be in the process of physiological recovery and susceptible to the ill-effects of recurrent head injury. The current findings support the concept of a graduated approach to resuming sporting activity after concussion, in which the athlete is closely monitored for a period of time after achieving full clinical recovery before full return to play. This approach is aimed at providing greater assurance that recovery is achieved both clinically and physiologically (i.e. at a *brain* level) before athletes resume full participation following sport-related concussion.

The current study has several strengths and limitations. Its major strength is that it utilizes and EEG-based algorithm of brain dysfunction (MTBI-DS) that was independently developed and tested using a population of mild head injury patients referred to and tested within a hospital emergency department environment (ED). It is important to note that reliable EEG data were obtained using current hand held EEG recording equipment in the ED environment and in the trainer's room after concussion in the current study. A weakness of the present study is that, despite 3 years of data collection, we have data on only 59 concussed individuals. While the size of this sample is large enough to make reliable comparisons within concussed individuals over time and between concussed and controls at separate time points, sample size is not large enough to test the reliability of findings across time in the individual concussed athlete, especially at longer time intervals. Future studies should increase the size of the concussed group, track MTBI-DS changes between 8 and 45 days and extend findings up to 6 months post-injury. It would also be of importance to identify a group of individuals who show persistent post-concussion symptoms and to follow the time course of TBI-DS change and its relationship to concussive symptomology.

In summary, the current study adds to a growing literature suggesting that the time course of physiological recovery after sport-related concussion extends beyond the point at which athletes demonstrate a full clinical recovery in symptoms, cognitive functioning and other functional domains. This extended period of cerebral dysfunction detected by advanced technologies such as QEEG or functional neuroimaging has significant implications to clinical management of athletes affected by sport-related concussion. These findings support approaches that call for a period of extended observation of the athlete beyond the point of clinical recovery, during which the athlete is not exposed to potential repetitive injury while still potentially in a vulnerable state during physiological recovery. Further research is necessary to investigate the influence of specific injury management strategies on recovery and prevention.

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***Declaration of Interest*:** Dr Barr, Dr Prichep and Dr Chabot serve as consultants to BrainScope, Inc. and Dr Prichep holds financial interest in BrainScope, Inc. through patented technology. None of the other authors have any conflict of interest to declare with respect to this study or manuscript. The authors have no other personal financial or institutional interest in any of the drugs, materials or devices described in the article. Aside from the author-investigators, representatives from BrainScope, Inc. did not play a role in the design or execution of the study beyond funding and had no involvement in the preparation of this manuscript.

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