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Preliminary investigation of a multimodal enhanced brain function index among high school and collegiate concussed male and female athletes

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ABSTRACT

Objective: The primary purpose of this study was to examine the longitudinal effects of sports-related concussion (SRC) on a multi-faceted assessment battery which included neuropsychological testing, symptom reporting, and enhanced brain function index (eBFI) among athletes with and without SRC. A secondary purpose was to explore longitudinal sex differences among these measures in athletes with and without SRC. **Methods**: A case-control, repeated-measures design was used for this study. A total of 186 athletes (concussed group:n = 87 controls:n = 99) participated in the study. A repeated-measures design was used in which each athlete was tested at four time points following an SRC: within 72 h of injury (Day 0; 2.0 ± 0.9 days following injury), 5 days following injury (Day 5; 5.0 ± 0.0), at return to play (RTP; 18.3 ± 13.8 days following injury), and within 45 days following RTP (RTP45; 66.2 ± 19.0 days following injury). All analyses were conducted separately using a 2 (Group: concussed, control) × 2 (Sex: male, female) × 4 (Time:Day 0, Day 5, RTP, RTP45) univariate multi-level model including the random intercept for each participant. A higher eBFI score indicates a better performance. Alpha level was set aprior at .05. This study was registered on clinicaltrials.gov (Objective Brain Function Assessment of mTBI/Concussion in College/ high school Athletes NCT02477943, NCT02661633, CAS 13–25 NCT03963804).

Results: Concussed athletes exhibited impaired eBFI within 72 h of SRC and at Day 5 compared to controls (p < .001). Analysis of eBFI scores between male and female athletes revealed a main effect of sex (p = .05), with female athletes exhibiting lower eBFI (33.9 ± 30.7) relative to male athletes (40.4 ± 33.0), however, it did not indicate interactions between sex, group, and time ($p's \ge 0.786$).

Conclusion: The eBFI appears to be a useful tool in determining concussed athletes during the acute stages of an SRC. However, this index may lack the sensitivity to detect sex-related differences between groups at various time points during recovery.

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KEYWORDS

eBFI; sex differences; concussion; SCAT

Introduction

A multifaceted assessment approach that includes symptoms, neurocognitive, balance, vestibular, and oculomotor measures is considered best practice for the assessment and management of sport-related concussion (SRC) [1,2]. This approach, combined with a thorough clinical exam and medical history, affords the clinician the ability to capture the heterogeneous presentation of symptoms and impairments of SRCs. Despite the advantages, this comprehensive assessment approach is comprised of the assessment of clinical behaviors and symptom presentations, which are subject to patient interpretation and effort. Moreover, these measures do not directly assess the neurophysiological changes that may occur following SRC. Alternatively, a neurophysiological or neurocognitive function could provide an objective assessment of SRC and address the limitations of self-reported measures, which can complicate management.

Researchers have used electroencephalography (EEG) to measure the neurophysiological changes that occur following SRC [3,4]. EEG assesses changes in brain electrical activity at a higher temporal resolution (i.e., more frequent sampling of the area, resulting in more accurate measurements in regard to time) than other neuroimaging modalities (e.g., MRI, CT) [5]. Several researchers have reported changes in EEG frequency spectra, power relationships, and coherence between brain regions in individuals with SRC compared to non-injured controls [3,4,6,7]. Collectively, these findings support the utilization of EEG as an objective assessment of SRC.

Recently, researchers have developed an enhanced Brain Function Index (eBFI), which incorporates a multimodal assessment of SRC including neurocognitive measures, vestibular/balance symptoms, and EEG [8]. Initial support for this novel eBFI was presented by Jacquin and colleagues [8] who indicated that concussed athletes demonstrated lower eBFI scores compared to controls both at time of injury (defined as within 72 h of injury) and approximately 1 week following their injury. These researchers have also indicated the eBFI of concussed athletes was significantly improved at RTP compared to time of injury [8]. In addition to the accumulating evidence for the inclusion of EEG as a part of the multimodal assessment for SRC, the influence of risk factors affecting EEG outcomes following SRC is scant.

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Sex differences on SRC presentation and recovery are well documented [9–13], with sex differences also prevalent in the EEG literature [14,15]. Compared to their male counterparts, females have a greater risk for SRCs [16,17], report more symptoms and worse symptom severity [13,18], and are at a higher risk for a protracted recovery [19,20]. Moreover, males and females differ in brain structure and physiology. For example, females have lower overall brain volume [21], higher gray to white matter ratio [22], and more withinmatter network connectivity compared to males who have more between-network connectivity in regions underlying attention, hearing, memory retrieval, and default mode networks [12]. These sex differences are also documented on EEG outcomes, such as asymmetry of alpha activity during linguistic and visuospatial tasks [15] and differences in microstate transitions between males and females on EEG during rest [14]. The documented sex differences in neurophysiology between males and females warrant additional consideration when applying EEG measures as an assessment of SRC. To date, scarce literature on sex differences in EEG exists in concussed patients. To our knowledge, only one study has examined sex differences in changes in EEG spectral activity following a brain injury [23]. Laibow and colleagues [23] suggest that female patients reported reduced delta/theta bands and higher alpha/beta bands compared to male patients. However, key limitations include a small sample size, only examining TBI-related injuries from stroke or car accidents, and not characterizing the changes in spectral band power relative to normative populations. As EEG transitions from an experimental measure to a more clinically useful measure, it is important that sex differences are examined. Accordingly, the primary purpose of this study was to examine the longitudinal effects of SRC on a multi-faceted assessment battery that included cognition, symptom reporting, and eBFI among athletes with and without SRC. We hypothesized that concussed athletes would have lower cognition, higher symptom reports, and lower eBFI compared to athletes without an SRC. A secondary purpose of this study was to explore longitudinal sex differences on these measures in athletes with and without SRC. As the secondary purpose was exploratory in nature, we did not have a hypothesis for sex differences.

Material and methods

Research design

A case-control, repeated-measures design was used for this study.

Participants

A total of 186 high school and college varsity athletes with and without SRC participated in this study. This study was part of a larger multi-site investigation; however, athletes included in data analysis were recruited from multiple high schools and colleges in Michigan and Arkansas. The concussed group was comprised of 87 athletes (31 female, mean age = 18.1 ± 2.6 years), and the noninjured control group was comprised of 99 athletes (36 female, mean age = 17.8 ± 2.4 years) with similar athletic participation (i.e., high school varsity, college club, or college varsity teams). See Table 1 for demographics information and Figure 1 for a CONSORT flow diagram of enrollment. The inclusion criteria for the study consisted of being free of neurological disease, reporting normal or corrected-to-normal vision, and providing written informed consent in accordance with the institutions of the principal investigators. Athletes were excluded if they exhibited a loss of consciousness ≥20 min related to the concussive injury, evidence of abnormality visible on Computerized Tomography (CT) of the head related to the traumatic event (neuroimaging not required for enrollment), hospital admission due to either head injury or collateral injuries for >24 h, or were on central nervous system drugs (i.e., depression medication). The control group was excluded from the study if they had a concussion within the past year, a motor vehicle accident or were on central nervous system drugs.

Measures

Definition of sports-related concussion

SRC was defined as altered mental status resulting in short-term impairments [2]. Concussions were assessed by health-care providers using the following criteria: 1) observed and/or reported mechanism of injury (e.g., direct blow to the head, face, neck, or elsewhere on the body); and 2) the presence of at least one or more of the following: a) on-field signs (e.g., disorientation/confusion, loss of consciousness, balance difficulties, amnesia), b) symptoms (e.g., dizziness, nausea, headache), and/or c) any impairment on sideline assessments (e.g., SCAT).

Electroencephalography (EEG) and Enhanced Brain Function Index (eBFI)

A portable, hand-held EEG device (BrainScope Ahead 300iP©) was used for measuring the brain's electrical activity at [8] a sampling rate of 1 kHz and all electrical impedances set below 10 k Ω [8,24]. The eBFI uses a percentile score compared to a normative group and is a multimodal index consisting of quantitative features, including EEG, a subset of neurocognitive measures, and clinical sign/symptoms [8]. The eBFI* used in this

Table 1. Demographic characteristics as a function of sex and group (mean \pm SD).

	Concusse	Concussed athletes		Control athletes	
Measure	Male	Female	Male	Female	р
N	56	31	63	36	0.5
Age (years)	18.5 ± 2.7	17.6 ± 2.5	18.2 ± 2.4	17.2 ± 2.5	0.3
Race (% nonwhite)	30	23	17	19	1.0
Height (cm)	180.5 ± 9.1	167.7 ± 6.9	180.1 ± 7.9	166.2 ± 8.1	0.6
Weight (lbs)	181.8 ± 47.3	148.5 ± 27.8	164.5 ± 27.1	136.7 ± 23.1	.006*
History of Concussion (%)	4	13	0	0	0.02*

*denotes the *t*-test or chi-square was significant between concussed and control groups at p < 0.05.



Figure 1. CONSORT flow diagram of participants in each group with data through each testing period.

study was based on interim results from the algorithm development study. A higher eBFI score indicates a better performance. A more in-depth description of the eBFI can be found in the paper by Jacquin and colleagues [8].

Sport Concussion Assessment Tool (SCAT3)

The SCAT3 was administered as per the study protocol; however, the current study only included total symptom severity and the Standardized Assessment of Concussion (SAC) scores. The SCAT3 symptom evaluation is a subjective assessment of 22 symptoms on a scale of severity from 0 (none) to 6 (severe), providing an index of SRC symptom severity (maximum possible total symptom severity = 132) [25]. The SAC is a brief screening instrument used for neurocognitive assessment of concussion by health-care providers [26]. The SAC is comprised of four composite scores: orientation, immediate memory, concentration, and delayed recall. The SAC is scored out of 30, with orientation, concentration, and delayed recall scored out of 5, whereas immediate memory is scored out of 15 [27].

Recovery time

The total number of days from SRC occurrence to full unrestricted clearance from a physician. Full unrestricted clearance was granted after the concussed athlete had completed the entire step-wise progression and was back to unrestricted contact sport and school.

Procedure

The Institutional Review Board approved this study, prior to data collection. This study was registered on clinicaltrials.gov (Objective Brain Function Assessment of mTBI/Concussion in College/high school Athletes NCT02477943, NCT02661633, CAS 13-25 NCT03963804). All athletes in the concussed group were identified and enrolled in the study by a certified athletic trainer or team physician, who diagnosed the athlete with an SRC. All testing sessions were conducted in a controlled setting (e.g., classroom, laboratory). Prior to initial testing, a trained experimenter administered the Conley evaluation [28], which is a structured assessment used to assess the cognitive capacity of concussed individuals older than 18 years to provide informed consent; guardians provided informed consent for participants younger than 18 years old. Concussed athletes were recruited from varsity and collegiate club athletes with a sports-related concussion identified by a physician. A group of athletes with similar athletic participation (i.e., varsity or collegiate club

athletes) served as the noninjured control group and were recruited on the basis of age and sex.

Concussed athletes participated in testing within 72 h of their SRC (Day 0), 5 days $(\pm 1 \text{ day})$ following injury (Day 5), within 1 day of returning to full sport participation (RTP), and within 45 days (± 5 days) following return to play (RTP45). Concussed athletes returned to play within 5 to 69 days following injury $(M = 18.2 \pm 10.5 \text{ days})$. Non-injured control athletes participated in congruent periods of testing to those of the concussed athletes. For example, if the concussed athlete was administered the RTP session 10 days following their Day 5 session, the noninjured control athlete was administered their RTP 10 days following their Day 5. This strict testing protocol resulted in no differences in days between testing periods between concussed and noninjured control athletes at Day 5 (concussed: 7.3 \pm 4.6 days following injury; control: 7.2 \pm 5.1 days following initial testing), at RTP (concussed: 23.7 ± 14.9 days following injury; control: 19.1 ± 19.9 days following initial testing), or at RTP45 (concussed: 66.7 ± 24 days following injury; control: 64.9 \pm 23 days following initial testing), $t's(340) \le 1.8$, $p's \ge 0.07$, d_s 's \leq 0.28 [95% CI: -0.22 to 0.59]. Return to play times did not differ as a function of geographical location, age, or sex, t's (81) \leq 1.5, p's ≥ 0.1, d_s 's ≤ 0.29 [95% CI: -0.32 to 0.66]. Each athlete was administered the BrainScope Ahead 300iP© and SCAT3 during all test sessions. The athletes' forehead and earlobes were scrubbed and prepared in the following locations according to the International 10-20 placement system: Fp1, Fp2, AFz, Fpz, F7, F8, A1, and A2. Once the skin was prepared the headset was connected to the DAB. The EEG data collection was administered with athletes' eyes closed while attempting to limit all artifacts. After EEG data collection was complete the athletes were administered the SCAT3.

Statistical analysis

Data were analyzed using multi-level modeling as this approach is robust to unbalanced data (i.e., missing observations) and accounts for a number of sources of variability [29,30]. The eBFI score, SCAT3 symptom severity, and SAC were analyzed separately using a 2 (Group: concussed, control) \times 2 (Sex: male, female) \times 4 (Time: Day 0, Day 5, RTP, RTP45) univariate multi-level model, accounting for the random intercept for each participant. Analyses were conducted with α = 0.05 and Benjamini-Hochberg false discovery rate control = 0.05 for post-hoc decompositions. All analyses were performed using the Ime4 [31], ImerTest [32], and emmeans [33] packages in R version 3.4.0 [34] with Kenward-Roger degrees of freedom approximations. The experimental protocol required that all participants be tested within ± 1 day of Day 5 and RTP periods and within \pm 5 days of the RTP45 period. Participants with missing observations due to being unavailable for testing were retained in the analyses (missing cases: Day 5: 21 concussed, 33 controls; RTP: 4 concussed, 15 controls; RTP45: 12 concussed, 14 controls; see Figure 1). For each inferential finding, Cohen's d with 95% confidence intervals was computed as standardized measures of effect size, using appropriate variance corrections for between-subjects (d_s) and repeated-measures comparisons (d_{rm}) [35]. Given a sample size of 186 participants and beta of 0.20 (i.e., 80%

power), the present research design theoretically had sufficient sensitivity to detect *t*-test differences between concussed and noninjured control groups exceeding d = 0.41 (with a two-sided alpha) and between males and females exceeding d = 0.38 (with a two-sided alpha) as computed using G*Power 3.1.2 [36].

Results

A total of 186 high school and college varsity athletes with and without SRC participated in this study. All concussed athletes RTP approximately 18.2 \pm 10.5 days following injury. Concussed athletes reported significantly more previous concussions (0.5 \pm 0.7) compared to the non-injured control group (0.0) (t₍₁₇₎ = 2.8, p = .02, ds = 0.79 [95% CI: 0.33 to 2.77]) and heavier weight (169.9 \pm 44.2 lbs) compared to the non-injured control group (154.4 \pm 28.9 lbs) (t₍₁₈₄₎ = 2.8, p = .006, ds = 0.08 [95% CI: 0.12 to 0.70]). All other demographic variables were not significant between the two groups (see Table 1).

eBFI scores

Group differences

Analysis of eBFI scores revealed a Group × Time interaction, *F* (3,483) = 18.2, p < 0.001, $f^2 \le 0.83$ [95% CI: 0.54 to 1.26]. Post-hoc breakdown of this interaction was performed by examining the effect of Group within each Time. At Day 0, concussed athletes (7.0 ± 15.3) exhibited a lower eBFI score than the non-injured controls (41.4 ± 30.7), t (494) = 7.6, p < 0.001, $d_s = 1.11$ [95% CI: 0.82 to 1.41]. At Day 5, this difference persisted, with concussed athletes (26.8 ± 31.7) continuing to have decreased eBFI score relative to non-injured controls (44.2 ± 27.1), t (544) = 3.6, p < .001, $d_s = 0.58$ [95% CI: 0.26 to 0.90]. However, these differences were no longer apparent following RTP and at 45 days following RTP, t's (538) ≤ 0.3 , p's $\ge .8$, d_s 's ≤ 0.05 [95% CI: -0.29 to 0.35] (see Table 2).

Sex differences

Analysis of eBFI scores between male and female athletes revealed a main effect of Sex, F(1,181) = 3.9, p = .05, $f^2 = 0.06$ [95% CI: 0.00 to 0.13] such that female athletes exhibited lower eBFI scores (33.9 ± 30.7) relative to male athletes (40.4 \pm 33.0). However, there were no Sex \times Time or Group \times Sex \times Time interactions, *F*'s (3, 483) \leq 0.4, *p*'s \geq 0.786, *f* 2 's \leq 0.17 [95% CI: 0.00 to 0.06]. Given the secondary purpose of the manuscript for specifically investigating sex-related differences in the eBFI, planned analyses were conducted examining Group \times Time within each sex. Within only female athletes, there was a Group \times Time interaction, F(3, 234) = 4.2, p = 0.006, f^2 = 0.02 [95% CI: 0.00 to 0.08]. Breakdown of the interaction revealed lower eBFI scores for concussed female athletes relative to female noninjured controls at Day 0 and at Day 5 (t's (234)) \geq 3.0, p's \leq 0.003, d's \geq 0.78 [95% CI: 0.27 to 1.71]. This pattern of recovery was similar to concussed male athletes who exhibited lower eBFI scores relative to male non-injured control athletes at Day 0 and at Day 5 $(t's(351)) \ge 2.0$, $p's \le 0.05$, $d_s's \ge 0.41$ [95% CI: 0.00 to 1.50] (see Figure 2).

Group	Day 0	Day 5	RTP	RTP45
eBFI				
Concussed ($n = 87$)				
Males	10.3 ± 17.8	31.0 ± 33.7	49.0 ± 33.6	50.5 ± 31.3
Female	3.7 ± 7.5	22.7 ± 28.6	38.6 ± 34.4	38.8 ± 31.0
Matched Control ($n = 99$)				
Males	44.8 ± 31.5	43.3 ± 28.8	46.5 ± 32.5	47.9 ± 33.0
Female	38.0 ± 29.1	45.1 ± 24.4	44.0 ± 31.6	40.2 ± 30.7
SCAT Symptom Severity				
Concussed $(n = 87)$				
Males	28.0 ± 17.0	12.0 ± 13.0	1.2 ± 3.3	1.6 ± 2.9
Females	41.5 ± 22.7	15.2 ± 17.8	3.0 ± 5.0	3.1 ± 6.3
Matched Control ($n = 99$)				
Males	3.0 ± 4.7	1.8 ± 4.0	1.3 ± 2.2	1.8 ± 4.1
Females	2.9 ± 5.9	2.1 ± 4.0	1.5 ± 2.7	1.3 ± 2.3
SAC Overall Score				
Concussed $(n = 87)$				
Males	26.0 ± 2.4	26.3 ± 2.4	27.2 ± 2.0	27.3 ± 2.5
Females	26.6 ± 2.6	26.7 ± 2.6	27.6 ± 1.9	27.2 ± 2.0
Matched Control ($n = 99$)				
Males	27.1 ± 2.3	27.3 ± 1.7	27.8 ± 1.8	27.5 ± 2.3
Females	27.4 ± 1.8	27.4 ± 1.9	27.1 ± 1.7	27.7 ± 1.5

eBFI = enhanced brain function index percentile; symptom severity, 0 to 132; SAC overall score, 0 to 30.



Figure 2. Mean values (\pm SD) as a function of group and sex for eBFI. *denotes p < .05 for group differences between concussed and noninjured control athletes.

SCAT3 symptom severity

Analysis of SCAT3 total symptom severity revealed a Group × Sex × Time interaction, F(3, 483) = 5.8, p < .001, $f^2 = 0.04$ [95% Cl: 0.00 to 0.9]. Post-hoc breakdown of the interaction revealed that at Day 0 concussed females reported greater SCAT3 symptom severity scores than concussed males t (182) = 4.4, p < 0.001, $d_s = 0.99$ [95% CI: 0.54 to 1.44], with no significant differences observed at other time points, F's $(1,162) \le 1.7$, $p's \ge 0.2$, $f^{2's} = 0.0$ [95% CI: 0 to 0.02]. There were also no significant differences within the non-injured control group, t(182) = 0.0, p = 0.99, $d_s = 0.00$ [95% CI: -0.41 to 0.41] (see Table 2).

SAC overall score

Analysis of overall SAC scores revealed a main effect of Group with concussed athletes (26.9 \pm 2.4) exhibiting lower SAC scores than non-injured controls (27.4 \pm 1.9), t(182) = 2.3, $p = 0.025, d_s = 0.33$ [95% CI: 0.04 to 0.62]. A main effect of Time was observed in the concussed group for overall SAC scores at Day 0 (26.8 \pm 2.3) and at Day 5 (26.9 \pm 2.1), which were lower than at RTP (27.4 \pm 1.9) and at RTP45 (27.4 \pm 2.2), $t's(477) \ge 2.5, p's \le 0.012, d_{rm}'s \ge 0.20$ [95% CI: 0.04 to 0.46]. However, no differences were observed between Day 0 and Day 5 or between RTP and RTP45 in the non-injured control

group, $t's(479) \le 0.8$, $p's \ge 0.4$, $d_{rm}'s \le 0.06$ [95% CI: -0.17 to 0.20]. No Group \times Time interaction was observed, F(3, 479) = 2.4, p = 0.067, $f^2 \le$ 0.41 [95% CI: 0.22 to 0.66] and no main effects or interactions were observed with Sex, F(1, 479) \leq 1.3, p's \geq 0.3, f² \leq 0.22 [95% CI: 0.0 to 0.38] (see Table 2).

Discussion

The findings of the current study indicated that concussed athletes demonstrated impairments in the eBFI at 72 h and Day 5 following injury relative to non-injured controls, with brain activation recovery occurring at RTP. These findings are consistent with those reported elsewhere, with lower eBFI scores at Day 5 in concussed athletes compared to healthy non-injured controls [8]. These findings suggest that the eBFI may be a useful concussion tool during the acute stages of an SRC in high school and collegiate athlete. More importantly, the multimodal multivariate index composed of EEG, neurocognitive measures, and vestibular/balance symptoms provides a quantitative measure used to characterize brain function. Such a multimodal approach to characterizing brain function as it relates to the clinical assessment of SRC is particularly advantageous as it incorporates assessments across a number of levels of function. In particular, the addition of objective clinical assessments can aid with decisions for diagnosis and return to play that currently rely largely on subjective assessments. Further, when considered as a broader tool for the assessment of SRC, the multimodal nature coupled with normative approaches reduces the potential for athletes to intentionally bias baseline/preseason assessments in an effort to be able to return to play sooner following an SRC.

In contrast to the eBFI findings, the current study did not demonstrate impairments on the interaction between time and total SAC scores between concussed athletes and non-injured controls. These results are similar to a recent study that also reported no significant difference on total SAC scores between concussed athletes and healthy non-injured controls 3-5 days post-injury [37]. However, the results are also in contrast to previous researchers who have suggested that the SAC was able to differentiate between a concussed group and a healthy control group during the acute stages of injury [38]. The lack of findings on the SAC to differentiate between concussion and healthy controls may be due to the lack of sensitivity of the concussion measure. Therefore, the results of the current study further demonstrate the clinical utility of the added EEG-based measure within the eBFI into the clinical assessment. Moreover, the SAC has been shown to have a ceiling effect on immediate and delayed memory, suggesting that it may not be able to detect subtle cognitive impairments [26,39,40]. As a result, the newly created SCAT5 [41] has been revised to include a 10-word item recall to minimize this ceiling effect.

Female concussed athletes self-reported a higher severity of concussion symptoms on the SCAT3 at 72 h following their injury compared to concussed males. This is consistent with numerous previous studies that reported female concussed athletes had a greater severity in symptoms compared to concussed males [10,13,18,42]. There are several reasons why females may report a greater severity of concussion symptoms compared to males. First, female athletes have been shown to be more honest in reporting their SRC to a health-care professional than males [43]. Thus, females may be more honest in self-reporting their concussion symptoms to their athletic trainer or physician compared to males, which may be reflected in the current study. Second, the concussed females had a greater number of athletes who had a previous history of concussion compared to the concussed males. Previous research has shown that a history of concussion can indicate an increase in symptoms [44]. Third, healthy females have been found to have a higher incidence of migraine symptoms [45] and are almost twice as likely to report persistent posttraumatic headaches compared to healthy males [46]. Researchers have indicated that post-traumatic migraine headaches have been reported in 15-33% of athletes who incur an SRC [47-49]. In addition, concussed females have been found to exhibit greater cognitive-migraine-fatigue symptoms compared to concussed males following injury [18]. Finally, recent studies support that differences between male and female axonal structure and function after injury may be related to increased concussion symptom reporting in females compared to males [50,51]; however, more translational work is needed in this area.

The current study also indicated a main effect for Sex, such that the eBFI scores of females were lower compared to males. However, there were no Sex \times Time interactions in the newly created eBFI among concussed high school and collegiate athletes. This finding is in contrast to other researchers who have previously reported sex differences in EEG spectral activity [23]. Laibow and colleagues [23] indicated that females displayed reduced delta/theta bands and higher alpha and beta bands compared to males. However, the eBFI failed to detect sex differences among concussed athletes. One reason for the lack of sex difference findings may be due to the fact that BrainScope© derived this eBFI calculation using a multimodal assessment of concussion measures including neurocognitive, vestibular/balance symptoms, and EEG [8]. Recent systematic reviews [52,53] of acute and persistent concussion outcomes argue that sex differences may exist, especially in symptom reporting. However, the authors also caution the interpretation of such findings due to the variability in timing and methodologies and inconsistent results of the studies. Likewise, the eBFI additionally includes neurocognitive and EEG performance, in which previous literature provides inconsistent and scarce significant sex differences following concussion [53]. Such findings suggest that the EEG measures included in this eBFI may have negated the sex differences found in symptoms in the current study.

Despite the strengths of this study, there are a number of limitations warranting further discussion. First, this study was limited to a narrow age range (i.e., adolescents and collegiateaged subjects) and athletes on the milder end of the concussion spectrum; thus, findings cannot be generalized to adults older than 25 years old or individuals with more severe injury. Second, this study had a small proportion of females, thereby reducing the conclusions that can be drawn from the lack of significant sex differences observed in the eBFI. In addition, the concussed females had a greater number of athletes who had a previous history of concussion compared to the concussed males. Future research should include a larger sample size with a greater proportion of females. Finally, this study was conducted in only two states (Mid-West, Central Mid-West region), thereby limiting the degree to which these findings can be generalized across the country and other areas of the world. In addition, we could not control for potential differences in providers. However, physicians were told unrestricted clearance was full contact sport and return to school without academic accommodations.

Conclusion

In conclusion, preliminary findings from the present investigation indicate that the eBFI could be a useful tool in assessing an SRC as significantly lower eBFI scores were found in concussed athlete compared to controls at acute assessments post-injury (Day 0, Day 5). The results of this study suggest the utility of the eBFI as an objective measure of impairment following SRC beyond standard clinical assessments. However, this index may lack the sensitivity to detect sex-related differences in concussed athletes. Further research is necessary to examine differences in eBFI using concussed athletes with a more protracted period of recovery (i.e., years following injury) to examine the sensitivity of the eBFI for detecting long-term concussion-related decrements.

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Declaration of interest

Dr. Elbin served as a consultant for BrainScope, Inc.

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