

SEX DIFFERENCES IN NEUROPSYCHOLOGICAL FUNCTION AND POST-CONCUSSION SYMPTOMS OF CONCUSSED COLLEGIATE ATHLETES

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OBJECTIVE: Our purpose was to determine whether sex differences exist with respect to post-concussion symptoms and neurocognitive function in concussed collegiate athletes.

METHODS: A prospective dependent-sample cohort design was used to compare baseline and post-concussion neuropsychological test scores and endorsed symptoms as functions of serial post-concussion assessment with respect to time and sex. The Immediate Post-concussion Assessment and Cognitive Testing (ImPACT) battery was administered to a multicenter analysis group of 79 concussed athletes. This computerized neuropsychological test was given to the athletes during the preseason and, on average, 2 and 8 days postinjury.

RESULTS: Multivariate analyses revealed no significant between-group differences on baseline test performance with respect to sex on any of the ImPACT composite scores or on the total symptom score. Multivariate analyses of post-concussion data revealed a significant main effect of time on ImPACT scores, but no main effect of sex was identified, and no time-by-sex interaction existed. Post hoc analysis revealed that concussed female athletes performed significantly worse than concussed male athletes on visual memory tasks ($P = 0.001$), and analysis of endorsed post-concussion symptoms revealed that concussed men were significantly more likely than concussed women to report post-concussion symptoms of vomiting ($P = 0.001$) and sadness ($P = 0.017$). Athletes' scores were examined individually using the reliable-change methodology. At 2 days post-injury, 58% of concussed athletes had one or more reliable incidents of performance decline or increases in symptom reporting. At 8 days post-concussion, 30% of concussed athletes were still showing one or more reliable change from preseason values.

CONCLUSIONS: College athletes exhibit differences on visual memory composite scores and symptoms post-concussion as a function of sex. These data support the importance of evaluating neuropsychological status and post-concussion symptoms in concussed athletes. In addition, these data illustrate the importance of analyzing an individual athlete's recovery pattern, because individual differences in recovery trajectories may be overshadowed by global norm-group comparisons.

KEY WORDS: Concussion, Immediate Post-concussion Assessment and Cognitive Testing, Neuropsychological functioning, Sex differences

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Approximately 300,000 sport-related concussions are reported each year (40). To date, literature reporting concussions in athletes has been primarily concentrated on men's sports such as football, ice hockey, boxing, and soccer, with few comparisons with regard to sex in concussed athletes (2, 3, 10, 37). However, female athletes have been found to be at a greater risk for concussion in basketball and soccer than male athletes (10). Broshek et al. (6) reported significant declines on

measures of simple and complex reaction times relative to pre-season baseline values in female athletes. Because women's sports participation has expanded significantly during the last decade and brain function differs between the sexes, a comparison of baseline neuropsychological function and post-concussion symptoms is warranted (24, 25, 34, 36, 41).

A concussed athlete may present with numerous signs and symptoms that are not always observable to clinicians,

coaches, sports medicine personnel, or even the athlete. Moreover, an athlete who has suffered a concussion has a three-times-greater risk for experiencing a second concussion during the same season (16). Athletes may be motivated to minimize their symptoms if they wish to continue sport participation (23, 35), and there is evidence that compared with female athletes, male athletes may feel more pressure by their teammates or coaches to play while injured (14). Because of the difficulty of detecting the signs and symptoms of concussion, more objective methods that combine computer-based neuropsychological testing with clinical observation are now available for determining subtle cognitive changes associated with post-concussion in athletes (3, 9, 11, 15, 26). Several researchers have reported neurocognitive impairment of athletes after a concussion (3, 9, 11, 12, 28, 29, 32).

Despite the increase in women's sport participation (36) and sport-related concussion (10), very few researchers have compared sex differences among collegiate athletes who sustain concussion (2, 4, 10, 37). Covassin et al. (10) explored sex differences in the incidence and prevalence of concussion among collegiate athletes competing in soccer, lacrosse, basketball, gymnastics, baseball, and softball. Results of this assessment performed between 1997 and 2000 indicated that women were at a greater risk than men for experiencing concussion during games (9.5% versus 6.4%, respectively). Results also revealed women soccer players had the highest injury rate (1.72 per 1000 athlete-exposures) of concussions, whereas women's lacrosse was found to be associated with the highest inherent risk (14.1%) of sustaining a concussion during a game.

Based on the probability of sex differences in baseline measurements and post-concussion neuropsychological dysfunctions and symptoms, the purpose of our study was to determine whether sex differences exist in relation to post-concussion symptoms and cognition functioning in collegiate athletes.

SUBJECTS AND METHODS

Study Design

A prospective cohort design was used to compare baseline and post-concussion neuropsychological scores and symptoms. The independent variables were sex and time (baseline, up to 3 days, and 7–10 days post-concussion). The dependent variables were scores on a concussion symptom checklist and scores on a computerized neuropsychological test battery.

Subjects

The study population comprised 79 collegiate athletes (from five northeastern universities) who sustained concussion. Participants completed serial post-concussion assessments within the required timeline (as described under Protocol, below). Athletes participated in baseball, women's basketball, cheerleading, football, women's gymnastics, men's ice hockey, men's and women's lacrosse, men's and women's soccer, softball, volleyball, and wrestling (see *Table 1*). Athletes represented the full range of varsity sports and, on average, each athlete had 1.24 years of collegiate experience.

All athletes completed baseline and post-concussion assessments as a requirement for participation in varsity athletics. Inclusion in the research was optional, and we obtained appropriate consent from each

athlete who participated. Institutional Review Board approval for the research study was granted from each participating university, and permission was obtained from all team physicians, athletic directors, athletes, and certified athletic trainers. The sample in this study includes varsity athletes who sustained concussions that required serial testing across all three post-concussion time periods.

Outcome Measures

The Quality Standards Subcommittee of the American Academy of Neurology (AAN) describes cerebral concussion as an altered mental state that may or may not include loss of consciousness (1). The AAN grading scale criteria are used by physicians and certified athletic trainers to classify athletes who experience concussion (*Table 2*). The AAN grading scale is the only commonly used mechanism for categorizing concussions at the various universities. Although some universities also use the Cantu scale, the AAN system is universal across the sites. In our study, certified athletic trainers examined the athletes to identify concussion, and this diagnosis was then confirmed by physicians.

Version 2.0 of the Immediate Post-concussion Assessment and Cognitive Testing (ImPACT) battery was used for this study (30). The ImPACT instrument is a computer-based program used to assess neurocognitive function and concussion symptoms. The software consists of six neurocognitive tests that evaluate verbal recognition memory, visual working memory, visual processing speed, reaction time, numerical sequencing ability, and learning. The characteristics and psychometric properties of the ImPACT battery are well documented (8, 18–21, 27, 28, 30, 38), although it is important to note that these cited validation studies did not examine sex differences.

Protocol

Athletes reported to their own institution's training rooms and then were taken to the computer laboratory by the researchers, where the test procedures were explained. Athletes completed the ImPACT neuropsychological test battery on a computer, which required approximately 30 minutes. Concussed athletes were administered the ImPACT

TABLE 1. Athletes with concussion distributed by sport

Sport	Frequency, no of athletes (N = 79)	Percentage
Wrestling	12	15.2
Women's soccer	10	12.7
Football	9	11.4
Men's soccer	9	11.4
Women's gymnastics	8	10.1
Softball	6	7.6
Women's lacrosse	6	7.6
Men's lacrosse	5	6.3
Cheerleading	3	3.8
Women's basketball	2	2.5
Men's crew	2	2.5
Baseball	2	2.5
Field hockey	2	2.5
Volleyball	2	2.5
Men's ice hockey	1	1.3

TABLE 2. American Academy of Neurology concussion grading scale

Grade 1	Grade 2	Grade 3
Transient confusion	Transient confusion	
No loss of consciousness	No loss of consciousness	Brief or prolonged loss of consciousness
Concussion symptoms or mental status change resolves in 15 min or less	Concussion symptoms or mental status change resolves in more than 15 min	

test up to 3 days (mean, 1.89 days; standard deviation, 0.83 days) and 7 to 10 days postinjury (mean, 8.11 days, standard deviation, 1.1 days).

Data Analysis

The ImPACT series yields individual scores as well as composite scores for verbal memory, visual memory, processing speed, and reaction time. Higher scores on verbal memory, visual memory, and processing speed indicate better performance. Verbal memory and visual memory scores are presented as percentages of 100, and processing speed is indicated as a composite score. The composite score for processing speed is the average of two test scores: namely, the total correct number of X's and O's observed, multiplied by interference divided by four; and the average number of instances that three-letter groups were correctly identified, multiplied by three. A lower score on the reaction time test indicates better performance. All reaction-time scores are measured and presented in seconds. The ImPACT battery also yields individual scores for concussion symptoms. Athletes are required to indicate whether they are presently experiencing any of 22 noted concussion symptoms. The concussion symptoms are rated on a six-point Likert scale, with zero indicating the symptom is not present and five indicating the symptom is present and severe.

A two-sex (male, female) by three times post-concussion (baseline, up to 3 days, and 7–10 days) analysis of variance with repeated measures on the last factor was conducted to assess neuropsychological function and concussion symptoms. All four neuropsychological test scores were analyzed individually using a repeated-measure analysis of variance. The level of significance (P) was set at 0.05. All analyses were conducted using the Statistical Package for the Social Sciences version 11.1 (SPSS, Inc., Chicago, IL) (39).

RESULTS

Sample Characteristics and Comparisons at Baseline

During the 2-year study, a total of 79 athletes (41 men and 38 women) sustained concussions that warranted serial assessment, which was completed within the required time parameters. Of the 79 concussed athletes, 62% (49 athletes; 24 men and 25 women) were classified as Grade 1, 34% (27 athletes; 14 men and 13 women) were classified as Grade 2, and 4% (3 athletes, all men) were classified as Grade 3. A χ^2 analysis revealed no greater likelihood of sustaining a Grade 2 or 3 concussion as a function of sex ($\chi^2_1 = 0.44$; $P = 0.50$). A total of 41 concussed athletes (52%) reported a previous history of concussion, with 20% reporting a history of one concussion and 32% reporting a history of two or more concussions. However, multivariate analysis of variance revealed no significant differences for baseline tests or total symptom scores between concussed athletes on the basis of concussion history ($F_{10,144} = 1.67$; $P = 0.10$). In

terms of on-field markers, 10 male (24%) and 5 female (13.2%) athletes suffered loss of consciousness. Eight men (19.5%) and 6 women (15.8%) reported both retrograde and anterograde amnesia after concussion.

Multivariate analysis of variance revealed no significant between-group differences for baseline test performance with regard to sex on any of the ImPACT composite scores or on the total symptom score ($F_{5,73} = 0.80$; $P = 0.55$; Table 3). As such, baseline performance scores were not used as covariates when we compared the effects of sex on post-concussion performance.

Post-concussion Comparisons

A 3×2 mixed-factorial design multivariate analysis of variance was conducted with time (baseline, up to 3 days, and up to 10 days) and sex (male and female) as the factors, and the ImPACT indices and total symptom scores as the dependent variables. Wilke's Lambda revealed a multivariate repeated-measures effect (time) on ImPACT performance ($F_{2,76} = 1670$; $P = 0.0001$; $\eta^2 = 0.98$) with significant declines noted from baseline to 3 days ($\eta^2 = 0.56$) and from baseline to 10 days ($\eta^2 = 0.74$). No between-subject multivariate effect of sex ($F_{1,77} = 0.16$; $P = 0.69$; $\eta^2 = 0.002$), and no significant sex-by-time interaction ($F_{2,76} = 0.54$; $P = 0.59$; $\eta^2 = 0.01$) were identified.

Univariate post hoc analysis of post-concussion data revealed that concussed female athletes performed significantly worse than concussed male athletes on visual memory scores ($F_{1,77} = 11.26$; $P = 0.001$) at 3 days post-concussion (Table 4), with no significant univariate effects of sex noted on

TABLE 3. Baseline neuropsychological test values and total symptom scores distributed by sex^a

ImPACT index	Men, mean (SD)	Women, mean (SD)	F test	P value
Verbal memory	0.88 (0.09)	0.90 (0.08)	1.23	0.26
Visual memory	0.78 (0.11)	0.74 (0.18)	1.55	0.22
Reaction time	0.53 (0.06)	0.53 (0.09)	0.03	0.86
Processing speed	39.61 (5.85)	39.38 (7.14)	0.03	0.88
Total symptoms	7.83 (7.4)	8.29 (8.5)	0.06	0.80

^a SD, standard deviation; ImPACT, Immediate Post-concussion Assessment and Cognitive Testing battery; N = 79 athletes.

TABLE 4. Post-concussion ImpACT and total symptom scores distributed by sex^a

ImpACT index	Score		F	P
	Men, mean (SD)	Women, mean (SD)		
Visual memory				
Baseline	0.78 (0.11)	0.74 0 (0.18)	11.26	0.001
Post-test 1	0.75 (0.11)	0.61 0 (0.09)		
Post-test 2	0.76 (0.11)	0.74 0 (0.11)		
Reaction time				
Baseline	0.53 (0.06)	0.53 (0.09)	0.75	0.39
Post-test 1	0.58 (0.11)	0.58 (0.12)		
Post-test 2	0.57 (0.10)	0.53 (0.07)		
Verbal memory				
Baseline	0.88 (0.09)	0.90 (0.08)	0.70	0.41
Post-test 1	0.78 (0.13)	0.81 (0.13)		
Post-test 2	0.85 (0.09)	0.85 (0.10)		
Processing speed				
Baseline	39.61 (5.85)	39.38 (7.14)	0.79	0.38
Post-test 1	35.74 (9.58)	37.29 (9.06)		
Post-test 2	38.81 (6.77)	41.04 (7.98)		
Total symptoms				
Baseline	7.83 (7.38)	8.29 (8.53)	0.01	0.99
Post-test 1	20.85 (19.40)	20.61 (21.01)		
Post-test 2	12.71 (9.96)	12.53 (13.52)		

^a ImpACT, Immediate Post-concussion Assessment and Cognitive Testing battery; SD, standard deviation; N = 79 athletes.

TABLE 5. Symptom of vomiting as reported by men versus women with respect to time

Symptom: vomiting	Men	Women	F	P
Baseline	1.22 (1.6)	0.11 (0.4)	13.05	0.001
Post-test 1	1.98 (1.7)	0.87 (1.2)		
Post-test 2	0.73 (0.11)	1.08 (1.3)		

reaction time ($F_{1,77} = 0.75$; $P = 0.39$), motor processing speed ($F_{1,77} = 0.80$; $P = 0.38$), and verbal memory ($F_{1,77} = 0.70$; $P = 0.41$). Post hoc analysis of symptom scores revealed that concussed male athletes reported significantly higher symptom scores for sadness ($F_{1,77} = 13.05$; $P = 0.001$) and vomiting ($F_{1,77} = 5.95$; $P = 0.017$), with no other significant between-group differences for symptom scores. A significant time-by-sex interaction was also noted on reports of post-concussive vomiting ($F_{1,77} = 17.70$; $P = 0.001$), with no other time-by-sex interactions noted for any of the other post-concussion symptoms (Table 5).

TABLE 6. Reliable change indices with respect to time and sex

	1 Reliable change index	2 Reliable change indices
Baseline to Time 1	58.23%	26.58%
Men	58.54%	26.83%
Women	57.89%	26.32%
Baseline to Time 2	31.65%	7.59%
Men	31.71%	7.32%
Women	31.58%	7.89%

Reliable change indices were calculated to determine clinically significant decreases (or improvements) while reducing any effects of measurement error (Table 6). The use of reliable change index is well documented, and we used the original formula proposed by Jacobson and Traux (22). (A discussion of application and implementation of reliable change indices using ImpACT was recently published by Iverson et al. [17].) At Time 1 (up to 3 days postinjury), 58% of participants had one or more reliable declines in performance or increases in symptom reporting. At Time 2 (up to 10 days postinjury), 30% of participants were still showing one or more reliable changes from preseason levels.

DISCUSSION

This study identified post-concussion differences with regard to sex in only one of five cognitive domains of neuropsychological function. Specifically, concussed female athletes demonstrated significantly lower visual memory composite scores compared with male athletes. With respect to post-concussion symptoms, men reported post-concussion vomiting and sadness with greater frequency and intensity than women. At present, there is a paucity of literature on post-concussion sex differences. Chan (7) reported that a relatively large proportion of participants reported symptoms similar to those of patients with post-concussion syndrome, including longer time to think, forgetfulness, poor concentration, fatigue, and sleep disturbances, although no effects of sex were noted. With respect to post-concussion symptoms, in a meta-analysis of sex differences in traumatic brain injury outcome, Farace and Alves (13) reported that women fared worse than men on 85% of the measured variables, which were primarily somatic symptoms including poor memory, dizziness, fatigue, irritability in response to light and noise, impaired concentration, headache, anxiety, and depression, with men faring worse only on auditory symptoms.

More recently, Broshek et al. (6) identified post-concussion sex differences; in that study, women showed significantly decreased simple and complex reaction times and processing speed, as well as a greater number of post-concussion symptoms. However, their sample was composed of both high school and college athletes, with significantly fewer women than men (28 versus 72%). Our results are inconsistent with

these findings; in our study, male (not female) athletes were more likely to endorse specific symptoms (e.g., sadness and vomiting). Our results are also inconsistent with previous studies that have shown an increased likelihood of females reporting more symptoms after head injury (5). It is not clear why we identified post-concussion sex differences in only one domain of cognitive functioning. Our study was composed of nearly equal numbers of male and female collegiate athletes, and as such, there is no existing study in the literature for comparison. Given the limited focus on post-concussion sex differences in this growing body of literature on assessment and management of sports-related concussion, more research is warranted.

With respect to the increased incidence of men reporting specific symptoms, previous researchers have linked post-concussive vomiting with increased injury severity in males (31, 33). Granite and Carroll (14) suggest that male athletes often feel pressure from coaches and teammates to “play through pain,” so reactive depression (e.g., sadness) may occur as a result of removal from athletic competition. In this context, female athletes have been shown to be more concerned about the effects of an injury on their future health (14), and may not be as affected as male athletes when told they cannot participate.

Given that a significant portion of athletes showed reliable change from baseline in one or more cognitive domains at 3 days and at 7–10 days post-concussion, sports medicine personnel should closely monitor all athletes for symptoms or overt neuropsychological impairments. Post-concussive athletes should not be allowed to return to participation until they are free of symptoms and their cognition has returned to normal or baseline levels of functioning (19).

This study is not without its limitations. Foremost, the low sample size for concussed athletes may have lowered our ability to identify sex differences in recovery rates. However, as a preliminary report on sex differences found in post-concussion neuropsychological function and symptoms, the present research is well founded, and the results have clinical utility. Sports medicine professionals need to be cognizant of post-concussive symptoms to question and evaluate athletes who have sustained a concussion. For example, clinicians evaluating a concussed female athlete demonstrating a lower visual memory score should include additional follow-up tests that challenge visual awareness, such as the Rhomberg test. Furthermore, male athletes should be watched closely for changes in mood and expression. Future research should focus on the relationship between baseline differences and post-concussion symptoms, as well as the history of concussion, multiple concussions, and the potential for long-term permanent deficits.

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COMMENTS

The introduction of computerized neurocognitive testing has made the assessment of subtle sequelae related to cerebral and sports-related concussion a reality. As such, quantification of cerebral concussion is possible and data-driven approaches to sports concussion management and return-to-play decisions are becoming commonplace across all levels of sports participation. Studies that further introduce and expand upon our knowledge of the presentation of sports concussion are a valuable contribution to the literature. The current study is one such analysis, especially because a paucity of data exists examining potential gender differences in terms of presentation and recovery from sports-related concussion.

The current analysis provides data to suggest that female athletes may potentially respond differently in terms of recovery and presentation after sports-related concussion when compared with their male counterparts. Within this context, and per the authors' admission, the current data should be considered preliminary and further study is indicated. The relatively small sample size is a weakness of the analysis. Also, the authors seem to generalize from limited and attenuated differences between the two study groups. There were no symptom differences at baseline between the groups, which is somewhat surprising. Based on the existing literature, one would expect sex differences in

terms of both symptom reporting and aspects of the baseline neurocognitive data. Moreover, there were sex differences between only two of the 22 symptoms that were measured after injury. In addition, the authors found differences between vomiting and sadness, likely a statistical anomaly, especially because these are symptoms that are very infrequently reported by concussed athletes. The lack of differences between these groups is quite surprising and may actually reinforce similarities between men and women in terms of recovery. Within this context and in relation to the more objective neurocognitive data, it is felt that the statistically significant differences in terms of ImPACT visual memory scores may be a germane, meaningful finding that is certainly deserving of further study.

In summary, the current study provides an excellent methodology to study the phenomenon of sports-related concussion. The study is well thought-out and controlled. In addition, a paucity of data exists examining the meaningful question of sex differences in terms of presentation and recovery from sports-related concussion. The authors also provide a reasonable theory, albeit speculative, as to why physiological differences may occur across sexes in response to sports concussion. Lastly, the sensitivity and specificity of the ImPACT program is well established and current data support the utility of this approach in researching, as well as clinically managing, sports concussive injury. The current study should be considered a preliminary and meaningful first step, although further analysis is certainly indicated.

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Covassin et al.'s study attempted to determine if sex differences exist in post-concussion symptoms and neurocognitive function in concussed collegiate athletes. Although there was a small sample size of concussed collegiate athletes (79) in this study, results showed that female athletes performed significantly worse than males on visual memory scores and that male athletes were significantly more likely to report post-concussion symptoms of vomiting and sadness. This study further emphasizes the need for baseline and post-concussion neuropsychological testing as well as a reliable symptom reporting system. At our institution, we also perform baseline and post-concussion balance testing among our players involved in sports with the highest risk of concussion. We consider ourselves very fortunate to have experienced neurosurgeons as team physicians to direct us in treating trauma to the neurological system.

Russ Romano
Head Athletic Trainer
Los Angeles, California

Covassin et al. have conducted a prospective study of 79 collegiate athletes who sustained concussions, analyzing their results of neuropsychological testing and clinical recovery. They found that concussion in female athletes was associated with poorer performance in the cognitive domain of visual memory testing. In symptomatology, males reported a higher incidence of vomiting and sadness.

For those caring for the injured athlete, this study addresses an issue that is often underappreciated, i.e., that there may be significant differences related to physiology, performance capabilities, and expectations between the sexes, which influence diagnosis and return-to-play decisions. Although it may be considered preliminary data and limited by a specific population, this study adds to our knowledge and heightens our ability to discern these differences, especially as we are seeing

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more female athletes involved in contact or collisions in sports. Clinicians should be aware of these findings and incorporate them into their management schemes to optimize the care of the sports concussion patient.

Julian E. Bailes
Morgantown, West Virginia

This study is important because it shows the potential importance of an understudied area: sex differences in response to concussion. The authors conclude with a tone of appropriate puzzlement regarding

the disparity of their findings compared with those of the very small number of other comparable studies. Moreover, the authors clearly state that their study can demonstrate the potential importance of sex-related issues, but that further research is needed to clarify and resolve these issues. Sex and ethnic differences are increasingly being shown to be important in diverse areas of medicine, and this study is valuable in raising such questions regarding concussion.

Joseph Bleiberg
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The Old Guitarist by Picasso, 1903. Oil on wood. Courtesy of The Art Institute of Chicago.