

# Investigating baseline neurocognitive performance between male and female athletes with a history of multiple concussion

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## ABSTRACT

**Objective** The purpose of this study was to examine, using a dose—response model, sex differences in computerised neurocognitive performance among athletes with a history of multiple concussions.

**Design** Retrospective with randomly selected concussion cases from four levels/numbers of previous concussion.

**Setting** Multicentre analysis of NCAA student-athletes.

**Participants** Subjects included a total of 100 male and 88 female NCAA athletes.

**Intervention** Sex and four mutually exclusive groups of self-reported concussion history: (1) no history of concussion, (2) one previous concussion, (3) two previous concussions, (4) three or more previous concussions.

**Main outcome measurements** Neurocognitive performance as measured by a computerised neurocognitive test battery (Immediate Postconcussion Assessment Cognitive Testing (ImPACT)).

**Results** A dose—response gradient was found for two or more previous concussions and decreased neurocognitive performance. Females with a history of two and three or more concussions performed better than males with a history of two ( $p=0.001$ ) and three or more concussions ( $p=0.012$ ) on verbal memory. Females performed better than males with a history of three or more concussions ( $p=0.021$ ) on visual memory. Finally, there was a significant difference for sex on both motor processing speed and reaction-time composite scores. Specifically, males performed worse than females on both processing speed ( $p=0.029$ ) and reaction time ( $p=0.04$ ).

**Conclusion** The current study provided partial support for a dose—response model of concussion and neurocognitive performance decrements beginning at two or more previous concussions. Sex differences should be considered when examining the effects of concussion history on computerised neurocognitive performance.

Concussions remain a serious public health concern, with approximately 1.6–3.0 million sport concussions occurring every year in the USA.<sup>1</sup> Sports medicine professionals have recently promoted computerised neurocognitive testing as one objective component in a comprehensive concussion management approach that can be used to manage injured athletes.<sup>2–5</sup> Recent studies have identified certain factors, such as sex and history of concussion, which influence performance on neurocognitive tests both before (ie, baseline) and

after a concussion (ie, prolonged recovery).<sup>6–9</sup> Researchers have reported sex differences in cognitive performance at both baseline and post-concussion.<sup>10</sup> Specifically, athletes with a history of concussion demonstrated decreased neurocognitive performance on baseline neurocognitive measures when compared with athletes without any history of concussion. Moreover, females took longer to recover back to baseline neurocognitive levels following a concussion than males. However, other factors may play a role in these reported sex differences. For example, the decreased neurocognitive performance at both baseline and post-injury may be a function of the actual number of previously sustained concussions (ie, a dose—response) rather than sex per se.<sup>9</sup> Surprisingly, previous researchers have yet to explore sex differences pre- and postconcussion in neurocognitive performance among athletes with a history of multiple concussions.

Recent studies have documented sex differences on neurocognitive measures commonly used for managing concussion.<sup>6 11 12</sup> Barr *et al*<sup>11</sup> reported that female high school athletes scored higher than males on mental tracking, processing speed and verbal initiation. Using collegiate athletes, Covassin *et al*<sup>6</sup> reported that females performed significantly higher on verbal memory than males, whereas males demonstrated higher visual memory scores than females. Brown *et al*<sup>12</sup> also reported that male athletes performed faster on simple reaction time and higher on matching to sample pairs than female athletes. These researchers also reported higher scores on the Sternberg memory search task by females compared with males. These findings suggest a disparity between males and females on measures of neurocognitive performance. More importantly, other factors such as concussion history may interact with sex to further influence neurocognitive performance.

A history of concussion has been found to influence the risk for subsequent concussive injury.<sup>9 13</sup> Specifically, the risk for future concussion appears to be higher for athletes with a history of concussion.<sup>9 15</sup> Zemper<sup>13</sup> reported that athletes with a history of concussion are 5.8 times more likely to sustain a subsequent concussion than athletes without a history of concussion. Guskiewicz *et al*<sup>9</sup> found that college athletes with a history of three or more concussions had a higher risk (3.4 times) of sustaining a subsequent concussion than those with one (1.5 times) or two (2.8 times) previous concussions. Guskiewicz *et al*<sup>9</sup> suggested a dose—response relationship between

the number of previously sustained concussions and the risk for future concussion.

While there appears to be an increased risk for incident concussion in athletes with multiple concussions, the long-term neurocognitive effects of multiple concussions are unclear. Using a sample of college football players, Collins *et al*<sup>10</sup> found that athletes with a history of two or more concussions performed worse on baseline measures of executive function and processing speed than athletes with zero or one previous concussion. Similarly, Moser *et al*<sup>8</sup> found that high school athletes with a history of concussion demonstrated a similar neurocognitive performance to athletes who had sustained a concussion within the previous week of study, which suggests that there may be residual effects associated with previously sustained concussions. In contrast, Iverson *et al*<sup>14</sup> reported no differences between groups of athletes with zero, one or two previous concussions on verbal memory, visual memory, reaction time and processing speed. More recently, Bruce and Echemendía<sup>15</sup> did not find any differences on computerised or paper-and-pencil neurocognitive test batteries between athletes with and without a history of multiple concussions. Brown *et al*<sup>12</sup> also reported no differences on baseline neurocognitive function in athletes with a history of concussion.

There are mixed findings on the influence that multiple concussions have on concussion risk and neurocognitive outcomes. Extant literature supports a dose–response relationship, wherein there is a linear increase in concussion risk with each increase in previous concussions. However, few studies support a dose–response relationship for number of previous concussions and computerised neurocognitive performance. These studies have not examined the potential interaction that sex differences and previous concussions may have on neurocognitive performance. Therefore, the purpose of this study was to use a dose–response model to examine sex differences on computerised neurocognitive performance among athletes with a history of multiple concussions.

## METHODS

### Participants

Approximately 2500 collegiate and high school athletes participating in a multisite, sport-concussion surveillance project were recruited for study. Athletes participating in baseball, softball, football, lacrosse, volleyball, basketball, soccer, gymnastics, rugby and wrestling were administered a baseline computerised neurocognitive test battery. Participants who reported colour-blindness, learning disability, attention deficit disorder/attention deficit and hyperactivity disorder, treatment for migraines, psychiatric disorder or substance abuse were excluded from the current study. Athletes were also excluded from the study if they had an invalid baseline test as indicated by the Immediate Postconcussion Assessment Cognitive Testing (ImPACT) user manual.<sup>16</sup> Approximately 2100 athletes met the inclusion criteria. These athletes were categorised by their self-reported concussion history into one of four mutually exclusive groups: (1) no history of concussion, (2) one previous concussion, (3) two previous concussions or (4) three or more previous concussions. There were 1686 athletes (males=1170, females=516) with no history of concussion, 263 athletes (males=202, females=61) with one previous concussion, 89 athletes (males=66, females=23) with two previous concussions and 62 athletes (males=47, females=15) with three or more previous concussions. In order to provide for a more robust data analysis, 25 subjects were randomly selected from the overall sample for

inclusion in the study for each cell (concussion history by sex, for a total of eight cells). However, given the low numbers of females with a history of more than one concussion indicated above, only 23 and 15 females were included respectively in the two and three or more previous concussion groups.

### Instrumentation

#### Immediate Postconcussion Assessment Cognitive Testing (ImPACT)

The ImPACT (2006) computerised neurocognitive test battery was used to evaluate baseline neurocognitive function. This battery comprises three general sections: (1) demographics, (2) symptoms and (3) six neurocognitive modules. ImPACT takes approximately 25–30 min to complete. The demographic section includes a self-reported history of sport participation, history of alcohol and drug use, learning disabilities, attention deficit hyperactive disorders, major neurological disorders and history of previous concussion. The symptom section includes a self-reported inventory of 22 commonly reported concussion symptoms. The neurocognitive testing section consists of six neurocognitive modules which are compiled into four outcome composite scores (verbal and visual memory, reaction time, processing speed). These composite scores were the dependent variables in this study.

The test–retest reliability for ImPACT was assessed over 8 days across four administrations, yielding correlation coefficients ranging from 0.66 to 0.85 for the verbal memory index, 0.75 to 0.88 for the processing speed and 0.62 to 0.66 for the reaction time.<sup>17</sup> Using reliable change indices (RCI), repeated administrations over a 2-week period revealed no practice effects.<sup>18</sup> Schatz *et al* documented a combined sensitivity of 81.9% for ImPACT indices and total symptom score, and a specificity of 89.4%; the positive likelihood ratio was approximately 8:1, and the negative likelihood ratio was 2:1.

### Procedures

The research protocol was approved by the University Institutional Review Boards for the protection of human subjects at each participating institution. Prior to the study, the researchers obtained informed parental consent and assent for each minor (ie, under 18 years), and adult consent for each adult in the study. ImPACT testing was conducted at each participating institution's designated computer lab during preseason of each sport. Athletes were administered the baseline version of ImPACT in small groups (ie, 10 or fewer) to ensure a quiet environment for testing. All tests were then inspected for invalidity details according to ImPACT guidelines for scores outside normative ranges.<sup>16</sup>

### Data analysis

ImPACT yields four clinical composite scores for verbal memory, visual memory, processing speed and reaction time. Higher scores on verbal and visual memory, and processing speed are indicative of a better performance. Verbal and visual memory scores represent the percentage correct, and processing speed is a number composite score. Reaction time scores are presented in seconds, with lower scores being indicative of better performance.

A series of four 2 (sex=male/female)×4 (concussion history=0, 1, 2, 3+) factorial ANCOVAs (covaried for age) were performed on verbal and visual memory, reaction time and motor processing speed. Interactions were explored using a series of independent t tests where appropriate. Statistical significance for all tests was set at  $p=0.05$ . Analyses were conducted using the Statistical Package for the Social Sciences version 17.1.

## RESULTS

Male and female athletes were comparable in age, height and weight (see table 1). In addition, male and females were also similar on concussion recency. Both male and female athletes with a history of three or more concussions sustained their last concussive injury  $3.53 \pm 3.31$  and  $3.52 \pm 1.97$  years ago, respectively. Also, male and female athletes with a history of two concussions had their last concussion  $3.71 \pm 2.29$  and  $3.65 \pm 2.11$  years ago, respectively, whereas male and female athletes with one previous concussion were injured approximately  $5.02 \pm 4.28$  and  $4.73 \pm 3.90$  years ago, respectively. Independent t tests were performed to determine if there were any differences between the recency of last concussion between males and females in each of the groups. There were no significant differences between male and female athletes with one concussion ( $t_{(1,48)}=0.163$ ,  $p=0.872$ ), two concussions ( $t_{(1,48)}=0.122$ ,  $p=0.904$ ) or three or more concussions ( $t_{(1,48)}=0.007$ ,  $p=0.994$ ). Thus, it is unlikely that recency of concussion influenced the results of this study.

The results of a 2 (sex)  $\times$  4 (concussion history) ANCOVA for verbal memory supported a significant main effects for sex ( $F_{(1,179)}=22.43$ ,  $p=0.001$ ) and history of concussion ( $F_{(3,179)}=5.64$ ,  $p=0.001$ ), and the interaction between sex and history of concussion ( $F_{(3,179)}=2.67$ ,  $p=0.049$ ). Specifically, females performed better than males on verbal memory, and athletes without a history of concussion performed better than athletes with a history of two ( $p=0.016$ ) and three or more concussions ( $p=0.001$ ; see table 2).

Post-hoc independent samples t tests revealed that females with a history of three or more concussions performed better than males with a history of three or more concussions ( $t_{(3,38)}=2.71$ ,  $p=0.012$ ) on verbal memory. Females with a history of two or more concussions also performed better than males with a history of two or more concussions ( $t_{(3,46)}=4.59$ ,  $p=0.001$ ) on verbal memory. There were no other significant differences for verbal memory among the history of concussion groups.

The results for visual memory supported significant differences for sex ( $F_{(1,179)}=4.21$ ,  $p=0.042$ ) and history of concussion ( $F_{(3,179)}=2.96$ ,  $p=0.034$ ). Specifically, females performed better than males on visual memory, and athletes with a history of three or more concussions performed worse than athletes without a history of concussion ( $p=0.021$ ). The interaction between sex and history of concussion was not supported ( $F_{(3,179)}=0.50$ ,  $p=0.68$ ).

Finally, the results supported significant differences for sex on both motor processing speed ( $F_{(1,179)}=4.85$ ,  $p=0.03$ ) and reaction time ( $F_{(1,179)}=4.26$ ,  $p=0.04$ ). Specifically, males performed worse than females on both processing speed and reaction time. However, the analyses revealed no significant main effect in motor processing ( $F_{(1,179)}=0.7244$ ,  $p=0.54$ ) speed and reaction time ( $F_{(1,179)}=0.04$ ,  $p=0.99$ ) among the history of concussion groups or interaction between history of concussion and sex (motor processing= $F_{(1,179)}=0.89$ ,  $p=0.45$ ; reaction time= $F_{(1,179)}=0.46$ ,  $p=0.71$ ).

**Table 1** Demographic information for male and female athletes

	Males (n = 100)		Females (n = 88)	
	M	SD	M	SD
Weight (kg)	84.25	26.16	62.67	8.70
Height (inches)	69.48	10.73	65.08	2.73
Age (years)	18.35	2.77	18.29	2.24

## DISCUSSION

The purpose of the current study was to examine neurocognitive performance between male and female athletes with a history of multiple concussions. A secondary purpose was to reaffirm the dose-response gradient between concussion history and neurocognitive performance tentatively supported in the literature.<sup>8</sup> The results indicated that males with a history of three or more concussions performed worse than females with a history of three or more concussions on verbal memory. In addition, a dose-response gradient for history of concussion beginning with at least two or more previous concussions was partially supported by this study. Athletes with no history of concussion performed significantly better than athletes with a history of two and three or more concussions on verbal memory. Furthermore, athletes with a history of three or more concussions performed worse than athletes without a history of concussion on visual memory.

Athletes in this study demonstrated a dose-response gradient relationship between the number of previous concussions and cognitive performance. Specifically, athletes with a history of two and three or more concussions performed worse than athletes with no previous concussion on verbal memory. In addition, athletes with a history of three or more concussions scored worse on visual memory compared with athletes without a history of concussion. These results are consistent with Collins *et al*,<sup>10</sup> who found that athletes with two or more concussions performed significantly worse than athletes with one or no previous concussions on Trail-Making Test B and the Symbol Digit Modalities Test. These findings suggest that a history of a single concussion does not appear to result in long-term neurocognitive impairments as evidenced by computerised neurocognitive testing. However, a history of two or more concussions may be associated with long-term deficits in executive function<sup>10</sup> and verbal and visual memory. The notion that two or more previous concussions represent the threshold of a dose-response gradient for the relationship between previous concussion and neurocognitive performance is contrary to reports that three or more concussions were necessary for any long-term neurocognitive or other decrements.<sup>19</sup>

The dose-response observed in the current study may have been more evident for males with three or more concussions compared with females with three or more concussions due to males' possible under-reporting their previous concussions. Studies suggest that male football players<sup>20</sup> under-report concussions due to fear of being withheld from competition, not realising the injury was serious enough to warrant medical attention, and lack of awareness of concussions. As a result, the male athletes in our study with three or more concussions may in fact have had numerous concussions but did not report them to a medical professional. In addition to under-reporting concussions, male athletes may have incurred more severe concussions in this study compared with female athletes. This increased severity threshold could be related to that fact that males in the current study over-represented collision sports such as football and hockey, which generate high-velocity impacts. Males are also socialised to play through pain and minimise symptoms.<sup>21</sup> Consequently, males in the current study may have continued to participate with a mild concussion, thus exacerbating their injury and its effects. Unfortunately, the current study was unable to determine the severity of concussion as concussions were self-reported.

One explanation for the sex-based differences on history of concussion in our study may be oestrogen and progesterone

**Table 2** Means and standard deviations for Immediate Post-concussion Assessment Cognitive Testing composite scores by sex

Sex	N	History of concussion	Verbal memory (mean±SD)	Visual memory (mean±SD)	Motor processing speed (mean±SD)	Reaction time (mean±SD)
Males	25	0	0.901±0.069	0.820±0.114	39.69±7.79	0.559±0.077
	25	1	0.885±0.069	0.769±0.103	40.00±6.76	0.548±0.068
	25	2	0.828±0.069	0.774±0.085	37.89±4.26	0.553±0.076
	25	3+	0.817±0.069	0.732±0.081	41.69±6.70	0.559±0.073
Total	100		0.858±0.079	0.774±0.100	39.82±6.55	0.555±0.073
Females	25	0	0.931±0.070	0.821±0.106	41.13±8.39	0.528±0.061
	25	1	0.899±0.076	0.805±0.082	41.21±5.67	0.541±0.064
	23	2	0.913±0.060	0.811±0.108	42.79±6.11	0.539±0.055
	15	3+	0.894±0.0949	0.772±0.093	43.19±4.44	0.524±0.054
Total	88		0.991±0.074	0.806±0.098	40.812±6.58	0.545±0.067

acting as a neuroprotective factor for females following a concussion.<sup>22–25</sup> Oestrogen may increase the response to excitatory amino acids by acting directly on the glutamate NMDA receptor,<sup>25</sup> which has a role in the neurometabolic cascade following concussion.<sup>26</sup> However, oestrogen may also protect neurons from excitotoxic damage caused by ischaemia, which may mitigate cognitive impairments.<sup>24–27</sup> Furthermore, progesterone has been shown to bind to neuronal receptors (sigma receptor, GABA<sub>A</sub>), reduce cerebral oedema and down-regulate the inflammatory cascade in response to neurotrauma in animals.<sup>23</sup>

Sex differences were also observed in reaction time and motor processing speed, with females performing better than males on both these tasks. These results are in contrast to those of Brown *et al*,<sup>12</sup> who found a faster reaction time for male athletes than females on a computerised neurocognitive test (Automated Neuropsychological Assessment Metrics: ANAM). A possible explanation for this discrepancy may be that the IMPACT composite score for reaction time encompasses both choice and simple reaction time, while ANAM only includes a simple reaction time. Our results were similar to other researchers who reported that females performed better than males on processing speed.<sup>28–30</sup> Specifically, Barr<sup>11</sup> reported that female high school athletes demonstrated higher processing speed scores than male high school athletes.

There were several limitations in this study that must be considered when interpreting the results. History of concussion was self-reported and therefore was susceptible to recall, recency and other self-report effects. As a result, athletes may have under- or over-reported their concussion history. Another limitation of this study was the low representation of female athletes in the two and three or more history of concussion groups. Consequently, the generalisability of the current findings to female athletes in the higher concussion history groups is limited. Finally, the varying age (ie, college vs high school) of subjects was a potential confounding variable in this study. However, the confounding effects of age were statistically accounted for using the ANCOVA analysis.

The current study is the first to explore sex differences in athletes with and without a history of concussion using a concussion history dose–response gradient. Male athletes with a history of three or more concussions reported lower verbal memory scores compared with female athletes with a history of three or more concussions. As a result, clinicians may consider managing male and female athletes differently after multiple concussions. Also, a dose–response gradient was found for athletes with a history of two and three or more concussions

compared with athletes with no previous concussions. Future research should focus on sex and age differences in high school and collegiate athletes with and without a history of concussion. Further research is also warranted on sex differences and recovery rates in athletes with a history of multiple concussions. Finally, researchers should explore factors such as hormone levels, injury severity and the accuracy of concussion history reporting to better understand the sex differences reported in the current study

**Competing interests** None.

**Patient consent** Obtained.

**Ethics approval** Ethics approval was provided by the Michigan state University and Humboldt State University.

**Contributors** All authors have contributed to the three primary areas listed.

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