Cumulative effects of concussion in amateur athletes

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Primary objective: To examine the possibility that athletes with multiple concussions show cumulative effects of injury.
Methods and procedures: Amateur athletes with a history of three or more concussions were carefully matched (gender, age, education and sport) with athletes with no prior concussions. All completed a computerized neuropsychological test battery at preseason (ImPACT) and then within 5 days of sustaining a concussion (mean = 1.7 days).
Main outcomes and results: There were differences between groups in symptom reporting and memory performance. At baseline (i.e. preseason), athletes with multiple concussions reported more symptoms than athletes with no history of concussion. At approximately 2 days post-injury, athletes with multiple concussions scored significantly lower on memory testing than athletes with a single concussion. Athletes with multiple concussions were 7.7 times more likely to demonstrate a major drop in memory performance than athletes with no previous concussions.
Conclusions: This study provides preliminary evidence to suggest that athletes with multiple concussions might have cumulative effects.

Introduction

Children and adolescents frequently experience concussion in sports or other physical activities. Of particular concern is competition at the high school level, where at least 1.25 million athletes compete in contact sports. An estimated 62 816 cases of concussion occur annually at the high school level, with American football accounting for about 63% of cases [1]. It is well known that many people who sustain concussions experience post-concussion symptoms and decrements on neuropsychological testing during the first week post-injury [2–5]. Fortunately, the vast majority of people who sustain a single concussion recover relatively quickly and fully. Recovery has been demonstrated in trauma patients [5, 6], athletes [4], children [7], and the elderly [8, 9]. Although the vast majority of people who sustain concussions eventually recover, concussions can be significant injuries that
result in distressing symptoms and clear declines in measured cognitive abilities. Concussions should not be dismissed lightly, and young people with ongoing symptoms (e.g., headaches or feeling ‘foggy’) should be managed conservatively.

Unfortunately, there is very little research on concussions in high school athletes. This lack of research is alarming for several reasons. First, based on participation levels, the largest group of at-risk athletes is at the high school level or below. Second, at least 17 deaths related to second impact syndrome (which results from a second concussive insult closely following the first) were reported in the literature between 1992 and 1997 [10], and periodic cases continue to be reported. The majority of victims have been high school athletes between the ages of 13 and 18 years, suggesting the possibility of greater vulnerability to severe injury in children and adolescents versus adults. However, this vulnerability has yet to be established empirically. It is important to be aware of second impact syndrome, while keeping in mind that it is an extremely rare phenomenon. The vast majority of amateur athletes who sustain light concussions recover quickly and fully, typically within 3–10 days [4, 11–13].

In sport, the risk for long-term problems is rarely, if ever, associated with a single concussion. Rather, long-term problems are believed to be associated with multiple concussions. Awareness of the detrimental effects of repetitive concussions has existed in modern-era sports medicine for decades both anecdotally and in the clinical literature. Early examples from boxing include Martland’s [14] work on dementia pugilistica (punch-drunk syndrome) and later chronic [15] and traumatic boxer’s encephalopathy [16]. More recently, concussion in sport, and the aftermath of multiple concussions, has been witnessed by the masses as numerous professional athletes have had their careers prematurely ended due to these injuries.

Sports involving impact to the head such as American football, boxing and ice hockey provide an opportunity to explore the effects of multiple concussions. Peerless and Rewcastle [17] noted that boxers appear to make a rapid and full recovery from a single slight concussion, but after repeated episodes, there is a gradual appearance of permanent sequelae. The risk of sustaining a concussion in American football has been reported to be four-to-six times greater if the player has already sustained a concussion [18]. Permanent brain injuries due to multiple concussions have been reported in ice hockey players [19]. In a study employing neuropsychological testing, researchers suggested that cumulative effects of concussion might be detectable in amateur soccer (i.e., Association football) players [20]; however, other researchers have reported no adverse effects associated with participation in competitive soccer [21]. In a large study involving college American football players, athletes with a history of two or more concussions reported more preseason (i.e., baseline) symptoms, and they performed more poorly on two tests designed to measure information processing speed than athletes with no previous concussions [11]. In the most frequently cited study, Gronwall and Wrightson [22] reported that trauma patients, some with multiple concussions, scored significantly lower on an auditory processing task than patients with only one concussion. In addition, a recent study demonstrated statistical differences in post-concussion symptoms and cognitive event-related potentials at baseline for young amateur hockey players with zero versus three or more concussions [23].

Animal models of neurotrauma suggest that limited but significant damage to neurons can result from a single concussion (although the animal research typically involved much more serious traumatic brain injuries than the concussions sustained
in sports). The notion of a continuum of injury [17, 24] implies that as acceleration/deceleration forces increase, the number of cells damaged will increase and that damage will progressively occur in deeper structures. Gennarelli [25] described a continuum of injury with four stages based on increasingly severe strains on nodal and paranodal regions of axons. Stage 2 damage (axonal ‘stretch’ from 5 to 10%) resulted primarily in transient cellular dysfunction and marked the initiation of limited cell death.

Different types of neurons appear to be susceptible to acceleration/deceleration forces, that are largely dependent on the amount of force and the direction of movement of the head. In addition, neurons may be differentially susceptible to acceleration/deceleration forces. For instance, when axons change direction to accommodate the presence of a blood vessel, enter target nuclei (e.g. the grey/white interface), decussate, or are of large calibre, they may be more susceptible to injury [26–29]. Although researchers who employ animal models have demonstrated the effects of single injuries on subsequent brain functions and structure, little evidence is available on the effects of multiple concussions. Early studies employing animal models designed to contrast repetitive versus single impact of concussive and subconcussive injuries suggested that after a single subconcussive impact, no change was observed in animal behaviour or histology. In contrast, repetitive subconcussive episodes between 5 and 20-s intervals often resulted in permanent injury [30, 31]. Obviously, it is very difficult to extrapolate from animal research to concussions sustained by humans in sport. Nonetheless, a basic science foundation for possible cumulative effects is apparent.

The purpose of this study was to replicate and extend the results of previous studies that reported increased post-concussion symptoms at baseline for amateur athletes who sustained multiple concussions versus those who had not sustained a concussion. In addition, the severity of on-field markers and symptoms following a subsequent concussion were examined to determine whether athletes with a history of multiple concussions experience more severe symptoms and greater measured neuropsychological decrements than athletes with no prior concussions.

**Methods**

**Subjects**

All subjects participated in the University of Pittsburgh Medical Center Sports Concussion Program. The programme uses preseason and post-injury neuropsychological testing protocols to help determine return to play in athletes sustaining concussions. Immediate Post Concussion Assessment and Cognitive Testing (ImPACT), a computer-based demographic, symptom and neuropsychological test program, was used at baseline and at each post-concussion follow-up assessment.

Amateur athletes with three or more concussions were selected from a large database of players who took part in the programme. Only subjects with complete data at baseline and at 1–2 day follow-up were included. A sample of 19 athletes, 11 high school and eight college, were identified. A sample of athletes who were matched on age, education, level (high school or college), gender, sport, and days post-injury was then carefully selected. The results of this matching are presented in table 1. Therefore, the total sample consisted of 38 players, 19 with a history of three or more concussions and 19 with no prior concussions. Because of the careful
matching, there obviously were no statistically significant differences between groups on the demographic variables.

**Measures**

ImPACT is a computer-administered neuropsychological test battery that consists of seven individual test modules that measure aspects of cognitive functioning including attention, memory, reaction time and processing speed. It also contains a post-concussion symptom scale.

The memory index is comprised of five subtest scores measuring different aspects of memory including verbal (word) learning and recognition memory, visual associative memory, visual working memory, and letter memory. This composite index represents the average per cent correct score for these five scores. The test battery is designed to minimize practise effects by randomizing the stimuli. With the exception of the recognition word memory test, presentation of all stimuli is varied automatically for each examination. For example, for each administration of the symbol match, three letter memory, and visual memory tasks (X’s and O’s), the computer automatically randomizes the stimuli presented to minimize memorization of the presented sequences across multiple evaluations. The word memory module has five separate forms. To make up the five word lists, the words were randomly selected from a group of single syllable nouns. In addition to the 12 target words, each word is paired with a similar but not identical word (e.g. ‘snow or ice’, ‘doctor or nurse’).

<table>
<thead>
<tr>
<th>Variable</th>
<th>No previous concussions</th>
<th>Three or more concussions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>17.9 (median = 17, SD = 2.7)</td>
<td>17.8 (17, 2.5)</td>
</tr>
<tr>
<td>Education-years</td>
<td>11.8 (median = 11, SD = 2.5)</td>
<td>11.9 (11, 2.5)</td>
</tr>
<tr>
<td>Gender</td>
<td>18 male</td>
<td>17 male</td>
</tr>
<tr>
<td>Education level</td>
<td>11 high school, 8 college</td>
<td>12 high school, 7 college</td>
</tr>
<tr>
<td>Sport</td>
<td>15 American football, 3 football, 1 baseball</td>
<td>14 American football, 2 football, 2 basketball, 1 lacrosse</td>
</tr>
<tr>
<td>Days post-injury</td>
<td>1.8 (median = 1, SD = 1.3)</td>
<td>1.6 (1, 1.5)</td>
</tr>
<tr>
<td>Number of athletes</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Preseason</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjective symptoms</td>
<td>5.6 (SD = 8.1)</td>
<td>14.1 (15.8)</td>
</tr>
<tr>
<td>Reaction time</td>
<td>0.57 (SD = 0.09)</td>
<td>0.55 (0.06)</td>
</tr>
<tr>
<td>Processing speed</td>
<td>35.7 (SD = 8.1)</td>
<td>34.4 (10.1)</td>
</tr>
<tr>
<td>Memory</td>
<td>89.1 (SD = 6.5)</td>
<td>84.7 (12.0)</td>
</tr>
<tr>
<td>Post-concussion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjective symptoms</td>
<td>21.5 (SD = 23.4)</td>
<td>31.3 (26.4)</td>
</tr>
<tr>
<td>Reaction time</td>
<td>0.57 (SD = 0.11)</td>
<td>0.56 (0.10)</td>
</tr>
<tr>
<td>Processing speed</td>
<td>36.6 (SD = 8.0)</td>
<td>35.6 (7.8)</td>
</tr>
<tr>
<td>Memory</td>
<td>84.7 (SD = 12.0)</td>
<td>74.5 (12.7)</td>
</tr>
<tr>
<td>On-field markers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Retrograde amnesia</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Post-traumatic amnesia</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Disorientation</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Five or more min of</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>mental status change</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The module yields per cent correct recognition scores for both learning (per cent correct recognition after two presentations) and delayed recognition (per cent correct recognition approximately 15 min after the initial presentation).

The reaction time index represents the average time (s) to respond. All stimuli are randomized to minimize practise effects. Three scores are used in the calculation of the composite index. First, the distractor task for the X’s and O’s test module (choice reaction time) requires the athlete to mouse click the left button if a blue square appears on the screen and alternatively to right mouse click if a red circle appears. The second score is the average correct reaction time score from the colour-match module. For this test module, the athlete is presented with three words (red, green, or blue) presented either in the same colour ink of the work (e.g. the word ‘blue’ presented in blue ink) or in a different colour ink (‘red’ in blue or green ink). Therefore, this task requires the athlete to respond rapidly while inhibiting the impulse to respond to non-target words. Third, the average correct reaction time score from the symbol match module consists of the average time to respond to this task, which requires the athlete to mouse click on a given number, when a specific symbol appears on the screen. The average correct reaction time is divided by three to produce a score proportional to the other two scores. This final score represents the reaction time composite index.

The visual–motor speed composite index consists of the average of two scores. First the total number of blue squares or red circles correctly clicked during the previously described X’s and O’s distractor task is divided by four. Second, the distractor task from the three letters module is calculated and multiplied by three. The three-letters module is a verbal working memory test that measures the ability of the athlete to remember a series of three consonants that are immediately followed by a distractor task that requires the athlete to click a randomly displayed array of numbers in backward order from 25 to one. Therefore, the distractor task provides a measure of visual search and visual–motor speed. The weighting of the two scores that make up the visual processing composite index produces results in a similar numeric range for both scores.

The post-concussion symptom scale has 21 symptoms (graded 0–6 in terms of severity) commonly associated with concussion (e.g. headache, photosensitivity, feeling slow, etc.). This scale was originally developed for use with the Pittsburgh Steelers (a professional American football team) and is now used throughout professional and amateur sports [32, 33]. The athlete is asked to choose (via a mouse click) the point on the scale that most accurately reflects his/her status with regard to each symptom at that time.

**Procedures**

Athletes underwent a baseline evaluation and were administered the computerized test battery before the 2000 and 2001 athletic seasons. ImPACT consists of a detailed symptom and demographic questionnaire (e.g. relevant sport/medical/concussion history information), as well as seven individual test modules that measure aspects of cognitive functioning.

A standardized concussion history questionnaire contained within the ImPACT test battery was administered with the supervision of the test administrator. Before athletes completing this section, test administrators communicated to them that they were to document each prior episode of cerebral concussion that was formally
diagnosed by a team physician or certified athletic trainer. Athletes also documented any prior concussion that resulted in loss of playing time. Test administrators were trained to define concussion as a ‘traumatically induced alteration in mental status that may or may not be accompanied by a loss of consciousness’. Non sports-related concussions were also included in the tally only if diagnosed by a physician. Based on these criteria, athletes, under the supervision of the test administrator, entered in the total number of concussions experienced in their history.

Administration of the computerized neuropsychological test battery was supervised by a team of clinical neuropsychologists, certified athletic trainers, or physicians who were thoroughly trained in the administration of the measures. Given that ImPACT is a self-administered test battery, all information is gathered in a standardized manner.

All athletes were re-administered the computerized battery within 5 days of injury (mean = 1.7 days). In-study concussions were characterized by the on-field presentation of one or more of the following symptoms after a blow to the head or body: (1) any observable alteration in mental status or consciousness; (2) a constellation of self-reported symptoms, such as post-traumatic headache, ‘fogginess’, nausea/vomiting, dizziness, etc.; and/or (3) the presence of loss of consciousness, disorientation, post-traumatic amnesia (PTA) or retrograde amnesia (RTA) as identified by on-field examination. Sports medicine practitioners present on the sideline at the time of injury made the diagnosis of concussion.

Sports medicine practitioners carefully documented information pertaining to markers of injury severity. On-field disorientation was assessed by questioning the athlete’s post-injury awareness and orientation to surroundings (e.g. name the current stadium, city, opposing team, current month/day). On-field PTA was assessed through immediate and delayed (e.g. 0, 5, 15 min) memory for three words (e.g. girl, dog, green). PTA was further documented at the post-injury follow-up evaluation by assessing the athlete’s ability to recall all information after trauma. Any loss of memory in this latter regard indicated positive presence of PTA. On-field retrograde amnesia was assessed by having the athlete recall events that occurring just before their injury (e.g. events in the first quarter, memory for play preceding trauma, score of the game). Retrograde amnesia was further documented at the post-injury evaluation by assessing the athlete’s ability to recall information just before trauma. Any loss of memory in this latter regard indicated positive presence of retrograde amnesia. Loss of consciousness was documented when an athlete was unresponsive to external stimuli as documented by on-field evaluation by team medical personnel. By definition, athletes experiencing loss of consciousness (LOC) also experienced a concomitant PTA. For the purposes of the present study, athletes with any degree of LOC were categorized in the positive LOC group rather than the PTA or retrograde amnesia group.

Results

A mixed-model 2 × 2 ANOVA was used to determine if there were between- and within-group effects on each of the dependent variables (i.e. total symptoms, reaction time, processing speed, and memory). For the total symptoms score, there was a significant main effect for time; $F(1, 36) = 29.4, p < 0.00001, \eta^2 = 0.45$. This is a large effect size; approximately 45% of the variability in symptom scores was related to the differences in performance across the two time intervals. There was not a
statistically significant group effect, although the observed power in this analysis was very low (i.e. 0.35). In other words, there was only a 35% chance of correctly rejecting a false null hypothesis. However, exploratory independent t-tests revealed a significant difference between groups at preseason, with the athletes who had multiple concussions reporting more symptoms ($p < 0.05$, observed power = 0.53, $d = 0.71$, large effect). The groups did not differ in total symptoms during the post-injury follow-up assessment ($p = 0.24$; observed power = 0.22, $d = 0.39$, small–medium effect). Again, however, low power could have affected this finding. There was a trend toward an effect (table 1 and figure 1) and as demonstrated in the effect size of 0.39. Specifically, the two groups differed by more than one-third of a pooled standard deviation unit.

For the reaction time and processing speed composite scores, there were no significant between- or within-group effects. Moreover, exploratory analyses revealed no trends toward differences between groups.

For the memory composite score, there was a significant main effect for time; $F(1, 36) = 13.1$, $p = 0.001$, $\varepsilon^2 = 0.27$. This is a medium-to-large effect size; approximately 27% of the variability in memory scores was related to the differences in performance across the two time intervals. There was also a group effect, with the multiply concussed athletes showing greater decrements in memory functioning than the mildly concussed subjects ($F(1, 36) = 7.0$; $p = 0.012$, $\varepsilon^2 = 0.16$, observed power = 0.73). There was a clear trend toward lower memory performance in the multiply concussed group at preseason ($p = 0.08$, two-tailed test, observed power = 0.42, $d = 0.59$, medium effect size). These results are presented in table 1 and figure 2. If the effect size between groups remained constant and the sample size in each group was increased from 19 to 25, then the two-tailed $p$ would be 0.04. The athletes with multiple concussions obtained significantly lower memory composite scores during the post-injury assessment ($p = 0.015$, observed power = 0.70, $d = 0.83$, large effect).

A 14-point drop in memory performance represents a major decline in function between preseason and immediate follow-up (i.e. greater than 1.5 pooled SD decline in performance). The 38 subjects were divided into two groups based on whether they demonstrated this major decline in memory performance.
(i.e. 11 subjects demonstrated a major decline). A significantly greater proportion of the athletes with multiple concussions (47.4%) versus no previous concussions (10.5%) demonstrated a major decline in memory performance, $\chi^2 (1, 38) = 6.3, p < 0.013$. The athletes with multiple concussions were 7.7 times more likely to demonstrate a major drop in memory performance than the athletes with no previous concussions (95% CI = 1.4–42.7).

In terms of on-field markers, the groups did not differ in their experience of LOC, retrograde amnesia or disorientation (table 1). Importantly, there was very low power in all of these $\chi^2$ analyses due to small sample sizes and some missing data. There was a prominent trend toward a difference in post-traumatic amnesia ($p = 0.08; \text{odds ratio} = 6.4, 95\% \text{CI} = 0.7–61.2$). The athletes with multiple concussions were six times more likely to experience sideline-assessed post-traumatic amnesia. Moreover, the athletes with a history of multiple concussions were significantly more likely to evidence 5 or more min of sideline-assessed, broadly defined, mental status disturbance ($p = 0.036; \text{odds ratio} = 8.3, 95\% \text{CI} = 0.9–77.6$).

**Discussion**

The main findings of the current study were that young athletes who sustain multiple concussions reported significantly more symptoms and demonstrated a clear trend toward lower memory scores at baseline. Given the closely matched samples, the preseason symptom and memory findings were interpreted to be suggestive of cumulative, lingering effects of multiple concussions. In addition, athletes with multiple concussions showed worse on-field severity markers associated with their next concussion as compared with athletes who were experiencing their first concussion. They were six times more likely to experience post-traumatic amnesia and approximately eight times more likely to experience 5 or more min of mental status disturbance, broadly defined (i.e. RTA, PTA or disorientation). Finally, athletes with multiple concussions had more adverse consequences in the acute recovery period (i.e. 2 days) from their next concussion. That is, multiply concussed players performed much lower on the memory testing at 2 days post-injury than the singly concussed players. Athletes with multiple concussions were eight times more likely
to evidence a marked drop in memory functioning from baseline to 2 days post-injury (i.e. a 1.5 pooled SD drop in functioning). A major strength of this study was the careful matching of athletes on important demographic variables. Major limitations include the retrospective, quasi-experimental component of the study and the small sample sizes.

The present findings are consistent with those of Gaetz et al. [23] who reported that at baseline, subjects who sustained three or more concussions reported greater numbers of post-concussion symptoms than those who had never sustained a concussion. Variables such as headache, memory problems, and problems with ‘the ability to think’ were more highly endorsed by those with multiple concussions. In addition, athletes had significant increases in event-related potential latency compared with the group with no concussions. The results are also consistent with the findings of Collins et al. [11] in a large sample of college football players. Those with two or more concussions reported more symptoms and performed more poorly on two information processing speed tests than athletes with no prior concussions.

The results of the present study have potentially important implications for the clinical care of concussed athletes. If indeed multiple concussive injuries result in a decline in neuropsychological performance over time, this information may be important in helping athletes and their families make informed decisions about the risk of continued participation in contact sports.

Not all recent studies reported evidence for cumulative effects. For example, Macciocchi et al. reported that in matched groups of football players with either one or two concussions, no statistical differences were observed on neuropsychological tests such as the PASAT, Trails A and B, or the Symbol Digit Test [34]. However, their sample sizes were very small (i.e. $n = 12$). Perhaps there is a point where statistical increases in symptoms occur following multiple concussions. There might be a linear progression where cognitive problems and subjective symptoms increase with the number of concussions sustained. Of course, severity of concussion is likely as important, or even more important, than number of concussions. Further research is required to understand these issues better.

Researchers have reported post-concussion symptoms in trauma patients who are 1 or more years post-injury [35–37]; however, the underlying causes of these persistent, long-term symptoms are subject to considerable debate. Moreover, a carefully controlled, large-scale, prospective study of trauma patients with uncomplicated mild traumatic brain injuries demonstrated that long-term post-concussion symptoms were rare [38]. In addition, it is well known that the so-called post-concussion symptoms are non-specific; they occur in day-to-day life and are associated with multiple other factors and conditions such as depression, chronic pain, life stress and personal injury litigation [39–46]. Therefore, it is possible that due to some unknown sampling bias, the present study has inadvertently selected a group of multiply concussed players who have increased baseline symptom reporting as a result of other factors. Although possible, this seems unlikely. Nonetheless, replication of the current results, ideally with a larger sample, is recommended.

In conclusion, this study provides preliminary and provocative evidence to suggest that young athletes with multiple concussions might have cumulative effects. Specifically, these athletes are more likely to report ongoing post-concussion symptoms, and they performed slightly worse on preseason memory testing. Moreover, they appear to be more susceptible to sustaining injuries of greater
severity in the future. Finally, those athletes with multiple concussions had greater adverse consequences in the acute recovery period (i.e. 2 days) from their next concussion.

References


