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Timing of Concussion Diagnosis is Related to Head Impact Exposure Prior to Injury

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Abstract

Purpose—Concussions are commonly undiagnosed in an athletic environment because the postinjury signs and symptoms may be mild, masked by the subject, or unrecognized. This study compares measures of head impact frequency, location and kinematic response prior to cases of immediate and delayed concussion diagnosis.

CONFLICT OF INTEREST

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Joseph J. Crisco, Richard M. Greenwald, Jeffrey J. Chu, Jonathan G. Beckwith and Simbex have a financial interest in the instruments (HIT System, Sideline Response System (Riddell, Inc)) that were used to collect the data reported in this study. The remaining authors have no financial interests associated with this study.

Methods—Football players from eight collegiate and six high school teams wore instrumented helmets during play (n=1,208), of which ninety-five were diagnosed with concussion (105 total cases). Acceleration data recorded by the instrumented helmets was reduced to five kinematic metrics: peak linear and rotational acceleration, GSI, HIC₁₅, and change in head velocity (v). Additionally, each impact was assigned to one of four general location regions (Front, Back, Side, and Top), and the number of impacts sustained prior to injury was calculated over two time periods (one and seven days).

Results—All head kinematic measures associated with injury, except peak rotational acceleration (p = 0.284), were significantly higher for cases of immediate diagnosis than delayed diagnosis (p<0.05). Players with delayed diagnosis sustained a significantly higher number of head impacts on the day of injury (32.9 ± 24.9 ; p < 0.001) and within seven days of injury (69.7 ± 43.3 ; p = 0.006) than players with immediate diagnosis (16.5 ± 15.1 and 50.2 ± 43.6). Impacts associated with concussion occurred most frequently to the Front of the head (46%) followed by the Top (25%), Side (16%), and Back (13%) with the number of impacts by location independent of temporal diagnosis ($\chi^2(3) = 4.72$; p = 0.19).

Conclusions—Concussions diagnosed immediately after an impact event are associated with the highest kinematic measures, while those characterized by delayed diagnosis are preceded by a higher number of impacts.

Keywords

HIT System; impact biomechanics; MTBI; TBI; injury threshold; symptomatology

INTRODUCTION

Sports related concussion, a type of mild traumatic brain injury, is diagnosed following assessment of several clinical domains including athlete reported symptoms, physical signs (e.g., change in behavior, balance, sleep, etc.), and cognitive functioning.(26) Current strategies for injury management suggest that abnormalities in any one or more of these domains should place an athlete in the category of suspected concussion. On the athletic field, loss of consciousness (LOC) is arguably the most identifiable sign of concussion; however, it has been well documented that most sports related concussions do not result in LOC.(7, 14, 27, 29) Because the post-injury changes in signs and symptoms used for identification may be mild, masked by the athlete, or go unreported, it is common for concussions to go undiagnosed.(25) It is also not uncommon for an athlete to self-report signs and symptoms in the day or days following their onset, further confounding efforts to understand the circumstances surrounding the injury.(12)

Although a majority of sports related concussion cases are attributed to a single impact, in many cases the athlete has been exposed to multiple head impacts prior to injury and potentially multiple head impacts after initial onset of symptoms when the injury goes unreported.(3) For example, it has been reported that college football players sustain up to 2,400 head impacts per season(10) with the average player sustaining 14.3 impacts per game.(9) At this time it is unknown whether multiple head impacts influence the pathophysiology of the brain and the clinical manifestation of the injury, but, at the very

least, a player's history of head impact exposure (frequency, location, and kinematics of head impact) makes associating a single impact with injury a complicated task,(2, 3, 31) and, if an athlete does not recall when onset of symptoms occurred, the reliability of correctly identifying a single impact associated with injury is likely to be quite low.

Published research to date has demonstrated that single head impact kinematic measures (e.g., peak linear acceleration, peak rotational acceleration, etc.) are sensitive to diagnosed concussion; however, these measures have low specificity. Injuries typically occur following an impact with kinematics in the highest percentile of all impacts, but there are many impacts with similar characteristics that do not result in diagnosed injury.(4, 19) Both the sensitivity and specificity increase when kinematic measures are combined with additional factors such as head impact location, into composite measures, (5, 17, 32) but a single concussive injury threshold that is specific to all cases of injury has remained elusive due to the wide variance in values reported for single head impacts associated with injury.

To better understand the association between head impact and diagnosed concussion, we previously reported the frequency and associated kinematic response of head impacts sustained by football players on days with and without diagnosis of concussion.(2) Ninety-five of 1,208 athletes participating on 14 collegiate and high school football teams who wore instrumented helmets to record their head impact exposure (HIE) during play sustained at least one diagnosed concussion, yielding 105 distinct cases of recorded injury (9 players sustained multiple injuries). Players sustained both an increase in impact frequency and magnitude of kinematic parameters (linear and rotational acceleration magnitude, change in head velocity (v), and composite measures Gadd Severity Index (GSI) and Head Injury Criterion (HIC₁₅) on days of diagnosed concussion than on days without. Additionally, kinematic measures derived from linear head acceleration were the most sensitive predictors of immediately diagnosed concussion. We also reported that 57% of the 105 cases of concussion were not diagnosed later that day or in the following days. These cases (n = 60) have been termed 'delayed diagnosis of concussion' for this study.

There are several potential explanations for why delayed concussion diagnosis occurs, including, but not limited to, athletes not wanting to be removed from play, athletes not knowing they were injured, or symptoms developing at a later time.(18, 23, 25) In our previous study, we postulated that variation in head impact exposure (HIE) may be associated with this observed difference in clinical presentation (i.e., immediate vs. delayed diagnosis). The aim of this study was to test that theory by comparing measures of HIE prior to cases of immediate and delayed diagnosis of concussion. Specifically, we tested the hypotheses that impacts associated with delayed diagnosis; players would sustain more impacts prior to delayed diagnosis of concussion than immediate diagnosis; and that the location distribution of impacts associated with concussion would not depend on whether the injury was diagnosed immediately or delayed.

PARTICIPANTS AND METHODS

Methodology Review

As part of a multi-institutional study to examine the Biomechanical Basis of Mild Traumatic Brain Injury, football players from eight collegiate and six high school teams wore instrumented helmets (Head Impact Telemetry (HIT) System, Simbex, Lebanon, NH) to record measures of HIE (frequency, location, and kinematic response of head impacts) while playing football (Figure 1). The following analyses focus on 105 cases of diagnosed concussion experienced by 95 of those players who were diagnosed with injury during a six year period (2005 – 2010).(2) Nine of the players were diagnosed with concussion multiple times during the study period with eight players sustaining two injuries and one player sustaining three. At all institutions participating in the research, approval for data collection and reduction was received by an Institutional Review Board and informed consent was obtained, including parental consent in the case of minors.

Helmet Instrumentation

Description of the HIT System technology has been reported in the literature including discussion of algorithmic, (8, 30) laboratory, (1, 13, 15, 24) and on-field descriptions of system performance (5, 6, 9–11, 13, 17, 28, 31). Briefly, helmets were fitted with a wireless, sealed in-helmet unit designed to isolate head from helmet acceleration. (24) The in-helmet unit contains six single-axis accelerometers, data acquisition hardware, and a rechargeable battery. When any one of the six accelerometers exceeded a threshold of 14.4 g, data from all accelerometers were recorded, time stamped, and transmitted to a sideline computer. Once downloaded, acceleration data were processed for impact location and linear and angular acceleration of the head center of gravity (8 ms pre-trigger and 32 ms post-trigger). (8, 30) Additional measures derived from the linear acceleration time series data, HIC₁₅,(21, 22) GSI,(16) and (v), were then computed. Head impact data from all schools were consolidated into a single database and redacted of personal identifiers for all subsequent analyses.

Measures of Head Impact Exposure

Head impact exposure (HIE) is a broad term used to describe the frequency, location, and kinematic response (both acceleration and measures derived from acceleration) to head impacts.(9–11) For analyses presented here, acceleration data was used to compute five kinematic metrics: peak linear acceleration, peak rotational acceleration, HIC₁₅, GSI, and v. To allow for comparison by impact location, each impact was assigned to one of four

general location regions – Front, Back, Side, and Top – from the continuous impact location measurement provided by the in-helmet unit.(9, 17) Impact frequency was defined as the number of impacts sustained over two periods of time, one day and seven days. For each of these time periods, both the total number of impacts (*Freq*) and the number of impacts exceeding the 50th (*Freq*₅₀) and 95th percentile (*Freq*₉₅) peak linear acceleration level for all players are reported. Peak linear acceleration was selected as the measure of interest because it was previously shown to be the best predictor of immediately diagnosed concussion.(2) Cutoff values for peak linear acceleration (50th = 20.5 g, 95th = 62.2 g) used in this study

was previously established by Crisco et al and represent levels at which only 50% and 5% of all impacts sustained during play are expected to exceed.(10)

Clinical Diagnosis

Diagnosis of concussion was made by the medical staff at each participating institution (athletic trainer (AT), team physician, etc.). Following symptom resolution, each institution provided the date of injury, the suspected time of injury, the approximate time of diagnosis, day of symptom resolution, and player age, height, and weight. Anecdotal descriptions of the events surrounding injury (e.g., description of the impact, method of identifying the injury, and on-field observations regarding clinical presentation) were also provided by each team when available.(2)

While it was common for teams to associate a single impact with injury, it was observed that concussion was not always diagnosed immediately following head impact. For these cases, the diagnosis did not occur until later that day or in the days following when signs of injury were observed by the staff or symptoms were self-reported by the athlete. Because of this observation, injury cases were classified into two timing categories: 1) immediate diagnosis – a case of diagnosed concussion where a single identifiable head impact preceded onset of symptoms that led to the player being immediately removed from play without re-entry, 2) delayed diagnosis – a case of diagnosed concussion where the player was not immediately identified with injury, continued to play, and was diagnosed later that day or the following days. No distinction was made between players who indicated a delayed onset of symptoms and those who failed to immediately report symptoms to medical personnel. For single impact analyses, cases of immediate diagnosis were associated with the head impact sustained prior to diagnosis and delayed diagnosis cases were associated with the highest level impact, by peak linear acceleration, sustained on the day of injury.

Statistical Analysis

Descriptive statistics (mean, standard deviation, range) are provided for single impact kinematic measures and impact frequency and location by timing category. Prior to statistical comparison of impact kinematics and frequency, Lilliefors tests were first conducted to verify assumptions of normality. If normality assumptions were met, distributions of kinematic measures and impact frequency were compared using a Student's t-test. If the distributions of data for either immediately or delayed cases were found to be skewed, a Kruskal-Wallis Nonparametric one-way analysis of variance was used. A chi-squared test for independence was used to determine if the location of impacts associated with concussion are dependent on whether the injury is diagnosed immediately or delayed. All statistical analyses were performed using Matlab (version 7.11, The MathWorks Inc., Natick. MA). A significance level of $\alpha = 0.05$ was set *a priori* for all statistical tests.

RESULTS

161,732 head impacts were recorded over 10,972 player days (day where an athlete sustained at least one head impact) from 95 athletes clinically diagnosed with concussion (Figure 1). Eight of the subjects sustained two diagnosed concussions and one had three,

yielding 105 identified cases of injury.(2) Forty-five (43%) of all injury cases were classified as immediate diagnosis, with seven of these cases involving loss of consciousness. Of the 60 cases of delayed diagnosis, 7 were reported during the period of play but after stated onset of symptoms, 16 were reported on the same day but following the practice or game, 22 were reported in the days following, and in 5 cases the player was not removed from play but it was indeterminable from available clinician notes whether the injury was reported after play on the same day or in the days following. Time between injury and symptom resolution was reported for 89 of the 105 cases, and, of these, symptoms resolved in 5.9 ± 7.4 days (15 min – 59 days). No statistical difference in length of symptom resolution was found between cases of immediate (35 reported, 6.1 ± 5.8 days) and delayed (54 reported, 5.8 ± 8.3 days) diagnosis (p = 0.56).

Average peak linear and angular acceleration for all impacts associated with diagnosis of concussion (n= 105) were 102.5 g \pm 33.8 g (29.3 – 205.3 g) and 3,977 rad/s² \pm 2,272 rad/s² (183 – 10,484 rad/s²). Average HIC₁₅, GSI, and v were 249 \pm 203 (11 – 994), 345 \pm 270 (14 – 1,188), and 3.74 \pm 1.55 m/s (1.32 – 8.99 m/s) respectively. The distributions of peak linear and rotational acceleration and v for the impact associated with concussion diagnosis were normally distributed for both the immediate and delayed diagnosis classifications. Measures of these three kinematic metrics were higher for immediately diagnosed cases, but only peak linear acceleration (p = 0.011) and v (p = 0.001) were statistically significant (Table 1). HIC₁₅ and GSI were not normally distributed and measures for both metrics were significantly higher for cases of immediate diagnosis than those associated with delayed diagnosis (Table 1).

Impacts associated with diagnosed concussion occurred most frequently to the Front of the head (46% of all, 16 immediate and 32 delayed diagnosis), followed by the Top (25% of all, 11 immediate and 15 delayed diagnosis), Side (16% of all, 10 immediate and 7 delayed diagnosis), and Back (13% of all, 8 immediate and 6 delayed diagnosis) (Figure 2). The frequency of impacts by location did not differ by classification of immediate or delayed concussion diagnosis, $\chi^2(3) = 4.72$ (p = 0.19).

Players diagnosed with concussion sustained an average of $25.8 \pm 22.7 (1 - 108)$ impacts on days of injury and $61.3 \pm 44.3 (1 - 216)$ impacts within seven days previous to the injury. Impact frequency was non-normally distributed for both one and seven day time windows and at all levels of acceleration evaluated (all impacts, top 50^{th} percentile, and top 95^{th} percentile). On the day of injury, players with delayed diagnosis sustained twice as many total head impacts (Table 2) and significantly more impacts with peak linear acceleration higher than the 50^{th} percentile of all impacts than players with immediate diagnosis (p < 0.001); however, the number of head impacts above the 95^{th} percentile of all impacts did not differ by diagnosis classification (p = 0.135). Players with delayed diagnosis also sustained a higher number of total impacts (p = 0.006) and 50^{th} percentile impacts did not differ statistically during this time (p = 0.129).

DISCUSSION

Recently, several studies have attempted to identify a [biomechanical] threshold for concussive injury in sports.(4, 17, 19) While the sporting environment offers a unique opportunity to study concussion, identifying a single head impact associated with injury is often difficult because athletes are frequently exposed to repetitive head impacts over the course of practices and games.(9, 10) Additionally, the diagnosis of sports concussion is often difficult due to variability in on-field presentation of signs and symptoms,(27, 31) the athletes' willingness to report,(25) and the potential for delayed symptom on-set.(18, 23) This investigation is the second in a series of analyses designed to elucidate the Biomechanical Basis of Mild Traumatic Brain Injury and focuses on the relationship between head impact exposure and timing of clinical diagnosis. Specifically, head impact exposure recorded from collegiate and high school football players diagnosed with concussion by medical personnel were separated into cases of immediate and delayed diagnosed concussion and compared.

All evaluated kinematic measures of impact, except peak rotational acceleration, were found to be significantly higher for impacts associated with immediately diagnosed concussions than the highest severity impact recorded on the day of delayed diagnoses injury (Figure 3). Additionally, the frequency of impacts by head impact location was not found to be significantly dependent on injury classification. Considering rotational acceleration is more likely to be influenced by impact location than linear acceleration and no dependence on location was found, it is understandable that kinematic measures derived from linear acceleration differed between cases of immediate and delayed diagnosis while rotational acceleration did not. Sixty-nine percent of all concussion-related impacts were either to the Front or Top of the head. These ratios of injury are similar to those reported by Crisco et al. who, when evaluating head impact exposure from three collegiate football teams, found that the highest peak linear accelerations occur for athletes not diagnosed with concussion following impacts to the Top, Front, Back, and Side of the head, respectively.(10) Since the impacts associated with both injury timing categories are in the highest percentile of all impacts by linear acceleration, it is not altogether surprising that the most frequent locations for concussive injury are the same as the locations where sub-concussive impacts result in the highest accelerations.

A key finding from our initial report was that athletes sustained significantly more head impacts on days of diagnosed concussion $(25.8 \pm 22.7 \text{ impacts per day})$ than on days without $(14.6 \pm 15.6 \text{ impacts per day}).(2)$ When separated into cases of immediate and delayed diagnosis; however, a sharper contrast emerges. Athletes with immediate diagnosis sustain a similar number of impacts on injury days $(16.5 \pm 15.1 \text{ impacts per day})$ as on non-injury days,(2) but athletes with delayed diagnosis sustain twice as many impacts $(32.9 \pm 24.9 \text{ impacts per day})$ on days of injury than on days without. Additionally, athletes with delayed diagnosis. By isolating this analysis to only include impacts in the top 50th and 95th percentile, it can be seen that the additional impacts sustained by athletes with delayed diagnosis are primarily of lower severity.

The first step in evaluating the relationship between head impact biomechanics and concussion is to make an association between an impact event and injury. During this process, we unexpectedly found that many injuries were not easily identifiable due to the frequency of head impacts experienced by football players and a high propensity for delayed injury reporting. Others reporting an association between head impact and injury have correlated video with data recorded from instrumented helmets to best identify the time of injury; (17, 20) however, this method requires a reliable athlete report of approximate time of injury and is still confounded by the potential influence of head impacts within a temporal proximity. Because of this, we chose to separate cases of diagnosed concussion into two general categories, those that were clearly associated with a single impact because the player was immediately removed from play and those diagnosed concussions that did not have an easily identifiable impact because diagnosis was delayed. This distinction is not based on the number or severity of symptoms experienced by the athlete or the length of those symptoms, so it cannot be assumed that athletes with immediate diagnosis had a higher severity of injury than those with delayed diagnosis, rather the symptoms associated with these injuries appear to differ in presentation and over time and/or illicit a different subject response, which leads to immediate removal from play for some, but not others.

For impact kinematics and location comparisons, biomechanical measures associated with delayed concussion diagnosis were linked with the impact resulting in the highest peak linear acceleration sustained on the day of injury. While it cannot be certain that the injury did not result from another impact, or a series of cumulative impacts, this conservative, systematic approach of associating impact with injury does allow us to illustrate differences between these two groups. By implementing this method, we potentially overestimate the head impact severity associated with delayed diagnosis, but the statistical significance between the two groups would be unaffected. This approach is also supported by 22 cases of delayed diagnosis where an approximate time of symptom onset was identified by the player, even though they continued to play. In 16 of these cases, the approximate time of injury corresponded with the recorded time for the highest peak linear acceleration impact of the day. In each of the 6 remaining cases, the athlete was initially evaluated by the team's medical staff following the impact where symptom on-set was thought to occur, but the player was not initially diagnosed with injury and allowed to re-enter play. Each athlete then sustained an impact with higher linear acceleration later that day before being diagnosed with concussion. Further support is found in the immediately diagnosed cases, where 38 (84.4%) of the impacts associated with concussion were the highest peak linear acceleration impact of the day. While any of the impact severity measures could have been chosen for these analyses, peak linear acceleration was used because it has previously been shown to be the most predictive of diagnosed concussion.(2) The same impact would have been chosen in 36, 47, 50, and 38 cases of delayed diagnosis if peak rotational acceleration, HIC15, GSI, or change in head velocity would have been used.

This study has several limitations that should be considered when interpreting the results. First, variability in injury diagnosis and methods used to identify injury most likely exists due to the large number of represented teams, inclusion of teams from two levels of play, and the progressively increasing public emphasis placed on concussion awareness during the six year period of this study. While level of play might be thought to have a significant

influence on the number of cases with immediate versus delayed diagnosis based on the theory that collegiate athletes may be more reluctant to self-report symptoms and that high school teams may not have the same resources to identify injuries immediately as they occur, this was not the case. The ratio of immediate to delayed cases of injury was nearly identical for high school (16 immediate, 21 delayed) and collegiate players (29 immediate, 39 delayed).

Additionally, the analyses presented focus on individual athletes who were selected for inclusion based solely on whether they sustained a diagnosed concussion while wearing an instrumented helmet. Because of this, extrinsic variables associated with these players such as position group and session participation (i.e. games vs. practices) were not matched to the general football population. This focus on individual players provides a means for identifying which biomechanical variables are most related to concussion diagnosis but, unfortunately, is not particularly well suited for directly correlating extrinsic variables to concussion risk. From a qualitative perspective, however, it does appear that lineman (offensive line, defensive line, and linebackers) tend to sustain a higher percentage of delayed diagnosis cases (70.4% delayed diagnosis) than skill position players (defensive backs, quarterbacks, running backs, wide receivers; 46.6% delayed diagnosis) and the percentage of immediate and delayed cases associated with games, practices, and scrimmages is similar (immediate diagnosis: game - 62.2%, practice - 33.3%, scrimmage 4.5%; delayed diagnosis: game – 58.3%, practice 33.3%, scrimmage 8.4%). These numbers suggest that lineman, who have been shown to sustain more head impacts than skill position players,(9) are more likely to sustain concussions with delayed diagnosis that skill position players who typically sustain impacts with higher kinematic response,(11) but further analysis on cohorts controlled for normal distributions of athletes are required to determine if these trends are statistically significant.

Finally, the study design only tracked concussion history during the period of time players wore instrumented helmets. Of the 105 cases, there were 9 subjects who sustained multiple concussions. This sample or repeat concussions is currently not large enough to draw meaningful conclusions on how concussion history affects either injury tolerance or clinical presentation; however, we do plan to present this data as individual case studies within separate communications.

This communication is the second in a series exploring the Biomechanical Basis of Mild Traumatic Brain Injury. This analysis compared head impact exposure for two groups of concussed athletes, those that were immediately diagnosed with injury and those with delayed diagnosis. While both injured groups sustained impacts with higher associated kinematic measures on days of diagnosed injury than on days without diagnosed injury, a clear differentiation between these cases exists with immediately diagnosed cases more closely associated with single impacts with high kinematic response and delayed cases associated with moderately high kinematic response and an increased number of impacts with low kinematic response. These data suggest differences in head impact exposure can result in different clinical presentation, and, therefore, diagnosed concussion should not be treated as a dichotomized outcome variable when determining injury risk. Additionally,

further exploration into the relationship between head impact exposure and other aspects of clinical presentation (e.g., balance, cognition, neuroimaging, etc.) is warranted.

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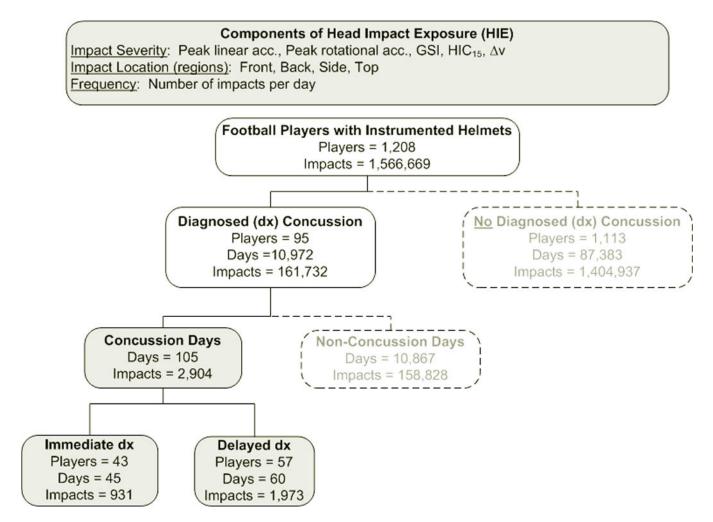


Figure 1.

Hypotheses tested within this communication are based on a subset of biomechanical and clinical data that was collected as part of a longitudinal study to investigate the biomechanical bases of mild traumatic brain injury. Data reported in this study are derived from the samples highlighted in the above flowchart.

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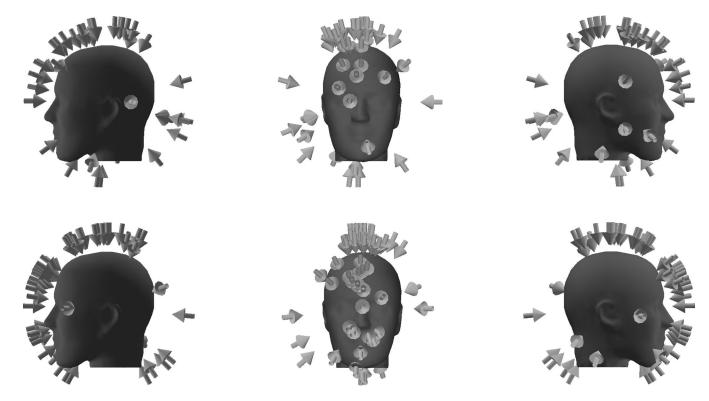


Figure 2.

Locations of impacts associated with immediate (top, N=45) and delayed (bottom, N=60) concussion diagnosis. The percentage of impacts by location did not differ by classification of immediate or delayed diagnosis, $\chi^2(3) = 4.72$ (p = 0.19)

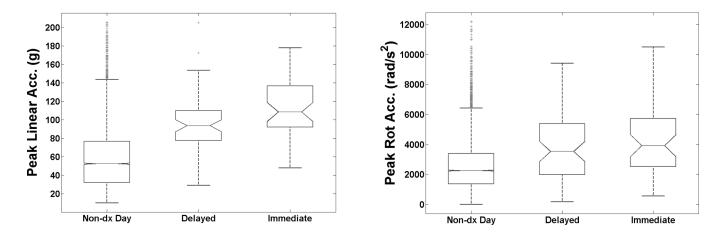


Figure 3.

Peak linear and rotational acceleration for impacts associated with immediate and delayed cases of diagnosed concussion compared to the highest severity impact recorded for those players on each playing day without diagnosed injury. Non-diagnosis day data previously reported by Beckwith et al.(2)

Table 1

Mean (SD) values of head kinematics following single head impacts associated with diagnosis of concussion. Immediately diagnosed concussions were associated with significantly higher mean head kinematics (all measures except peak angular acceleration) than injuries with delayed diagnosis.

Single Impact Kinematics	Timing of Diagn	osed Concussion	P Value
	Immediate	Delayed	
Peak Linear Acc. (g)	112.1 (35.4)	95.3 (30.9)	0.011
Peak Angular Acc. (rad/s ²)	4,253 (2,287)	3,771 (2,258)	0.284
HIC ₁₅	331.2 (239.4)	194.8 (150.6)	0.004
GSI	439.3 (315.2)	274.2 (206.4)	0.005
v (m/s)	4.29 (1.71)	3.33 (1.29)	0.001

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Table 2

The mean (SD) number of head impacts sustained on the same day and within seven days of injury. Delayed diagnosis concussions were preceded by more total impacts and impacts with peak linear acceleration higher than the median (top 50th percentile) of all impacts than injuries with immediate diagnosis.

Days Prior to Injury	Ę	All Impacts		Top :	Top 50 th Percentile	a	Top 95 ^t	Top 95 th Percentile ^b	e p
	Immediate	Immediate Delayed	d	Immediate Delayed	Delayed	d	Immediate Delayed	Delayed	d
Same day	16.5 (15.1)	$16.5(15.1) 32.9(24.9) < 0.001 \qquad 8.7(8.9) \qquad 18.7(15.6) < 0.001 \qquad 1.8(1.2) \qquad 2.6(2.5) 0.135(1.2) \qquad 0.135(1.2)$	< 0.001	8.7 (8.9)	18.7 (15.6)	< 0.001	1.8 (1.2)	2.6 (2.5)	0.135
7 days of injury	50.2 (43.6)	50.2 (43.6) 69.7 (43.3) 0.006	0.006	24.3 (38.4)	24.3 (38.4) 38.4 (26.2) 0.006	0.006	3.9 (3.5) 5.3 (5.4)	5.3 (5.4)	0.129