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# Sex Differences in Vestibular/Ocular and Neurocognitive outcomes following Sport-related Concussion

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## Abstract

**Objective—**To examine sex differences in vestibular and oculomotor symptoms and impairment in athletes with sport-related concussion (SRC). The secondary purpose was to replicate previously reported sex differences in total concussion symptoms, and performance on neurocognitive and balance testing.

**Design—**Prospective cross-sectional study of consecutively enrolled clinic patients within 21 days of a SRC.

**Setting—**Specialty Concussion Clinic

**Participants—**Included male (n = 36) and female (n = 28) athletes ages 9–18 years

**Interventions—**Vestibular symptoms and impairment was measured with the Vestibular/Ocular Motor Screening (VOMS). Participants completed the Immediate Post-concussion Assessment and Cognitive Test (ImPACT), Post-concussion Symptom Scale (PCSS), and Balance Error Scoring System (BESS).

**Main Outcomes Measures—**Sex differences on clinical measures.

**Results—**Females had higher PCSS scores ($p = .01$) and greater VOMS VOR score ($p = .01$) compared to males. There were no sex differences on BESS or ImPACT. Total PCSS scores together with female sex accounted for 45% of the variance in VOR scores.

**Conclusions—**Findings suggest higher VOR scores following SRC in female compared to male athletes. Findings did not extend to other components of the VOMS tool suggesting that sex

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differences may be specific to certain types of vestibular impairment following SRC. Additional research on the clinical significance of the current findings is needed.

**Keywords**

concussion; adolescents; vestibular; ocular; sex differences

## INTRODUCTION

Sport-related concussion (SRC) continues to be a major health concern for children, with an estimated 3.8 million per year in the U.S.[26]. Recently, the role of sex on SRC outcomes in children has received considerable attention from researchers [11–14]. Following a SRC, females endorse more overall symptoms than males [5, 8, 11, 36] and experience slower resolution of those symptoms [36]. Specific differences in post-concussion symptom presentation have also been identified, with females endorsing more cognitive symptoms [18], as well as symptoms related to migraine [11] and dizziness [5] than males. Similarly, females experience worse neurocognitive impairment in the acute stage of recovery following SRC. Specifically, females were 1.5 times more likely than males to experience neurocognitive impairment following SRC, and demonstrated a greater decline in scores compared to baseline [5, 13, 16]. However, little is known about sex differences in vestibular and oculomotor impairment and symptoms following concussion.

Researchers have recently reported that 60 – 70% of children experience vestibular and/or oculomotor impairment and symptoms following SRC [9, 32]. Vestibular impairment and symptoms may include disequilibrium and impaired balance, dizziness, vertigo, blurred/unstable vision, discomfort in busy environments and nausea often occur with disruption to the vestibulo-ocular system [19]. Oculomotor impairment and symptoms may include blurred vision, diplopia, difficulty reading, eyestrain, headache, reading difficulties, and problems with visual scanning [4]. Previous investigations of sex differences in post-concussion vestibular functioning have focused on vestibulo-spinal impairments (i.e., imbalance) associated with SRC. Researchers have documented that among healthy children, females demonstrate better balance compared to males [27, 30]. High school male athletes performed worse than females on a clinical assessment of balance (i.e., Balance Error Scoring System [BESS]) following SRC [13]. Further assessments of sex differences in vestibular and ocular functions, which are neurologically distinct from balance [35], are warranted. Researchers suggest that females with vestibular conditions unrelated to head injury report more symptomatic and present more psychiatric distress than males [17, 31]. Migraine and hormonal differences, both of which influence vestibular functioning [23, 34], have been posited for these exacerbated vestibular outcomes in females post-concussion [5]. However, little is known about these outcomes following SRC. One reason for the dearth of research in this area is the lack of assessments that focus on vestibular and oculomotor impairment following SRC.

Recently, we reported findings for a new tool, the Vestibular/Ocular Motor Screening (VOMS), that assesses vestibular and oculomotor impairment and symptoms following SRC [32]. The VOMS consists of brief, standardized assessments of pursuits, saccades, near point convergence (NPC), vestibular ocular reflex (VOR), and visual motion sensitivity (VMS). Our preliminary findings indicated that over 60% of adolescent athletes experience one or more vestibular/ocular motor impairments or symptoms following SRC [32]. We also reported that the VOMS was nearly 90% accurate in identifying patients with concussion from controls. However, we did not examine sex differences in this initial study. Given the reported sex differences in concussion risk and outcomes, additional research examining the role that sex may have on vestibular and oculomotor outcomes following SRC is needed.

The primary purpose of the current study was to compare vestibular and oculomotor impairment and symptoms following SRC between male and female youth athletes. We expected that females would experience more vestibular and oculomotor impairment and symptoms following SRC than males. Given that SRC is a heterogeneous phenomenon involving different clinical outcomes or trajectories [7] we also compared balance and neurocognitive impairment, and concussion symptoms between males and females following SRC. With the exception of balance, we expected that females would experience more impairment and symptoms following SRC than males.

# METHODS

## Participants and Design

We conducted a cross-sectional study of patients aged 9–18 years who were consecutively enrolled at a sports concussion clinic with a diagnosed SRC within 21 days of their injury. All participants were injured while playing scholastic or other organized sports, and referred by certified athletic trainer, team physician, primary care physician, or pediatrician. Diagnosis was confirmed by licensed medical professionals with specialized training in concussion per the definition from McCrory et al.[29]. A total of 85 patients who were eligible for the study (per the exclusion criteria below) were consented and enrolled into the study between August 2013 and December 2013. Exclusion criteria included history of two or more concussions, brain surgery, neurological disorder (e.g., migraine, seizure disorder), vestibular (e.g. benign paroxysmal positional vertigo, unilateral or bilateral vestibular hypofunction) or visual (e.g., strabismus, diplopia, saccadic/pursuit deficiencies) dysfunction, treatment for substance abuse, and/or psychiatric disorder.

## Instrumentation

**The Vestibular/Ocular Motor Screening (VOMS) Assessment—**The VOMS was developed to assess vestibular and ocular motor impairments following SRC. The VOMS consists of brief assessments in the following five domains: (1) smooth pursuit, (2) horizontal and vertical saccades, (3) near point of convergence (NPC), (4) horizontal VOR, and (5) visual motion sensitivity (VMS). Patients report symptom provocation for each of four symptoms - headache, dizziness, nausea, and fogginess - on a 10-point scale from 0 (none) to 10 (severe) after each assessment. Symptom totals for each of the five domains are then calculated to provide a total symptom provocation score. In addition to symptom provocation, NPC distance is measured with a standard Gulick anthropometric tape measure (cm) and fixation stick that included a target letter in 12 pt font. Three consecutive measures of NPC are conducted. In previous research the internal consistency of the VOMS was high

(Cronbach α = .92) [32]. The VOMS takes 5 min to administer, and is described elsewhere in more detail [32].

**Neurocognitive Assessment—**The Immediate Post-concussion Assessment and Cognitive Testing (ImPACT) is a computer-based neurocognitive test battery comprised of 6 subtests designed to examine neurocognitive impairment in individuals with a SRC. The ImPACT test yields four composite scores for verbal memory, visual memory, processing speed, and reaction time. The ImPACT has adequate reliability and validity as reported elsewhere [1, 33]. The ImPACT takes approximately 20 – 25 min to administer.

**Concussion-related Symptoms—**The Post-concussion Symptom Scale (PCSS) is a computerized self-report inventory of 22 items representing somatic (e.g., nausea, headache), cognitive (difficulty concentrating, memory problems), affective (e.g., anxiety, depression), and sleep-related symptoms. Participants rate each symptom on a 7-point Likert scale from 0 (none) to 6 (severe). The PCSS has adequate reliability and validity for assessing and monitoring of SRC-related symptoms [28]. The PCSS takes 5 min to administer.

**Balance—**The Balance Error Scoring System (BESS) is a clinical balance assessment developed to evaluate static and dynamic postural stability following SRC [21]. A trained observer assesses 6 balance conditions (3 conditions with feet on the floor, and 3 conditions with feet on a foam pad) with eyes closed. A total BESS score is determined by counting the number of errors across all conditions, with higher scores representing worse balance. A comprehensive description and detailed psychometric properties for the BESS are described elsewhere [20]. In this study a single trained therapist was used to eliminate potential concern with interrater reliability.

## Procedures

The study protocol was approved by the University of Pittsburgh Human Subjects Institutional Review Board. All participants were evaluated by a trained physical therapist. Participants were administered the assessments during their initial clinical visit following a SRC, in the following order: 1) symptom self-report, 2) neurocognitive, 3) balance, 4) vestibular/oculomotor. All assessments were conducted in a private exam room by the same therapist.

## Data Analysis

Mann-Whitney U or chi-square tests were used to compare males and females on demographic variables, ImPACT composites, total PCSS scores, BESS scores, and VOMS scores. Significant sex group differences on VOMS symptom scores and NPC distance were tested for optimal cut points to dichotomize the measure. Any VOMS item demonstrating a significant sex group difference was dichotomized at the optimal cut point that maximized sex difference using receiver operating characteristic (ROC) curve with are under the curve (AUC) analysis. The symptom cutoff score was selected that demonstrated the maximum sum of sensitivity and specificity for identifying female subjects while retaining a significant univariate association with sex. The effect of sex on VOMS scores was tested using a generalized linear model (GLM) to estimate the effect of sex on VOMS scores with adjustment for significant demographic and concussion-related covariates demonstrated identified in the sex group comparisons. The assumption of residual value normality was tested using the Shapiro Wilk test. A logistic regression model was also used to test the association of sex and dichotomized VOMS scores identified from ROC AUC analysis with adjustment for significant covariates for group difference. A $p < .05$ was used for all statistical tests.

# RESULTS

## Sex Differences

Complete data were available for a total of 64 (36 males, 28 females) of 85 (75%) participants enrolled in the study. A summary of demographic and concussion related data for the sample is provided in Table 1. The results of a Mann-Whitney U test supported higher mean total concussion symptom scores for females compared to males ($p = .01$). The results did not support any other statistical differences between males and females on demographics, signs of concussion at time of injury, or balance and neurocognitive outcomes following SRC. A summary of VOMS data for the sample is provided in Table 2. The results of a Mann-Whitney U test supported a significantly greater VOR score for females compared to males ($p = .01$) (Table 2). Males and females were not significantly different on any other VOMS item.

## The Effect of Sex on VOMS

Analysis of the ROC for the VOR score demonstrated a significant AUC = .72 (*95% CI* = .59–.86, $p = .002$). A VOR symptom score cut-point of >= 3 optimally identified female subjects at 68% sensitivity and 72% specificity. With adjustment for total symptoms score (mean = 28.2), mean VOR scores were significantly greater in females (5.0, *95% CI* = 3.5–6.5) compared to males (2.7, *95% CI* = 1.4–4.0, $p = .03$, Figure 1). A linear regression model with sex and total symptom score predicted 45% of the variance in VOR total symptom score with residual values conforming to a normal distribution at $p = .18$ (Table 3).

The results from a logistic regression model demonstrated that sex ($p = .025$) and total symptoms score ($p = .016$) were independent and significant predictors of the likelihood of a VOR score >=3 (−2 log likelihood compared with constant = 70.76, $p < .001$). Females were more likely to demonstrate a VOR symptom score greater than or equal to the cutoff score of 3. This two-factor model predicted 32% of the variance in the likelihood and correctly identified 75% of subjects with VOMS VOR symptoms score >=3.

# DISCUSSION

In the current study we examined post-concussion sex differences in vestibular and oculomotor impairment and symptoms using the recently developed VOMS screening tool. There were two primary findings from our study: 1) females reported more symptoms on the VOR component of the VOMS and more total concussion symptoms than males following SRC; and 2) previously reported sex differences on neurocognitive and balance outcomes following SRC were not supported in the current findings. Our hypothesis that females would report more symptoms on the VOMS was partially supported, with only the VOR component of the VOMS demonstrating this pattern. A cutoff value for horizontal VOR (symptom score >=3) demonstrated significant accuracy to discriminate concussed female athletes from males.”. Moreover, total concussion symptom scores together with female sex accounted for 45% of the variance in VOR scores in our study. It is important to note that although the findings supported only one statistical difference between males and females for the VOR, females demonstrated a non-significant trend for higher scores across all other VOMS components (see Table 2). The results did not support sex differences in neurocognitive or balance outcomes.

The primary finding of the current study supported higher VOR scores following SRC for females compared to males. Although VOR was the only score that was higher for females, the effect size was medium to large. In previous research, VOR was best at distinguishing concussed athletes from controls compared to the other VOMS items [32]. VOR is among the most common vestibular impairments following SRC [9, 35]. It is possible that females’ SRCs may represent different clinical trajectories than males, as reported by Collins and colleagues [7]. Specifically, females may be more likely to follow a vestibular trajectory, with persistent vestibular dysfunction and symptoms weeks to months following SRC, compared to males. It has also been suggested that VOR may relate to migraine symptoms [24] and motion sickness [25], which are more prevalent in females and common sequelae of SRC. These relationships may underlie the sex differences reported for VOR in the current study, and may be relevant for clinicians to assess following SRC. Further, this finding offers explanation for why some female athletes perform normally on neurocognitive and balance testing, but remain symptomatic following SRC.

Researchers have suggested that sex differences in concussion outcomes are prevalent [5, 8, 11, 36]. Consistent with this prior research, female athletes in our study reported higher total concussion symptom scores following SRC than males. In fact, higher reported total symptom scores following SRC among females is the most consistent finding supporting sex differences reported in the literature [5, 8, 11]. Our findings are consistent with Berz et al [2], who examined a similar sample (9–17 years old athletes) and found female athletes to be more symptomatic for a longer period following injury, in the absence of differences in neurocognitive scores. With the exception of Berz et al., the lack of sex differences in neurocognitive performance in our study is not supported by previous literature [5, 11, 16]. However, in contrast to these studies that examined sex outcomes in the acute stage of recovery in a select age group, our study included athletes with a longer time since injury (up to 21 days), and the current sample is younger, with a mean age around 14 years of age. As such, the lack of support for sex differences in the current study may suggest that sex does not play a role in outcomes following SRC until post-adolescence (i.e., high school and college aged). This supposition makes sense, as post-pubertal differences between males and females are more substantial than differences prior to puberty [15] and hormonal changes have been linked to vestibular symptoms [3, 22]. With regard to balance, the current sample included a younger sample, and previous research with high school aged samples reported no differences in balance following SRC [10]. This finding may be related to the influence of age- i.e., the lack of reported differences in children and adolescents. Given that the time since injury in the current study ranged up to 21 days post-injury, the previously reported reduced sensitivity of balance testing beyond 72 hours post injury [13] may have played a role in the lack of balance findings in the current study.

Our study was the first to examine sex differences in vestibular and oculomotor impairment and symptoms following SRC. Although sex differences were supported for VOR with a medium to large effect size, there were methodological limitations to the study that may have influenced our findings. For example, the sample size was fairly small, included uneven group sizes, and was largely heterogeneous in nature. The participants were enrolled into the study in a convenient manner using consecutive patient enrollments. The large age range (9–18 years) of participants represented various developmental stages, and younger participants may have had less insight and difficulty articulating their symptoms. Even though we excluded participants with pre-existing vestibular conditions, the younger ages of our sample may have precluded them from a formal diagnosis at this point in their lives. The variability in time since injury (e.g., up to 21 days post injury) could influence outcomes. However, as reported there were no significant differences between males and females on time since injury. Nonetheless, the variability in time since injury for the overall sample may have influenced the results. This sample was drawn from a concussion specialty clinic, and may be subject to referral bias for participants with more severe injuries. The prevalence of vestibular dysfunction following concussion is limited to research conducted in specialty clinics [9, 32], and may not be reflective of less severe injury. We employed subjective symptom reports that are subject to recall bias. Further, baseline neurocognitive testing was not available for participants, and there was no measure of effort or engagement during testing.

Moving forward, researchers should collect data at more succinct time points and examine the interaction of age and sex. Studies with larger samples sizes that include both collegiate and high school aged samples are warranted. In addition, a temporal comparison of VOMS and other assessments would help elucidate recovery trajectories and aid in clinical decision making. Given that the range of scores across the VOMS components was much larger for females, researchers should examine potential moderating factors that might have explained the variability in these scores. Additional participant characteristics that may influence vestibular and oculomotor outcomes following SRC such as history of migraine should be included in future studies. Finally, researchers should extend the current study and examine VOMS and other outcomes in regard to the efficacy of vestibular and vision therapies.

## CONCLUSION

The current study was the first to examine sex differences in vestibular and oculomotor impairment and symptoms following SRC. The current findings provide preliminary evidence for higher VOR scores following SRC in female compared to male athletes evaluated <21 days post injury. Clinicians should pay close attention to VOR in females following this injury. The difference in VOR did not extend to other components of the VOMS tool used in the current study, suggesting that sex differences may be specific to certain types of vestibular and oculomotor impairment and symptoms following SRC. As expected, females reported higher total concussion symptom scores than males. However, the current study's findings did not support sex differences in neurocognitive or balance impairment. Additional research on the clinical significance of the current findings, and the nature of the relationship between the VOMS and other concussion risk factors (e.g., migraine history, age) that moderate sex differences is needed.

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## TABLE 1

Demographic and Concussion-related Characteristics for Male (n = 36) and Female (n = 28) Participants following a Sport-related Concussion.

| Characteristic | Male mean ± SD (range) | Female mean ± SD (range) | $p^*$ |
|---|---|---|---|
| Age (years) | 13.6 ± 2.8 (9–18) | 14.3 ± 2.1 (10–18) | .26 |
| Days Since Injury | 4.5 ± 3.3 (1–16) | 6.0 ± 4.7 (1–21) | .12 |
| Number (%) with previous concussions | 8 (22) | 6 (21) | .94 |
| Number (%) with Learning Disability | 1 (3) | 1 (4) | *.86* |
| Number (%) with LOC | 4 (13) | 3 (11) | *.80* |
| Number (%) with Post-traumatic amnesia | 6 (17) | 1 (4) | *.09* |
| Number (%) with Confusion/Disorientation | 9 (25) | 7 (25) | *.99* |
| Verbal Memory | 79.3 ± 15.7 (42–100) | 77.6 ± 17.3 (32–100) | .80 |
| Visual Memory | 67.6 ± 16.1 (35–94) | 65.6±18.1 (19–96) | .61 |
| Motor Processing | 31.5±9.4 (18.7–52.1) | 31.6±10.4 (10.5–48.0) | .77 |
| Reaction Time | .70±.12 (.45–1.03) | .74 ± .24 (.47–1.49) | .74 |
| PCSS | 20.8±17.0 (0–63) | 37.7±26.2 (0–99) | .01 |
| BESS | 12.5±8.2 (2–50) | 13.0±10.2 (6–60) | .84 |

*Mann-Whitney U non-parametric or Chi-square for categorical variables

## TABLE 2

A Comparison of Vestibular/Ocular Motor Screening Assessment Scores between Male (n = 36) and Female (n = 28) Participants following Sport-related Concussion

| VOMS Item | Male mean ± SD (range) | Female mean ± SD (range) | Group Difference Significance* |
|---|---|---|---|
| Smooth Pursuits | 1.4 ± 2.7 (0–10) | 3.1 ± 6.5 (0–31) | $p = .44$ |
| Horizontal Saccades | 1.9 ± 3.1 (0–11) | 3.3 ± 6.4 (0–29) | $p =.67$ |
| Vertical Saccades | 1.6 ± 3.2 (0–11) | 2.86 ± 5.9 (0–29) | $p = .46$ |
| Convergence (Symptoms) | 1.8 ± 3.0 (0–11) | 2.8 ± 5.1 (0–20) | $p = .80$ |
| Horizontal Vestibular Ocular Reflex | 1.78 ± 2.5 (0–11) | 6.1 ± 6.4 (0–22) | $p =. 01$ |
| Visual Motion Sensitivity | 1.9 ± 3.2 (0–12) | 4.6 ± 7.5 (0–35) | $p = .18$ |
| Near Point of Convergence Distance (cm) | 4.5 ± 4.6 (0–21) | 7.5 ± 10.4 (0–41) | $p = .72$ |

*Mann-Whitney U non-parametric

## TABLE 3

Generalized Linear Model for Sex as Predictive of Horizontal Vestibular Ocular Reflex Scores in Males (n= 36) and Females (n= 28) following Sport-related Concussion with Adjustment for Total Symptom Score (beta coefficients, significance levels, coefficients of determination)

| Variable | β | SE β | Significance | Partial R-Squared[†] |
|---|---|---|---|---|
| Total Symptom Score | .122 | .023 | <.01 | .32 |
| Female Sex | 2.33 | 1.04 | .03 | .07 |

[†]Total Model R-squared = 45%