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Acute Effects and Recovery After Sport-Related Concussion: A Neurocognitive and Quantitative Brain Electrical Activity Study

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Objective: To investigate the clinical utility and sensitivity of a portable, automatic, frontal quantitative electroencephalographic (QEEG) acquisition device currently in development in detecting abnormal brain electrical activity after sport-related concussion. **Design:** This was a prospective, non-randomized study of 396 high school and college football players, including cohorts of 28 athletes with concussion and 28 matched controls. All subjects underwent preseason baseline testing on measures of postconcussive symptoms, postural stability, and cognitive functioning, as well as QEEG. Clinical testing and QEEG were repeated on day of injury and days 8 and 45 postinjury for the concussion and control groups. **Main Outcomes and Results:** The injured group reported more significant postconcussive symptoms during the first 3 days postinjury, which resolved by days 5 and 8. Injured subjects also performed poorer than controls on neurocognitive testing on the day of injury, but no differences were evident on day 8 or day 45. QEEG studies revealed significant abnormalities in electrical brain activity in the injured group on day of injury and day 8 postinjury, but not on day 45. **Conclusions:** Results from the current study on clinical recovery after sport-related concussion are consistent with early reports indicating a typical course of full recovery in symptoms and cognitive dysfunction within the first week of injury. QEEG results, however, suggest that the duration of physiological recovery after concussion may extend longer than observed clinical recovery. Further study is required to replicate and extend these findings in a larger clinical sample, and further demonstrate the utility of QEEG as a marker of recovery after sport-related concussion. **Keywords:** *brain injury*, *concussion*, *electroencephalography*, *neuropsychological tests*

SPORT-RELATED CONCUSSION is now widely recognized as a significant public health issue in the United States and worldwide.[1,2] The Centers for Disease Control and Prevention estimate the annual incidence of nonfatal traumatic brain injuries from sports and recreation activities to be in the order of 2 million per year in the United States, with the overwhelming majority of injuries classified as mild traumatic brain injury (mTBI) (ie, concussion).[3] Within organized athletics, epidemiologic studies reveal that concussion is among the most frequently observed injuries in most contact or collision sports (eg, football, hockey, wrestling).[4,5] Furthermore, additional studies suggest that the true incidence of sport-related concussion may actually be much higher than that captured in conventional epidemiologic studies, in large part from a tendency on the part

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of athletes to either not recognize or not report these injuries.[6]

Clinically, sports medicine professionals now commonly consider the diagnosis and clinical management of concussion as among their greatest challenges. Beyond injury detection and diagnosis, the chief responsibility of clinicians is to accurately monitor the course and extent of an athlete's clinical recovery after concussion, and, in turn, determine the athlete's readiness for safe return to competition. The advent of neuropsychological testing and other standardized assessment tools over the past decade now enables clinicians to more precisely measure the acute effects and extent of recovery after concussion, thereby affording a more objective means for determining that an athlete has had a full resolution of postconcussive symptoms and cognitive or other functional impairments after injury.

Recent studies have also made great gains in advancing our understanding of the true natural history of *clinical* recovery after mTBI, including sport-related concussion.[7] Prospective studies have consistently demonstrated that the overwhelming majority of athletes achieve a complete recovery in symptoms, cognitive dysfunction, and other impairments over a period of approximately 7 to 10 days after injury.[8–10] Contrary to earlier reports in the general MTBI literature,[11] the incidence of persistent symptoms or impairments beyond several weeks after concussion appears to be very low.[12] Our advancement in the scientific understanding of the true natural history of recovery after concussion provides an evidence base for clinicians in determining recovery and making clinical decisions at the individual case level.

Our understanding of the natural history and time course of *physiological* recovery after concussion, however, remains less clear. The dilemma still facing clinicians and researchers alike is knowing when recovery has been fully achieved at a *brain functional* level. It has long been held that there is a window of cerebral vulnerability that may extend beyond the point at which full clinical recovery has been observed. Findings from recent studies that have used advanced functional neuroimaging techniques suggest that physiological abnormalities can be detected beyond the point at which individuals achieve a complete recovery in symptoms and cognitive functioning.[13,14] In fact, most published guidelines for the management of sport-related concussion recommend a symptom-free waiting period that disallows an athlete to return to competition for a period of several days after they have reached a full recovery.[15] Therefore, determining the time course of physiological recovery after concussion has significant implications not only to our understanding of the clinical science of MTBI, but also to clinical decision making.

Recent reports have further supported the theory that concussion is associated with metabolic and physiological changes in the brain, which correlate with the report of postconcussive symptoms and performance on neurocognitive testing during the acute postinjury periods. There is also growing evidence to suggest an interaction between the time course of physiological recovery after concussion, persisting postconcussive symptoms, and activity level during the early postinjury recovery period.[16–18]

Quantitative electroencephalogram (QEEG) studies in mTBI or concussion, have reported abnormalities in many features reflecting changes in brain function, including reduced mean frequency of alpha, reduced power in the alpha and beta frequency bands, hypercoherence between frontal regions, and decreased gamma frequency.[19–23] Using these features, normal controls have been discriminated from patients with mTBI in previous studies with a reported 96.2% sensitivity and 90.5% specificity.[21] Alterations in brain function of concussed individuals were reported using wavelet features of the EEG, which increased when second concussive events occurred.[24] QEEG features have also been used in multivariate classifier functions to discriminate between mild and severe TBI, with sensitivity a reported 95% and specificity of 97%.[20] The variables contributing primarily to this discrimination include measures of coherence, phase and amplitude differences. It was noted that frontal and frontotemporal regions contributed more than other regions to such discrimination, suggesting increased vulnerability of these areas. In addition, the disruption of brain function reflected in QEEG measures has also been demonstrated to reflect such abnormalities for long periods postinjury in those patients who report persistence of symptoms[22,25–27] and to correlate with recovery of function at 1 year after injury.[23]

Because conventional 19-lead EEG is not a tool feasible as a sideline device, in this study a limited montage on the frontal scalp locations of the standardized system 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 acceleration affects a freely moving head.[28,29] The frontal regions are 3 times more likely to be affected than other cortical regions.[30] Neuropathologic and neuroimaging studies show that frontal regions are the most vulnerable for focal deficits after closed head injury.[31] The most common postconcussion symptoms were characteristic of frontal and/or temporal lobe dysfunction.[32] Further, children with moderate TBI were most likely to show diffusion tensor imaging abnormality in inferior frontal, superior frontal, and supracallosal regions.[33] This increased susceptibility of the frontal regions to damage after closed head injury most likely results from direct contusions to this region and the

TABLE 1 *Concussion group and control group characteristics and baseline test results*[a,b]

	Injured		Control					
Demographics	**Mean**	**SD**	**Mean**	**SD**	**Mean diff**	***t***	***P***	**95% CI**
Weight, lb	205.92	50.24	202.87	39.73	3.05	0.25	.80	−21.5 to 27.6
Academic year	12.92	1.80	12.55	2.23	0.372	0.673	.504	−0.735 to 1.48
Grade point average (4.0 scale)	2.87	0.93	3.18	0.34	−313	−1.69	.10	−0.685 to 0.058
Baseline test results								
WTAR	105.86							−8.03,5.42
CSI total score	3.95	4.47	2.94	4.09	1.012	0.820	.416	−1.47,3.49
SAC total score	27.40	2.137	27.06	2.568	0.335	0.485	.630	−1.05,1.72
BESS	24.65	7.48	15.53	6.76	−0.883	−0.434	.666	−4.98,3.21
ANAM CDD	47.28	14.60	46.83	12.90	0.48	0.114	.910	−7.65,8.56
ANAM CDS	55.88	12.15	53.50	9.98	2.38	0.736	.466	−4.13,8.88
ANAM M2S	34.61	14.34	35.89	9.10	−1.28	−0.361	.720	−8.42,5.86
ANAM MTH	19.58	7.01	20.03	7.09	−0.454	−2.18	.828	−4.65,3.74
ANAM SRT	182.30	17.04	180.09	20.73	2.20	0.388	.700	−9.2,13.65
ANAM SR2	182.40	26.00	185.60	16.95	−3.20	−0.515	.609	−15.7,9.31

[a]ANAM abbreviations for specific tasks: Automated Neuropsychological Assessment Metrics; CDD, Coding Substitution Delayed; CDS, Coding Substitution Learning; CSI, Concussion Symptom Inventory; MTH, mathematical processing; M2S, matching to sample; SAC, standardized assessment of concussion; SRT, simple reaction time; SR2, simple reaction time (second administration); WTAR, Wechsler test of adult reading. All ANAM data reported are based on throughput scores.

[b]Range of values for normal controls on matching variables: weight (145–325), academic year (10–16), grade point average (2.3–3.7), WTAR (88–120), CSI (0–18), and SAC (23–30).

disruption of the extensive connections between the frontal region and other cortical regions.[34] On the basis of these results and the results from previous EEG studies that stress the contribution of frontal measures, we postulated that although different from that derived from 19-lead data, leads over the frontal regions would allow us to demonstrate high sensitivity to mTBI.

The current study was designed to extend previous work by using innovative quantitative brain electrical activity techniques to gain a better understanding of the early electrophysiological effects and recovery after sport-related concussion, and to measure the window of cerebral vulnerability after concussion, during which athletes may be at greatest risk for additional brain injury.

METHODS

Subjects

A total of 396 football players from 8 high schools and 2 colleges in the midwestern United States were enrolled in the study before the 2008 football season. In total, 527 players from 10 high schools and colleges were eligible to participate; of those, we were able to obtain written informed consent from a parent or guardian for 417 athletes (79.1%). We completed baseline testing on 95% (396) of the 417 athletes who consented to participate. Dropouts were due to players missing the baseline testing sessions at their respective school or quitting the football team before baseline testing. Twenty-eight players who sustained a concussion (7.0% of players enrolled) were studied.

Twenty-eight noninjured controls matched to injured subjects on the basis of age, years of education, cumulative grade point average, and baseline performance on concussion assessment measures were administered the identical protocol at baseline and follow-up. Controls subjects are "yoked" to individual athletes based on the best fit to the aforementioned matching variables. This is done manually by the investigators searching the electronic database for the closest control match for each injured athlete based on the combined matching variable set. Our research team has refined this approach while conducting studies of sport-related concussion of the past 15 years. Table 1 provides compares the injured and controls groups on matching variables and other baseline measures, along with the range of values for the control group on each matching variable. Normal controls were excluded from consideration if there was any reported history of concussion, learning disability, attention-deficit/hyperactivity disorder, other developmental disorder, or current use of psychotropic medications.

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.

TABLE 2 *Study protocol and clinical outcome measures*

Baseline	Acute injury	Day 1 P-I	Day 3 P-I	Day 5 P-I	Day 8[a] P-I	Day 45[a] P-I
History	CSI	CSI	CSI	CSI	CSI	CSI
CSI	SAC	SAC	SAC	SAC	SAC	SAC
SAC	BESS	BESS	BESS	BESS	BESS	BESS
BESS	B-Scope				B-Scope	B-Scope
B-Scope	ANAM				ANAM	ANAM
ANAM						

Abbreviations: ANAM, Automated Neuropsychological Assessment Metrics; B-Scope, BrainScope; BESS, Balance Error Scoring System; CSI, Concussion Symptom Inventory; P-I, post-injury; SAC, Standardized Assessment of Concussion.
[a]Study protocol allowed for +/− 1 day for day 8 assessment point and +/− 5 days for day 45 assessment point.

Design and procedures

All subjects underwent a preseason baseline evaluation on all concussion assessment measures prior to the football season, including EEG studies with the BrainScope device. An extensive health history questionnaire was also administered at baseline to generate a database of demographic information, concussion history, and preexisting developmental, neurological, or other medical conditions.

Injured subjects were identified and enrolled in the study protocol by a certified athletic trainer present on the sideline during an athletic contest or practice. *Concussion* was defined as an injury resulting from a blow to the head causing an alteration in mental status and 1 or more of the following symptoms prescribed by the American Academy of Neurology 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.[15,35] Criteria contributing to the identification of a player with a concussion also included the observed mechanism of injury (eg, acceleration or rotational forces applied to the head), symptoms reported or signs exhibited by the player, and reports by medical staff or other witnesses regarding the condition of the injured player. Loss of consciousness (LOC), posttraumatic amnesia (PTA) (eg, inability to recall exiting the field, aspects of the examination), and retrograde amnesia (RGA) (eg, inability to recall aspects of the play or events before injury, score of the game) were documented immediately after injury.

All players identified by the certified athletic trainer as having sustained a concussion according to the study's injury definition and criteria were tested with the Concussion Symptom Inventory (CSI)[36] and the Standardized Assessment of Concussion (SAC)[37] on the sideline immediately after injury. Certified athletic trainers then paged the principal investigator, who conducted a systematic interview with the athletic trainer regarding injury characteristics (eg, mechanism, alteration in mental status or level of consciousness, amnesia, chief symptoms) and early course. The principal investigator then arranged for the follow-up protocol of the player with concussion and the respective control subject. In addition to the CSI and SAC, follow-up assessments on the day of injury, as well as postinjury days 8 and 45 included a computerized neuropsychological testing battery, postural stability testing, and QEEG. The protocol matrix and listing of clinical outcome measures administered at each assessment point is presented in Table 2. Because research data were collected in the context of direct clinical care delivery, examiners were not blinded as to the player's group assignment (injured vs control) at the time of evaluation.

Clinical outcome measures

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

CSI:[38] a brief screening measure that assesses for the presence and severity of 12 common postconcussive symptoms. A Likert-type scale is used to assess symptom severity (range 0–6 per item). Total score range is 0 to 72 for the full CSI; higher scores on the CSI indicate more severe symptoms reported.

SAC:[8,39] a brief cognitive screening tool that has been used extensively to assess the cognitive effects of concussion. The SAC includes brief subtests of orientation, immediate memory, concentration, and delayed recall. Total score range on the SAC is 0 to 30; lower scores on the SAC indicate poorer cognitive performance.

Balance Error Scoring System (BESS):[40,41] a brief clinical measure of postural stability. The BESS assesses balance during 6 separate trials, including 3 stances (single-leg, double-leg, and tandem) on 2 surfaces (firm and foam). Standardized errors are summed for each trial. Score range for each BESS trial is 0 to 10 (0–60 for total

BESS score); higher scores on the BESS indicate poorer performance.

Automated Neuropsychological Assessment Metrics (ANAM):[42–45] 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 subtest, a lower throughput score indicates poorer performance.

All of these measures have demonstrated reliability and accuracy in the evaluation of sport-related concussion. Clinicians also recorded information on injury mechanism, severity, management, recovery, and return to play.

EEG data acquisition

Patients and controls underwent 10 minutes of eyes closed resting EEG recording on the BrainScope 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 lower than 5 kΩ. Amplifiers had a bandpass from 0.5 to 70 Hz (3 dB points), with a 60-Hz notch filter. Setup was accomplished in all cases in less than 5 minutes. The collected EEG data were subjected to artifact rejection by an artifact algorithm built into the BrainScope device, 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 (60–120 seconds) can be obtained from this 10-minute recording.

Quantitative analysis of brain electrical activity

As stated previously, the continuous electrical activity was subjected to artifact rejection algorithms in the BrainScope devise to remove any biologic or nonbiologic contamination, such as that from eye movement or muscle movement, This EEG was then visually inspected by an experienced EEG technologist to confirm quality of selection. Previous experience has demonstrated that sufficient artifact-free data can be obtained from this 10-minute recording. The EEG technicians processing the EEG were blinded to whether or not the individual had a concussion or was a control. In all cases, the first 1 to 2 minutes of artifact-free EEG were used.

The artifact-free data were then submitted for quantitative analyses offline. Power spectral analysis was performed using fast-Fourier transform. For all monopolar and bipolar electrode derivations, absolute and relative (%) power, mean frequency, inter- and intrahemispheric coherence, and symmetry was 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.

Using neurometric methods, 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,[46] as are test-retest reliability[47] and independent replications of the neurometric normative data of brain electrical activity.[48] Thus, this dataset is unique in its use of log-transformed and age-regressed features derived from the frontal EEG in a multivariate approach to the identification of a profile of abnormality in mTBI.

Statistical analysis

Descriptive statistics were generated on the injured and control group characteristics to ensure precise matching of groups on demographic variable, estimate of premorbid cognitive functioning, and baseline test performance on the main clinical outcome measures.

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 postinjury assessment point. This basic approach was undertaken because of concerns about applying more extensive statistical analysis (eg, standardized regression-based methods, reliable change indices, or receiver operating characteristics) in a relative small study sample. The straightforward approach of comparing group means at each postinjury assessment point is strengthened significantly by the lengths taken in the study design to ensure extremely accurately matching of the injured and controls groups on both demographic and performance measures (ie, yielding no preinjury group differences).

For the CSI, BESS, and SAC, raw scores were used 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 subtest 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. As a performance index, it blends accuracy and response speed into a single measurable unit of behavior. Relative to scores of accuracy and speed in isolation, it is considered more sensitive to behavioral change, and is more reliable over time, particularly when one would expect a decline (or improvement) in both accuracy and speed after an experimental manipulation or event. For

a more detailed discussion of theory and characteristics associated with throughput scores, please see Thorne.[49] Throughput scores have been reported as a robust performance measure in previous studies using ANAM, including studies on the cognitive effects of sport-related concussion.[45]

The statistical methods employed to analyze data from our clinical outcome measures is consistent with those used in prior studies of sport-related concussion, including those conducted by our research group. We elected not to use a Bonferroni correction or other methods that control for multiple comparisons on the basis that we are treating data from the various clinical instruments as independent comparisons within and across assessment time points. Further, a Bonferroni correction could potentially reduce power in detecting arguably very mild effects of concussion on these measures.

All QEEG analyses were accomplished offline using the extracted QEEG features described previously. Seven QEEG features were identified based on their clinical and scientific relevance, their ability to distinguish the control from the concussion patients (analysis of variance *F*' ratios) at the time of injury, and their intercorrelation with each other. Multivariate analysis of variance (MANOVA) techniques were then used to compare the control and concussion patients at each time point and to compare all time points within each group of patients. This was possible because all 7 QEEG features were expressed as standard *z*scores and were minimally correlated with each other. The use of MANOVA procedures obviates the need for corrections in power from running multiple *t* tests or univariate analysis of variance procedures. These QEEG variables included 4 variables reflecting changes in interhemispheric (left vs right) power relationships (asymmetry), 1 variable associated with interhemispheric coherence relationships (independent of power), and 2 variables reflecting changes in high and low beta absolute power.

RESULTS

Acute injury characteristics

Twenty-eight athletes who sustained a concussion during a football practice (50% of injuries) or game (50%) were studied. Two subjects (7.1%) had an observed period of LOC associated with their injury, with a mean duration of less than 1 minute. PTA (17.9% of injuries; median duration 10 minutes) and RGA (28.6% of injuries; median duration 60 minutes) were relatively more common characteristics observed. There was significant overlap in the occurrence of LOC, PTA, or RGA; 3 of the 5 subjects with PTA also had RGA. Overall, 64.2% of subjects had no LOC, PTA, or RGA observed in connection with their injury event. These findings on acute injury characteristics are highly consistent with those previously reported from considerably larger study samples of sport-related concussion.[8,39]

At baseline (preinjury), there were no differences between the injured and control groups on any demographic variables, an estimate of premorbid intellectual functioning (WTAR), or performance on the main clinical outcome measures (Table 2), which was planned and anticipated given the strict methods used to select a matched control group.

Clinical recovery

There were statistically significant differences between the injured and control groups on CSI, SAC, and ANAM at select postinjury assessment time points. No group differences were observed on the BESS. Table 3 indicates that injured subjects as a group reported a significantly more severe level of postconcussive symptoms than controls on the CSI through day 3 postinjury, with a trend of greater symptoms also evident on day 5 postinjury. There were no statistically significant differences in symptom reporting by the injured and control groups on

TABLE 3 *Concussion group and control group results on CSI, SAC, and BESS*

	CSI				SAC				BESS			
	Injured		Control		Injured		Control		Injured		Control	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Time of injury	18.82[a]	15.14	2.13	3.36	25.50[a]	3.32	27.90	1.60	20.04	15.09	17.64	6.58
Day 1	13.33[a]	13.62	2.47	3.15	25.86	3.62	26.63	1.86				
Day 3	6.95[a]	7.93	2.33	3.21	27.30	2.32	27.50	1.75				
Day 5	5.07	7.0	2.94	3.19	27.54	2.04	28.38	1.63				
Day 8	2.58	8.32	2.63	3.40	28.23	1.82	27.97	1.54	14.62	7.11	16.97	7.57
Day 45	0.88	3.78	5.24	10.64	27.92	2.17	28.11	1.93	13.33	5.69	15.33	6.83

Abbreviations: BESS, Balance Error Scoring System; CSI, Concussion Symptom Inventory; SAC, Standardized Assessment of Concussion.

[a]Significant difference, $P < .05$.

TABLE 4 *ANAM test results for concussion group and control group at time of injury and at day 8 and 45 after injury*[a]

	Time of injury				Day 8				Day 45			
	Injured		Control		Injured		Control		Injured		Control	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
ANAM CDD	46.56	17.56	52.11	11.12	52.10	12.29	52.89	12.65	53.59	11.42	48.42	11.96
ANAM CDS	52.67	15.11	57.71	8.61	61.01	12.16	60.75	9.84	59.67	10.90	58.77	10.23
ANAM M2S	35.29	16.16	39.16	8.22	39.43	11.84	40.82	12.12	37.28	13.88	40.11	11.54
ANAM MTH	20.63[b]	6.54	24.04	5.13	22.53	6.16	23.60	8.22	23.71	6.56	25.30	6.40
ANAM SRT	163.80[b]	38.38	192.15	16.35	188.78	26.11	195.61	19.15	192.86	27.42	193.57	19.59
ANAM SR2	157.01[b]	46.34	186.92	26.28	181.27	31.02	189.30	31.79	187.15	24.71	15.33	22.11

[a]ANAM abbreviations for specific tasks: ANAM, Automated Neuropsychological Assessment Metrics; CDD, Coding Substitution Delayed; CDS, Coding Substitution Learning; MTH, mathematical processing; M2S, matching to sample; SAC, standardized assessment of concussion; SRT, simple reaction time; SR2, simple reaction time (second administration); WTAR, Wechsler test of adult reading. All ANAM data reported are based on throughput scores.
[b]Significant difference, $P < .05$.

day 8 or day 45. The injured group, on average, made more errors than the control group on the day of injury, but this difference did not reach statistical significance and there were no group differences on the BESS on days 8 or 45 post injury.

In terms of cognitive recovery, the injured group performed significantly more poorly than matched controls on the SAC on the day of injury, but not beyond that assessment point. Similarly, group differences were evident on select neuropsychological subtests of ANAM on only the day of injury, but not on day 8 or day 45 postinjury. Specifically, the injured group demonstrated impairments on measures of mathematical processing and simple reaction time relative to uninjured controls. Trends toward poorer performance by injured subjects were suggested on other ANAM subtests (Coding Substitution – Leaning and Delayed, Matching to Sample) on day of injury, which did not reach statistical significance. Table 4 provides a summary of throughput scores for the injured and control groups on all ANAM subtests at each assessment point.

Electrophysiological recovery

Concussion was generally associated with increased left/right power asymmetry, decreased left/right hemisphere coherence, and increased power in the beta frequency band. Table 5 presents the MANOVA *F* values and significance levels (*P*) for the MANOVAs comparing baseline with the second evaluation, baseline with the day-8 evaluation (8 days after injury or control), and baseline versus day-45 evaluation (45 days postinjury or control). In general, none of the MANOVA results reached significance for the control group, indicating that QEEG variables were stable over 45 days. However, for the group suffering concussions the QEEGs obtained at injury and 8 days postinjury were significantly different from the baseline evaluation. Significance at day 8 is higher than at point of injury, suggesting that abnormalities in brain function progress after time of injury.

Table 6 presents MANOVA results for comparisons done between the concussion and control groups. Note that the number of subjects in these comparisons is 18, because only 18 of the 27 injured subjects had data for all longitudinal comparisons. The concussion and control groups did not differ at baseline, with significant differences found at the time of injury and 8 days postinjury, with these differences not present at day 45 postinjury.

Figure 1 shows the multivariate composite *Z* score for the features included in the MANOVA for each group at each evaluation point. Significant differences can clearly be seen between the groups at time of injury and at day

TABLE 5 *Within-group comparisons for injured group (n = 18) and controls (n = 18)*[a]

	F (*P*)	
Comparison	Injured group	Control group
BL vs injury	2.5 (.039)[b]	0.52 (.81)
BL vs day 8	3.3 (.013)[b]	0.56 (.78)
BL vs day 45	1.5 (.20)	0.86 (.55)

Abbreviation: BL, base line.
[a]Multivariate *F* values from the multivariate analysis of variance analysis and probability for which *F* values are shown.
[b]Significant difference, $P < .05$.

TABLE 6 *Between-group comparisons for BL, injury/retest, day 8, and day 45*[a]

Between-group comparisons	*F* (*P*)
BL	1.65 (.164)
Injury/retest	4.4 (.002)
Day 8	2.53 (.04)
Day 45	0.60 (.74)

Abbreviation: BL, base line.
[a] Multivariate *F* values from the MANOVA analysis and probability for that *F* value are shown.

8 after injury. Unexplained differences can be seen in the figure at baseline between the injured and control groups, although it did not reach statistical significance. It was also noted that, although the baseline of the controls was different from its follow-up scores, this difference was not statistically significant. At injury and all follow-up time points the standard deviation of the injured group is much larger than that of the controls, suggesting that the injured group may be heterogeneous with respect to progression. Likewise, although differences between the means can be seen at day 45, this does not reach significance because of a large variance at this evaluation point. The large variance at day 45 in the injury group suggests that some of the subjects were still showing persistent abnormalities at this time point, although not statistically significant for the group.

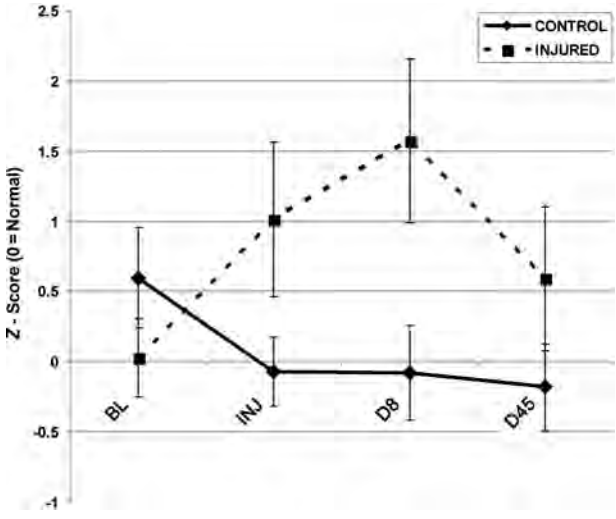

Figure 1. Composite *Z* score of the 7 quantitative electroencephalographic features in the multivariate analysis of variance between groups, shown at BL, injury/retest, day 8, and day 45 after injury. Standard error of the mean shown for each group average point. Clear differences between the groups at point of injury and day 8 can be seen. BL indicates base line; INJ, time of injury.

DISCUSSION

Our findings pertaining to the physiological effects and recovery after concussion have relevance to the existing literature from both animal and human studies. Animal research has suggested a lengthier time course of neurophysiological recovery than the recovery timeframe often reported in clinical studies of sport-related concussion. Additionally, recent studies that employ more innovative functional neuroimaging techniques have reported abnormalities in brain function well beyond the observed 7- to 10-day window of typical clinical recovery. Preliminary QEEG findings from the current study are in line with earlier discoveries from animal and functional neuroimaging research, suggesting the possibility of lingering cerebral dysfunction beyond the observed clinical recovery period. In turn, the collection of these findings now adds increasing empirical support to the concept of a "window of cerebral vulnerability," during which the brain has not yet returned to a normal state of metabolic and cerebral function. Further study is required to more precisely clarify the risks (eg, susceptibility to recurrent injury, poor outcome) imposed during this proposed period of suspected cerebral vulnerability after concussion.

The pathophysiology of concussion, or mTBI, has been nicely delineated by several scientific breakthroughs over the past decade or more. Several experts have provided detailed reviews of the pathophysiology of concussion, citing primarily findings from animal models of traumatic brain injury.[50–52] These studies consistently demonstrate a sequential pattern of neuronal dysfunction due to ionic shifts, altered metabolism, impaired connectivity, and changes in neurotransmission, which some have commonly coined as the "neurometabolic cascade" that ensues after trauma to the brain.[52] In animal models, the time course of these physiological changes and return to normal homeostasis is typically a period of many days, similar to the QEEG findings in the current study. Further study is required to determine how these findings generalize to the time course of physiological recovery after concussion in humans. Perhaps surrogate instrumentation such as electrophysiological or functional neuroimaging methods will help in the translation of the animal findings to the advancement our under understanding of the pathophysiology of concussion in humans.

Findings from the current and previous studies on physiological recovery after concussion have a potentially translational value to the clinical management of sport-related concussion. Specifically, our findings generally support the concept of a "no exposure" and recovery period that extends beyond the simple point at which the athlete is symptom-free and clinical testing returns to normal. Given the consistency of our findings

with prior studies on the time course of clinical recovery after sport-related concussion, it is considered unlikely that are findings are due to type I error. The clinical utility of a portable, real-time QEEG device could possibly aid in the identification and evaluation of subtle brain dysfunction during the acute and subacute period after concussion. Obviously, further study is required to provide additional evidence to support use of QEEG in the assessment of concussion in sport. Ultimately, this issue has major implications for injury prevention strategies, particularly with regard to preventing recurrent concussion and the risks of possible catastrophic outcome in sports.

The application and generalizability of findings from the current study are somewhat limited because of sampling and other issues. We are reporting on a relatively small data set, which is made up of all male football players. It is uncertain as to whether or not the findings might be different based on gender or when studying a broader sample of athletes across sports. Future studies will be aimed at replicating these findings in a larger, broader sample of sport-related concussion. The possible heterogeneity of recovery within the injured group will also require a larger group for study. In addition, large sample sizes using this methodology will enable the utilization of more advanced statistical methods to examine the utility, sensitivity, and specificity of QEEG in identifying abnormalities in brain electrical activity at the individual case level that would influence clinical decision making. Ultimately, future studies should look at the incremental value of all clinical measures (eg, symptom checklists, neurocognitive testing, balance testing, QEEG) and the unique contribution they make in detecting clinical abnormalities in athletes who are otherwise reporting to be symptom free and would be returned to competition, perhaps prematurely.

In conclusion, findings from the current study expand our understanding of physiological recovery after sport-related concussion and offer preliminary support for the potential utility of brief QEEG studies in the evaluation of sport-related concussion. Further research is required to better understand how quantitative studies of brain electrical activity may influence clinical the management of sport-related concussion.

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