*J Head Trauma Rehabil*
Vol. 33, No. 1, pp. 1–6


# The Use of an Electrophysiological Brain Function Index in the Evaluation of Concussed Athletes

*M. Alison Brooks, MD; Jeffrey J. Bazarian, MD; Leslie S. Prichep, PhD; Samanwoy Ghosh Dastidar, PhD; Thomas M. Talavage, PhD; William Barr, PhD*

**Objective:** To evaluate the effectiveness of the electroencephalographic (EEG) Brain Function Index (BFI) for characterizing sports-related concussive injury and recovery. **Participants:** Three hundred fifty-four (354) male contact sport high school and college athletes were prospectively recruited from multiple locations over 6 academic years of play (244 control baseline athletes and 110 athletes with a concussion). **Methods:** Using 5 to 10 minutes of eyes closed resting EEG collected from frontal and frontotemporal regions, a BFI was computed for all subjects and sessions. Group comparisons were performed to test for the significance of the difference in the BFI score between the controls at baseline and athletes with a concussion at several time points. **Results:** There was no significant difference in BFI between athletes with a concussion at baseline (ie, prior to injury) and controls at baseline ($P = .4634$). Athletes with a concussion, tested within 72 hours of injury, exhibited significant differences in BFI compared with controls ($P = .0036$). The significant differences in BFI were no longer observed at 45 days following injury ($P = .19$). **Conclusion:** Controls and athletes with a concussion exhibited equivalent BFI scores at preseason baseline. The concussive injury (measured within 72 hours) significantly affected brain function reflected in the BFI in the athletes with a concussion. The BFI of the athletes with a concussion returned to levels seen in controls by day 45, suggesting recovery. The BFI may provide an important objective marker of concussive injury and recovery.
**Key words:** *brain function index*, *brain injury*, *concussion*, *electrophysiological data*, *mild TBI*

***Author Affiliations:*** *Department of Orthopedics and Pediatrics, University of Wisconsin-Madison, Madison, Wisconsin (Dr Brooks); Department of Emergency Medicine, University of Rochester Medical Center, Rochester, New York (Dr Bazarian); Department of Psychiatry (Dr Prichep) and Departments of Neurology and Psychiatry (Dr Barr), New York University School of Medicine, New York; BrainScope Co, Inc, Bethesda, Maryland (Drs Prichep and Ghosh Dastidar); and Weldon School of Biomedical Engineering, Purdue University, West Lafayette, Indiana (Dr Talavage).*

*The authors acknowledge the contributions of those who made this research possible, including Michael Powers, and the athletic trainers and student athletes who participated in the studies.*

*Data acquisition for this study was supported in part by research grants to the clinical sites from BrainScope Company, Inc, and from GE NFL Head Health Challenge I. Drs Talavage and Brooks were principal investigators at clinical data acquisition sites. During the first 3 years of data acquisition, Dr Barr was an expert concussion consultant to BrainScope Company, Inc. Dr Bazarian was a principal investigator in a related data acquisition study and served as a thought leader in the field of concussion for BrainScope Company, Inc. Dr Ghosh Dastidar is a biomedical engineer who serves as a senior algorithm development specialist at BrainScope Co, Inc and holds company options. During the period of data acquisition, Dr Prichep was the Director of the Brain Research Laboratories, Department of Psychiatry, at NYU School of Medicine, and served as a paid consultant to BrainScope Company, Inc. Currently, Dr Prichep is the Chief Scientific Officer of BrainScope Company, Inc, and a Professor at NYU School of Medicine. Dr Prichep holds potential financial interest through patented technology licensed by BrainScope Company, Inc, from NYU School of Medicine and company options. BrainScope Company, Inc, had no role other than indicated above, in the conduct of these studies. Strict adherence to ethical concerns was followed and all subjects signed written informed consents for participation in the study.*

ESTIMATES OF THE INCIDENCE of mild traumatic brain injury (mTBI) or concussion in the United States are reported by the Centers for Disease Control and Prevention (CDC) to be 1.6 million treated and 3.8 million untreated sports-related concussions yearly on the basis of data from 2001 to 2005.[1] In 2010, the CDC reported a 70% increase in TBI-related emergency department visits over the previous decade, due in part to heightened awareness of concussion.[2] The current "gold standard" for sports-related concussion relies largely on subjective reporting of signs and symptoms, using assessment tools such as the Sport Concussion Assessment Tool (SCAT).[3] The subjective nature of the assessment makes diagnosis, intervention, and return-to-play decisions extremely difficult.

Current research in neuroimaging has contributed to a better understanding of the pathophysiology of sports-related concussion. Changes in "connectivity" have been demonstrated in studies of diffusion tensor

*The authors declare no conflicts of interest.*

***Corresponding Author:*** *Leslie S. Prichep, PhD, New York University School of Medicine, New York, NY 10016 (prichl01@nyumc.org).*

*DOI: 10.1097/HTR.0000000000000328*

imaging, providing evidence of the disruption of white matter tract integrity in concussive injury.[4–8] In addition, magnetic resonance spectroscopy results demonstrate evidence of changes in brain metabolism as a consequence of concussive injury.[9]

Such changes in brain physiology are also reflected in brain electrical activity, suggesting the utility of such measures as markers of functional brain injury.[10] In a study comparing diffusion tensor imaging and electroencephalographic (EEG) in blast-concussed soldiers, Sponheim and colleagues[11] reported a significant correlation between changes in mean fractional anisotropy of 4 major white matter tracts related to frontal interhemispheric communication and changes in phase synchrony of the EEG between frontal and frontotemporal regions. Another measure of brain electrical activity reported to reflect brain injury in mTBI is based on the "complexity" or entropy of the EEG signal, which decreases in concussive injury.[12] Changes in the frequency spectra of the EEG, power relationships, and coherence between regions have also been associated with concussive injury.[13–16]

Brain electrical activity has several advantages over other functional neuroimaging methods, considering both analytic and clinical aspects. On the analytic side, the superior temporal resolution of electrophysiological data results in better precision related to neuronal transmission, and sensitivity to both functional and structural brain injury. The clinical advantages include ready availability at the point of care, rapid acquisition, ease of use with limited training, nonradiation emitting, and cost-effectiveness.

The EEG Brain Function Index (BFI) is a derived marker that provides an index of functional brain abnormality following a head injury**.** The index, a novel composite measure, was recently validated in a blinded validation trial[17] of the BrainScope Ahead 300 device and received Food and Drug Administration 510(k) clearance (K161068). The BFI is derived from those EEG features associated with functional brain impairment, reflecting current consensus on the physiology of concussive injury. These features include those that reflect changes in brain region connectivity (eg, phase synchrony and coherence), EEG signal complexity (eg, fractal and scale-free dimension), and shifts in the frequency spectra (eg, alpha power). This study will demonstrate the potential clinical utility of the BFI in a population of athletes with a concussion studied longitudinally.

## METHODS

### Subjects

Male contact sport athletes ($N = 354$) from high schools and colleges (Male athletes were recruited from the University of Wisconsin-Madison and from high schools and colleges in the greater Milwaukee, Wisconsin, and West Lafayette, Indiana areas) who met inclusion criteria were enrolled in the study. The large majority of these athletes were football players (94.4%). Approval by the Institutional Review Boards at the host institutions of the principal investigators and written informed consent was obtained from all voluntary participants (or parent/guardian of minors).

### Design and procedures

All consenting contact sport athletes who met inclusion/exclusion criteria were enrolled into the study and participated in a preseason baseline EEG acquisition and evaluations on all concussion assessment measures used to make the concussion diagnosis. In addition to the assessments, a database was generated that included information such as patient demographics, concussion history, and any preexisting conditions (developmental, neurological, and medical).

#### *Inclusion/exclusion criteria*

The inclusion criteria included (1) no loss of consciousness of total duration of 20 minutes or more, (2) no neuroimaging evidence of structural injury, and (3) no hospitalization (no admission due to either head injury or collateral injuries). Subjects were excluded who met the following exclusion criteria by self-report: (1) evidence of illicit drug usage, (2) associated injuries (broken bones, sprained extremity joints), (3) did not speak or read English, (4) current central nervous system-active prescription medications, (5) skull abnormalities (eg, metal plate), and (6) attention-deficit hyperactivity disorder or learning disability (controls only).

#### *Concussion population*

During the course of the season, enrolled subjects who sustained a concussive injury were identified and moved to the injury group as per the 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 or to the body causing head deceleration, resulting in altered mental status and one or more of the concussion symptoms described by the American Academy of Neurology guideline for diagnosis and management of sports-related concussion[18] for consistency across sites (it is noted that this was the current version at time of data acquisition). These concussion symptoms included headache, nausea, vomiting, dizziness/balance problems, fatigue, trouble sleeping, drowsiness, sensitivity to light or noise, blurred vision, difficulty remembering, or difficulty concentrating.[18,19] The following additional symptoms were also documented after injury: loss of consciousness, posttraumatic amnesia (eg,

inability to recall exiting the field and aspects of the examination), and retrograde amnesia (eg, inability to recall aspects of the play or events prior to injury and score of the game) and other acute injury characteristics (not presented herein). All assessments and recording of symptoms were completed under the supervision of trained research technicians at the time of the EEG evaluation. This information was used for the determination of concussion and does not play a role in the analysis reported in this article.

Once an athlete suffered a concussion his or her preseason baseline was removed from the control population baselines and included in the injury group. There were no subjects who were in both the control group and the injury groups.

### *Assessment protocol*

The clinical "sideline" and electrophysiological evaluations were conducted preseason (when available), within 72 hours of sustaining a concussive injury and again 45 days postinjury (regardless of injury severity), in a controlled testing setting (eg locker room and classroom). All assessment time points included electrophysiological (EEG) testing, a computerized neuropsychological testing battery, and signs and symptom questionnaires (including the Standardized Assessment of Concussion [SAC][20,21] and the Concussion Symptom Inventory). Only the EEG data are presented herein. All examiners were trained to perform these evaluations, and quality control guidelines were followed rigorously.

## Electrophysiological evaluation

Subjects underwent 5 to 10 minutes of eyes closed resting EEG recording acquired on a hand-held device (investigational variants of BrainScope Ahead devices). The EEG recordings were made from frontal and frontotemporal sites of the extended international 10/20 electrode placement system using self-adhesive electrodes applied to the forehead, and referenced to linked ears. Electrode sites included FP1, FP2, AFz (located just anterior to Fz on the forehead, below the hairline), F7, and F8. All electrode impedances were below 10 kΩ. Amplifiers had a bandpass from 0.5 to 70 Hz (3-dB points). A sampling rate of up to 8 kHz was used for data acquisition and the data were subsequently downsampled to 100 Hz for processing. Electrode placement in all cases was completed in less than 5 minutes.

The EEG data were subjected to automatic artifact rejection algorithms to remove any biologic and nonbiologic contamination, including that from eye movement (vertical and lateral), muscle movement, patient or cable movement, external noise, significantly low-amplitude signal, and atypical electrical activity patterns.[22] Previous experience, as reported in Prichep et al,[22] has demonstrated that sufficient artifact-free data (60–120 seconds) for quantitative analysis can be obtained from such a 5- to 10-minute recording. It is noted that these artifact detection algorithms were part of procedures implemented in the Food and Drug Administration-cleared data acquisition devices used in this study.

## Computation of EEG BFI used in this study

The derivation of the BFI applied to patients in this study is described elsewhere.[17] To aid in understanding of the index, the steps taken in its derivation are summarized later. Artifact-free EEG data from head-injured and control subjects ($n = 2407$) were subjected to quantitative off-line analyses for feature extraction.

The set of features used to compute the BFI were those that are reflective of the physiology associated with concussive injury in the scientific literature. These included measure sets containing features related to "connectivity" (eg, phase synchrony and coherence), complexity of the signal (eg, fractal and scale-free dimension), and shifts in the frequency spectra (eg, decrease of alpha power). These features are thought to contain information about the architecture of the neural networks in the brain, neuronal transmission and changes in brain metabolism and neurochemistry, which are impacted on by head injury.[4–16] These features were age regressed and normalized to obtain feature *z* scores. See Prichep and colleagues[22] for a more complete description of the features and the feature extraction methodology.

### *Computation of the BFI*

The EEG BFI was computed as a linear combination of the selected QEEG feature z scores. The linear combination included additional weight assigned to values that are outside the age-expected normal range for that feature (to increase the relative contribution of the features with abnormal values to the index). The general formulation of the index (Y) for any EEG recording session was expressed as follows:

$$Y = w_N \sum_{i=1}^{N_N} x_i + w_A \sum_{i=1}^{N_A} x_i$$

where, $w_N$ is the weight associated with a feature value that is in the normal range for that feature, $N_N$ is the number of features for the given EEG recording session that are in the normal range, $x_i$ is the value of the $i$th feature, $w_A$ is the weight associated with a feature value that is outside the normal range, and $N_A$ is the number of features for the given EEG recording session that are outside the normal range.

During the development of the BFI, steps were taken to avoid overtraining. The feature set used as the basis for the BFI was limited not only by the informed data reduction but also by the conservative standard statistical

**TABLE 1** *Mean and standard error of Brain Function Index for each condition*[a]

| Group | N | Mean (standard error) | t statistic (compared with baseline) | P value |
|---|---|---|---|---|
| Control baseline | 244 | 155.52 (5.50) | – | – |
| Injury baseline | 49 | 166.33 (13.58) | − 0.7376 | .4634 |
| Injury day 0 | 94 | 190.87 (10.60) | − 2.9601 | .0036 |
| Injury day 45 | 55 | 171.15 (10.50) | − 1.318 | .191 |

[a]Results of *t* test (*t* statistic and associated *P* value) for comparisons between athletes with a concussion at each time point and baseline controls.

convention of 10:1 subject-to-feature ratio. In addition, the variability in the performance of the BFI across the development population was accounted for using a 5-fold cross-validation strategy. It is also important to note that, because the BFI was finalized a priori, only those specific features used for the BFI computation were extracted from the study population.[17*]

### Statistical analyses

Group comparisons for the BFI were made using a 2-tailed *t* test for independent samples, with unequal variances to test for the significance of differences in the BFI score between the controls and concussed athletes. The *t* tests were performed between (1) baselines of controls versus baselines of injured (those who sustain a concussion after baseline); (2) controls versus concussed at time of injury; and (3) controls versus concussed at day 45 following injury. It is noted that, although the BFI is a composite feature, it is tested in this model as a single measure and therefore does not require correction for multiple comparisons. (See earlier for discussion of protection from multiple measures used in derivation of the BFI.)

## RESULTS

A total of 244 control baseline cases and 110 cases that were diagnosed with a concussion during the course of the season were included in the study; 94.4% of study subjects were football players. The control group had a mean age of 18.27 years ($\sigma = 2.10$; range = 14.11–23.31). The injured/concussed subject group had a mean age of 18.36 years ($\sigma = 2.23$; range = 14.89–23.20). The mean SAC score for the control group at baseline was 27.45 (median = 28; $\sigma = 1.89$; range = 14–30). The mean SAC score for the injured group at baseline was 27.71 (median = 28; $\sigma = 1.78$; range = 24–30).

Of the 110 athletes with a concussion, 49 had received a preseason baseline assessment (note that preseason baseline was not included in all years of study), 94 received an assessment within 24 hours of injury, and 55 received a follow-up assessment (45 days after injury). The sample size is different for the various time points because of 3 main factors: (1) related to baselines, during 2 of the seasons of play the protocols did not include preseason baseline evaluations; (2) related to time of injury, some sessions were excluded because of excessive artifact, subjects tested outside the 24-hour time window, or subject withdrawal; and (3) related to follow-up at day 45, this last time point suffered from attrition.

Within the group of subjects who received an assessment within 72 hours of injury, 38 had baseline recordings and 56 did not. A comparison of the BFI scores for the 2 groups indicated that they were not different (*t* statistic = −1.1210; $P = .2653$). Therefore, it was deemed acceptable for the 2 groups to be combined for the purpose of this analysis, for the purpose of enriching the population and increasing the power of the analysis.

The characteristics of the BFI score for the control and injured populations are summarized in the Table 1, which shows the mean and standard error for the BFI score at each assessment time point for the injured subjects and the significance of the difference at each time point from control baselines. There was no significant difference between BFI at preseason baseline in athletes who were later concussed and those in the control group (*t* statistic = −0.7376; $P = .4634$). Injured athletes exhibited significant differences from controls at the time of injury (*t* statistic = −2.9601; $P = .0036$). No group differences (injured vs controls) were observed at 45 days (*t* statistic = −1.3180; $P = .1910$), which suggests normalization of the BFI, representing "recovery."

## DISCUSSION

In the absence of a biomarker as a gold standard for concussion, there is reliance on self-report and brief sideline evaluations, which are inconsistent in use, both in defining the injury and in making important

*It should be noted that the Ahead 300 device was cleared by FDA (K161068), for use within 72 hours of head injury, in patients between the ages of 18-85 years, with GCS of 13-15. The use of the BFI outside of the 72 hours post-injury window or pre-injury (baseline) discussed in this study were not evaluated as part of the FDA validation study.

return-to-play decisions. Unrecognized and untreated concussions can contribute to morbidity, with potentially debilitating and lingering postconcussive symptoms, including cognitive impairment, development of depression and anxiety, and somatization disorder.[23,24] In addition, there is a higher incidence of repeat concussion following a first concussion and when the injured athlete is allowed to return to play before symptom resolution.[25–26] The EEG BFI can provide important quantitative information about the status of brain function in concussion, aiding in the early identification, treatment, evaluation, and return-to-play decisions.

Although advanced neuroimaging can be used to distinguish between groups with concussive brain injury and controls in an experimental setting,[27] such technologies are not readily available at the sidelines or in the emergency department to aid in the assessment of concussive injury. Studies have suggested that EEG can act as a surrogate for other neuroimaging tools and can provide many advantages in sideline (including locker room or nearby venue) testing at the time of injury, including ease of use, rapid evaluation, and quantitative results, which can be expressed as a percentile of the normal population. To date, electrophysiological methods have been demonstrated to reflect persistence of alterations in brain function, beyond the window of abnormal findings demonstrated through clinical measures, focusing on assessment of reported symptoms, cognitive functioning, and sideline measures of vestibular functioning.

To facilitate the interpretation of the index in this work, the index may be mapped to a percentile scale developed using the range of values obtained for a large population of healthy individuals. Key points on the scale may be highlighted on the basis of clinical utility (eg, <10th percentile). Such displays are similar to those standardly used in presenting results of neurocognitive and other standard test results (and predicates for performance tasks).

Results of this study demonstrated no differences in BFI at time of preseason baselines but highly significant differences at time of injury. When compared 45 days following injury, no differences were found between the concussed and controls athletes, supporting the potential clinical utility of the BFI in providing a quantitative index for the evaluation of concussion and the sequelae that follow. It was also noted that although both preseason baseline and day 45 evaluations in the injured group showed no differences with the baseline controls, the *P* value for day 45 evaluations was lower than that for the preseason comparisons. This result suggests the heterogeneity of the population as related to the different trajectories of recovery, with some athletes still demonstrating abnormalities at this time point. Such findings underscore the need for such an objective biomarker of functional brain injury (BFI), which could contribute to more optimized assessment of return-to-play readiness. Studies underway will further investigate the persistence of abnormalities in the EEG as related to the rate of recovery.

Advances in signal-processing engineering, lessons learned from big data analysis in genomics and proteomics, and introduction of sophisticated classification methodology that takes advantage of machine learning, have greatly enhanced the field of quantitative electrophysiology, however, care must be taken to obtain high-quality data (elimination of artifact) and sufficient numbers of subjects to mitigate potential problems of overtraining. This study has followed this guidance. However, limitations of the current study include lack of female athletes and limited age range of the subject population. As such, applicability to individuals who differ significantly from the test population has yet to be demonstrated. Studies are currently underway to expand the concussed population to include females and a broader age range. Larger populations of athletes with a concussion including preseasons baselines would further facilitate validation of this approach. Another limitation of the study is that the reported group comparisons compare control and injured populations but was not designed to follow the trend of BFI for any given subject from baseline to injury and recovery. The expansion of the approach to include the baseline and longitudinal aspect along with "return-to-play" information (outside the time window currently cleared by the FDA for use of the BrainScope Ahead 300 device) will allow the relationship between the BFI and clinical decisions regarding return to play to be investigated.

The potential clinical utility of a biomarker on the basis of brain electrical activity in the acute assessment and quantitative tracking of recovery of brain functioning after concussion was demonstrated in this study. The ability to obtain such an index rapidly, at any point along the sequelae of concussion, suggests that such a measure can contribute greatly to the assessment of concussive injury, going beyond that obtained with the more traditional subjective clinical indices that are currently used in the sport setting.

## REFERENCES

1. Gilchrist J, Thomas KE, Wald M, Langlois J. CDC National Center for Health Statistics: nonfatal traumatic brain injuries from sports and recreation activities–United States, 2001–2005. *MMWR Morb Mortal Wkly Rep*. 2007;56(29):733–737.

2. Korley F, Kelen G, Jones C, Diaz-Arrastia R. Emergency department evaluation of traumatic brain injury in the US, 2009–2010. *J Head Trauma Rehabil*. 2016;31(6):379–387.
3. McCrory P, Meeuwisse W, Johnston K, et al. Consensus Statement, Sport Concussion Assessment Tool–3rd Edition. *Br J Sports Med*. 2013;47:259–262.
4. Cubon VA, Putukian M, Boyer C, Dettwiler A. A diffusion tensor imaging study on the white matter skeleton in individuals with sports-related concussion. *J Neurotrauma*. 2010;28(2):189–201.
5. Mac Donald CL, Johnson AM, Cooper D, et al. Detection of blast-related traumatic brain injury in U.S. military personnel. *New Eng J Med*. 2011;364(22):2091–2100.
6. Chu Z, Wilde EA, Hunter JV, et al. Voxel-based analysis of diffusion tensor imaging in mild traumatic brain injury in adolescents. *AJNR Am J Neuroradiol*. 2010;31(2):340–346.
7. Bigler E. Neuropathology of mild traumatic brain injury: relationship to structural neuroimaging findings. In:Slobounov SM, Sebastianelli WJ, eds. *Concussions in Athletics: From Brain to Behavior*. New York, NY: Springer Science + Business Media; 2014;181–204.
8. Wilde EA, McCauley SR, Hunter JV, et al. Diffusion tensor imaging of acute mild traumatic brain injury in adolescents. *Neurology*. 2008;70(12):948–955.
9. Vagnozzi R, Signoretti S, Cristofori L, et al. Assessment of metabolic brain damage and recovery following mild traumatic brain injury: a multicentre, proton magnetic resonance spectroscopic study in concussed patients. *Brain*. 2010;133(11):3232–3242.
10. Rapp PE, Keyser DO, Albano A, et al. Traumatic brain injury detection using electrophysiological methods. *Front Hum Neurosci*. 2015;9:11.
11. Sponheim AR, McGuire KA, Kang SS, et al. Evidence of disrupted functional connectivity in the brain after combat-related blast injury. *Neuroimage*. 2011;54(suppl 1):S21–S29.
12. Slobounov S, Cao C, Sebastianelli W. Differential effect of first versus second concussive episodes on wavelet information quality of EEG. *Clin Neurophysiol*. 2009;120(5):862–867.
13. Thatcher RW, North DM, Curtin RT, et al. An EEG severity index of traumatic brain injury. *J Neuropsychiatry Clin Neurosci*. 2001;13(1):77–81.
14. Prichep LS, McCrea M, Barr W, Powell M, Chabot RJ. Time course of clinical and electrophysiological recovery following sport-related concussion. *J Head Trauma Rehabil*. 2013;28(4):266–273.
15. McCrea M, Prichep LS, Powell MR, Chabot R, Barr WB. Acute effects and recovery after sport-related concussion: a neurocognitive and quantitative brain electrical activity study. *J Head Trauma Rehabil*. 2010;25(4):283–292.
16. Barr WB, Prichep LS, Chabot RJ, Powell MR, McCrea M. Measuring brain electrical activity to track recovery from sport related concussion. *Brain Inj*. 2012;26(1):58–66.
17. Hanley D, Prichep LS, Badjatia N, et al. A brain electrical activity (EEG) based biomarker of functional impairment in traumatic head injury: a multisite validation trial. *J Neurotrauma*. 2017, in review.
18. Practice Parameter: the management of concussion in sports (summary statement). Report of the Quality Standards Subcommittee. *Neurology*. 1997;48(3):581–585.
19. Kelly JP, Rosenberg JH. Diagnosis and management of concussion in sports. *Neurology*. 1997;48(3):575–580.
20. McCrea M, Guskiewicz KM, Marshall SW, et al. Acute effects and recovery time following concussion in collegiate football players: the NCAA Concussion Study. *JAMA*. 2003;290(19):2556–2563.
21. McCrea M. Standardized mental status testing on the sideline after sport-related concussion. *J Athl Train*. 2001;36:274–279.
22. Prichep LS, Jacquin A, Filipenko J, et al. Classification of traumatic brain injury severity using informed data reduction in a series of binary classifier algorithms. *IEEE Trans Neural Syst Rehabil Eng*. 2012;20(6):806–822.
23. Scholten AC, Haagsma JA, Cnossen MC, Olff M, van Beeck EF, Polinder S. Prevalence of and risk factors for anxiety and depressive disorders after traumatic brain injury: a systematic review. *J Neurotrauma*. 2016;33(22):1969–1994.
24. Kesinger MR, Juengst SB, Bertisch H, et al. Acute trauma factor associations with suicidality across the first 5 years after traumatic brain injury. *Arch Phys Med Rehabil*. 2016;97(8):1301–1308.
25. Guskiewicz KM, McCrea M, Marshall SW, et al. Cumulative effects associated with recurrent concussion in collegiate football players: the NCAA concussion study. *JAMA*. 2003;290(19):2549–2555.
26. Slobounov S, Slobounov E, Sebastianelli W, Cao C, Newell K. Differential rate of recovery in athletes after first and second concussion episodes. *Neurosurgery*. 2007;61(2):338–344.
27. Gardner A, Kay-Lambkin F, Stanwell P, Cao C, Newell K. A systematic review of diffusion tensor imaging findings in sports-related concussion. *J Neurotrauma*. 2012;29(16):2521–2538.