Incidence, Clinical Course, and Predictors of Prolonged Recovery Time Following Sport-Related Concussion in High School and College Athletes

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Abstract

Sport-related concussion (SRC) is typically followed by clinical recovery within days, but reports of prolonged symptoms are common. We investigated the incidence of prolonged recovery in a large cohort (n = 18,531) of athlete seasons over a 10-year period. A total of 570 athletes with concussion (3.1%) and 166 controls who underwent pre-injury baseline assessments of symptoms, neurocognitive functioning and balance were re-assessed immediately, 3 hr, and 1, 2, 3, 5, 7, and 45 or 90 days after concussion. Concussed athletes were stratified into typical (within 7 days) or prolonged (> 7 days) recovery groups based on symptom recovery time. Ten percent of athletes (n = 57) had a prolonged symptom recovery, which was also associated with lengthier recovery on neurocognitive testing (p < .001). At 45–90 days post-injury, the prolonged recovery group reported elevated symptoms, without deficits on cognitive or balance testing. Prolonged recovery was associated with unconsciousness [odds ratio (OR), 4.15; 95% confidence interval (CI) 2.12–8.15], posttraumatic amnesia (OR, 1.81; 95% CI, 1.00–3.28), and more severe acute symptoms (p < .0001). These results suggest that a small percentage of athletes may experience symptoms and functional impairments beyond the typical window of recovery after SRC, and that prolonged recovery is associated with acute indicators of more severe injury. (*JINS*, 2013, 19, 22–33)

Keywords: Brain injury, Concussion, Neuropsychological tests, Sport injuries, Neurological disorders, Closed head injury

INTRODUCTION

Based on its reported prevalence, acute effects, and fears over potential long-term neurological consequences, sport-related concussion has become the focus of increasing concern from clinicians, researchers, sporting organizations, and athletes themselves over the last 2 decades (DeKosky, Ikonomovic, & Gandy, 2010; Kelly, 1999; Langlois, Rutland-Brown, & Wald, 2006; McCrory et al., 2005, 2009; "Nonfatal traumatic

brain injuries from sports and recreation activities—United States, 2001–2005," 2007). Concussion is a frequent injury in contact and collision sports (e.g., football, hockey, wrestling) at all levels of participation, including youth sports (Guskiewicz, Weaver, Padua, & Garrett, 2000; Halstead & Walter, 2010; Powell & Barber-Foss, 1999). A recent study indicated that from 1997 to 2007 emergency department visits for 8- to 13-year-old children affected by concussion in organized team sports have doubled, and had increased by more than 200% in the 14- to 19-year-old group (Bakhos, Lockhart, Myers, & Linakis, 2010).

Extensive research over the last decade has significantly advanced our scientific understanding of the true natural

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history of clinical recovery following sport-related concussion. In general, the findings on acute recovery have been favorable. A 2003 report was the first to plot the continuous time course of acute recovery within several days after concussion, indicating that more than 90% of athletes reported a symptom recovery within 1 week (McCrea et al., 2003, 2005). Several other prospective studies have since consistently demonstrated that the overwhelming majority of athletes achieve a complete recovery in symptoms, cognitive functioning, postural stability, and other functional impairments over a period of approximately one to two weeks following concussion (Belanger & Vanderploeg, 2005; Broglio & Puetz, 2008; Collins et al., 1999; Guskiewicz et al., 2003; Macciocchi, Barth, Alves, Rimel, & Jane, 1996).

There are frequent anecdotal reports, however, of athletes who remain symptomatic or impaired on functional testing well beyond the window of recovery commonly reported in group studies. The greatest challenge arguably still facing sports medicine clinicians and public health experts is how to most effectively manage and reduce risk in this subset of athletes who do not follow the "typical" course of recovery. The precise frequency of athletes who do not follow the typical course of rapid, spontaneous recovery and instead exhibit prolonged postconcussive symptoms or other functional impairments after concussion remains unclear. While several studies have reported that the largest percentage of athletes achieve a complete recovery within one to two weeks (Belanger & Vanderploeg, 2005; Broglio & Puetz, 2008), limited research has suggested a lengthier recovery time in younger athletes (Field, Collins, Lovell, & Maroon, 2003), citing that roughly half of all high school athletes required more than 14 days to recover (Lau, Lovell, Collins, & Pardini, 2009; Lau, Collins, & Lovell, 2012). Unfortunately, these studies did not include controls, and applied criteria for "recovery" that may have resulted in high false positive rates due to criterion contamination that significantly complicate the interpretation of data from those studies. Furthermore, there is little empirical evidence on what risk factors may be associated with prolonged recovery time or poor outcome and how these risks can be modified in a clinical setting. A recent study of Australian Rules football players indicated that delayed return to sport after concussion was associated with acute symptom severity, but that study did not involve longitudinal tracking of concussed athletes beyond 7 days post-injury (Makdissi et al., 2010).

The current study used a longitudinal design to prospectively investigate the incidence, clinical course, and prediction of prolonged recovery time following sport-related concussion in a large sample of high school and collegiate athletes.

METHODS

Participants

This study combined datasets from three parallel, multi-center, prospective studies investigating the effects of sport-related concussion between 1999 through 2008. In total, 18,531 player seasons (i.e., total sport seasons of participation by all athletes)

were under surveillance during that 10-year period. Athletes who participated more than one year in the study had multiple sport seasons in the database. A cohort of 570 high school and collegiate athletes (3.1% of athlete seasons) who sustained a sport-related concussion in an organized team sport during this prospective research study was extensively studied. The injured cohort was 88.9 percent male and 11.1 percent female; 60.5% of injuries studied were at the high school participation level and 39.5% involved collegiate athletes. The distribution of concussions across sports was as follows: American football (80.7%), followed by soccer (13.3%), lacrosse (5.2%), and ice hockey (0.8%).

A control group (n = 166) of non-concussed athletes matched to the concussion group on demographic variables (i.e., sport, age, gender, years of education, level of competition) and baseline performance on the study's main outcome measures was administered the same assessment protocol as the concussed group. The method for control group sampling and matching used in this study has been demonstrated to be effective in closely matching control subjects to concussed subjects and controlling for non-injury variables in our prior studies of high school and college athletes (Guskiewicz et al., 2003; McCrea, 2001; McCrea et al., 2003, 2005). The control group was 63.3% (n = 105) high school athletes and 36.7%collegiate athletes (n = 61). Limited resources did not allow us to enroll a control group of 570 athletes, but the current control group was of sufficient size to allow adequate matching and ample statistical power.

This study was approved by the institutional review board for protection of human research participants at the host institution of the principal investigators (Drs. Guskiewicz and McCrea). Written informed consent was obtained from all participants or their parent/guardian before participation in the study.

Study Design and Procedures

All athletes underwent a preseason baseline evaluation on a battery of concussion assessment measures upon enrollment in the study. Injured subjects were identified and enrolled in the study protocol by a team physician or certified athletic trainer present on the sideline using the same procedures to identify concussed athletes during an athletic contest or practice. Throughout the entire study, concussion was defined according to the American Academy of Neurology Guideline for Management of Sports Concussion (i.e., "a trauma-induced alteration in mental status that may or may not involve loss of consciousness"), which was the most widely accepted definition in the clinical and scientific communities at the time this study was initiated [Kelly & Rosenberg, 1997; "Practice parameter: the management of concussion in sports (summary statement) report of the Quality Standards Subcommittee," 1997]. All athletes were closely monitored by medical staff over the course of their recovery.

Athletes were evaluated using the study's standardized outcome measures on the sideline immediately following injury, 2–3 hr later, and again at several time points during the

first week post-injury. More extensive neuropsychological testing was administered 1–2 days and 1 week post-injury. All measures were then re-administered 45 days or 90 days post-injury. Over the 10-year study period, this assessment point of remote recovery moved from 90 to 45 days.

Main Outcome Measures

The Graded Symptom Checklist (GSC), Balance Error Scoring System (BESS), Standardized Assessment of Concussion (SAC), and a brief neuropsychological test battery were used to assess post-concussive symptoms, postural stability, and cognitive functioning, respectively. The GSC required athletes to rate the presence and severity of 25 common concussion symptoms on a 0-6 (6 most severe) Likert scale. The SAC is a brief cognitive screening tool that assesses orientation, concentration, and immediate and delayed memory. The BESS is a brief clinical measure of postural stability. Total scores on the GSC (range, 0–150), SAC (range, 0-30), and BESS (range, 0-60) were used for analysis. The traditional (i.e., "paper and pencil") neuropsychological test battery used in this study included the Hopkins Verbal Learning Test (HVLT), Trail Making Test (Part B), Symbol Digit Modalities Test (SDMT), Controlled Oral Word Association Test (COWAT), and Stroop Color-Word Test. Several studies on the effects of sport-related concussion have demonstrated the reliability and validity of the GSC, SAC, BESS and selected neuropsychological tests in assessing the effects of sport-related concussion (Barr & McCrea, 2001; Collins et al., 1999; Guskiewicz, 2003; Lovell et al., 2003; McCrea, 2001; McCrea et al., 2003, 2005). The tests included in the neuropsychological test battery were commonly used in sports concussion studies and clinical programs during the early years of our study period and were retained throughout our study to maximize consistency of our main outcome measures.

All measures were administered by study personnel (e.g., certified athletic trainers, research assistants, neuropsychologists) fully trained and supervised by the investigators on standardized assessment methods. Alternate forms of all cognitive outcome measures except the Stroop were used to reduce practice effects over repeated administrations. The order of test administration was the same for all injured and control subjects. This conventional battery was implemented at the outset of our studies, before the proliferation of computerized test batteries, and maintained throughout our studies.

Statistical Analysis

For our current analyses directly relevant to the study's specific aims, injured players were stratified to one of two groups based on the following empirically-derived criteria:

Typical recovery group

Athletes were assigned to the typical recovery group if the change in their total score on the Graded Symptom Checklist (GSC) from pre-injury baseline to Day 7 post-injury was

inside the 95th percentile of the change score for the normal control group over the same period. Specifically, 94.7% of controls had a change of \odot 5 points from baseline to day 7 on the GSC, so injured players were assigned to the typical recovery group if their change score from baseline to day 7 on the GSC was ⊙ 5. The 95th percentile was applied based on the recognition that there is a small degree of variability in GSC score even among normal, non-concussed athletes. The day 7 time point was used because of consistent reports in the literature indicating that athletes typical achieve a complete recovery within one week after concussion. Applying the 95th percentile to the definition of recovery also suggests that 5% of normal control group would not meet the criterion of "typical recovery" (i.e., representing a 5% "false positive" rate). It was believed that this definition was sufficiently conservative to define "typical recovery" based on GSC score, while also allowing for the normal psychometric variability of the scale. We specifically elected to use symptom recovery time (as quantified by GSC score relative to individual pre-injury baseline, controlling for normal variability on the scale) to stratify between typical vs. prolonged recovery because we were interested in the indicator relied on most in the setting of clinicians determining an athlete's overall clinical recovery and fitness to return to play.

Prolonged recovery group

Conversely, injured players were assigned to the prolonged recovery group if their change score on the GSC from baseline to Day 7 was 6 or higher.

Our statistical analysis compared the typical recovery, prolonged recovery and control groups on several metrics relevant to the study's specific aims. Since serial observations on individuals were collected over the study period, mixed models with interaction between time and group were performed to study differences among the three groups at each time point in symptom recovery, cognitive recovery, postural stability recovery, and neuropsychological recovery [1]. The unstructured covariance structure was used in the mixed model since it showed the lowest Akaike information criterion (AIC) among compound symmetric, autoregressive order one, and unstructured covariance structures.

For symptom, cognitive, and postural stability recovery, nine assessment time points were included: pre-injury baseline, time of concussion, 3 hr, and days 1, 2, 3, 5, 7, and 45/90 post-injury. Four time points (baseline, day 1–2, day 6–7, and day 45–90) were observed for neuropsychological recovery. As noted, the final assessment point varied from 45 to 90 (\pm 5) days post-injury over the 10-year study. These data points were mutually exclusive, so they were combined as day 45/90 in the analysis. There were cases with missing data at one or more time points. Across all time points for all participants, 85% of data were complete. To account for the missing data, multiple imputation with 20 imputations was used (Rubin, 1987). This method is widely accepted in the biostatistics community and has been effectively used in studies previously published by our research group (McCrea et al., 2003).

Symptom, cognitive, and postural stability recovery curves for the three groups were created with 95% confidence intervals based on the estimated model. Since multiple testing was performed at each time point, Dunn-Sidak correction was considered to control Type I error. Using this conservative correction, we used a 0.002 level of significance for the *post hoc* comparisons on data from the GSC, SAC and BESS and 0.004 for the neurocognitive tests.

In addition, univariate logistic regression was used to identify risk factors associated with prolonged recovery (i.e., prolonged recovery group vs. typical recovery group). Multivariate logistic regression was not considered because some of the potential risk factors are highly correlated. Factors included in the regression model are listed in Table 4. A second logistic regression was implemented to investigate potential risk factors associated with prolonged recovery at day 45/90. For all logistic regression analyses, no imputation for missing values was used. All analyses were performed using SAS, version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

Incidence of Typical vs. Prolonged Recovery

Applying the study's empirically derived criteria, 90% (n = 513) of injured athletes were classified as the typical recovery group and 10% (n = 57) as the prolonged recovery group.

Table 1 provides a comparison of characteristics for the three study groups. As expected based on our matching algorithms, there were no statistically significant differences between the two injured groups or the control group on demographic (except for height), concussion history, or baseline test performance variables used to match control and injured subjects. The two injured and control groups were also not statistically different at baseline from the larger group of athletes enrolled in the study.

Typical vs. Prolonged Recovery Course

The prolonged recovery group had a significantly longer time course of recovery in symptoms, cognitive functioning and postural stability that was clearly distinct from the typical recovery group and control group.

As expected from the classification criteria, the prolonged recovery group had a longer course of symptoms than the typical recovery group. The prolonged recovery group reported more severe symptoms than the control group and typical recovery group at all assessment points from time of injury through day 45/90 post-injury (group \times time interaction; p < .001) (see Figure 1). The typical recovery group reported higher symptom levels than the control group through day 3 post-injury (p < .0001), without significantly elevated symptoms at day 5 or thereafter.

Beyond self-reported symptoms, the prolonged recovery group also showed a pattern of more severe and persistent cognitive impairment on standardized testing than the typical

Table 1. Comparison of sample characteristics for typical recovery group, prolonged recovery group, and control group

	Mean (95% CI)								
Characteristic	Typical recovery group $(n = 513)$	Prolonged recovery group $(n = 57)$	Control group $(n = 166)$	p					
Demographics									
Age (y)	17.51 (17.32–17.69)	17.04 (16.41–17.66)	17.39 (17.11–17.68)	.25					
Academic year (1–4)	2.53 (2.35-2.72)	2.75 (1.93–3.57)	2.66 (2.33–2.99)	.54					
Height (in)	70.65 (70.25–71.04)	70.09 (68.97–71.22)	71.52 (70.98–72.06)	.04					
Body weight (lbs)	191.00 (186.81–195.19)	186.29 (173.39–199.19)	196.50 (189.44–203.56)	.30					
Years played sport (y)	8.97 (8.54-9.40)	8.58 (5.85–11.31)	8.42 (7.67–9.16)	.44					
Self-reported concussion history									
Prior concussions – total (average per subject)	0.51 (0.41-0.61)	0.41 (0.15-0.66)	0.33 (0.20-0.46)	.49					
Prior concussions – sport-related (average per subject)	0.40 (0.32–0.49)	0.22 (0.04–0.40)	0.30 (0.19–0.41)	.15					
Baseline test results									
GSC total score	4.23 (3.58-4.89)	3.24 (1.69–4.79)	3.94 (2.79–5.09)	.60					
SAC total score	27.00 (26.78–27.22)	27.05 (26.39–27.72)	26.92 (26.63–27.22)	.89					
BESS total score	10.98 (10.26–11.70)	12.06 (10.54–13.57)	13.89 (13.09–14.69)	.30					
HVLT Immediate	25.15 (24.34–25.95)	22.70 (20.15–25.25)	25.31(24.23–26.40)	.18					
HVLT Delayed Recall	8.72 (8.31-9.12)	8.20 (6.95–9.45)	9.15 (8.58-9.72)	.29					
HVLT Recognition	22.71 (22.36–23.06)	22.42 (21.43–23.37)	22.94 (22.60-23.28)	.55					
Trail Making Test- B	65.41 (61.41–69.41)	68.82 (51.77–85.88)	57.30 (52.30-62.31)	.05					
SDMT	55.62 (53.42-57.82)	52.31 (42.87-61.73)	58.90 (55.63-62.16)	.13					
Stroop Color Word	46.95 (45.28–48.63)	48.71 (43.89–53.51)	48.66 (46.05–51.27)	.48					

Note. For academic year, value indicates year in high school or college for total combined sample.

GSC = Graded Symptom Checklist; SAC = Standardized Assessment of Concussion; BESS = Balance Error Scoring System; HVLT = Hopkins Verbal Learning Test; SDMT = Symbol Digit Modalities Test; 95% CI = 95% confidence interval.

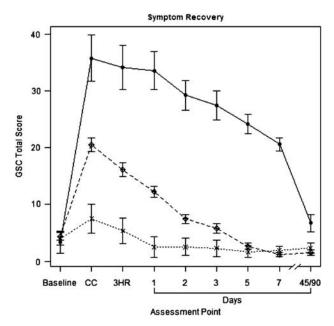


Fig. 1. Symptom recovery curve comparing typical recovery (open circles), prolonged recovery (filled circles), and normal control (Xs) groups. Group x time interaction, p < .001. Higher scores indicate more severe symptoms on the GSC. GSC = Graded Symptom Checklist; CC = time of concussion; 3 HR = 3 hours post-injury. Error bars indicate 95% confidence interval.

recovery group and control group, as measured by performance on the SAC (group \times time interaction, p < .001) (see Figure 2). The prolonged recovery group performed poorer than the typical recovery group and control group on the SAC through day 7 post-injury (p < .0001), while the typical recovery group showed cognitive recovery on the SAC relative to controls by day 2 post-injury. There were no significant group differences on the SAC at day 45/90.

Among the neurocognitive measures, only a few significant group findings were identified and there were no significant interactions (group \times day effects; all p-values > .08). Applying our conservative correction for level of statistical significance (p < .004), the prolonged recovery group showed significantly lower immediate memory scores on the Hopkins Verbal Learning Test (HVLT Immediate Memory) than the typical group (estimated difference: -2.88; 95% CI: -1.00 to -4.76; p = .0028) at day 6–7, but neither the typical or atypical recovery groups showed a statistically significant difference from the control group. For the other neuropsychological measures, we did not find any statistically significant group differences at any time points (see Table 3).

The prolonged and typical recovery groups performed more poorly than controls on postural stability testing immediately after injury (p < .001) (see Figure 3 and Table 2), but there were no differences between the prolonged and recovery group. There were no statistically significant group differences on balance testing beyond 3 hr post-injury.

Tables 2 and 3 provides detailed data on estimated differences and effect sizes between the typical recovery, prolonged recovery and control groups on the GSC, SAC, BESS,

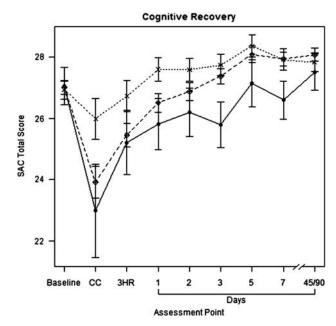


Fig. 2. Cognitive recovery curve comparing typical recovery (open circles), prolonged recovery (filled circles), and normal control (Xs) groups. Group x time interaction, p < .001. Lower scores indicate poorer cognitive test performance on the SAC. SAC = Standardized Assessment of Concussion; CC = time of concussion; 3 HR = 3 hours post-injury. Error bars indicate 95% confidence interval.

and neuropsychological tests at each post-injury assessment point. Overall, the prolonged recovery group reported elevated symptoms that persisted through the day 45/90 time

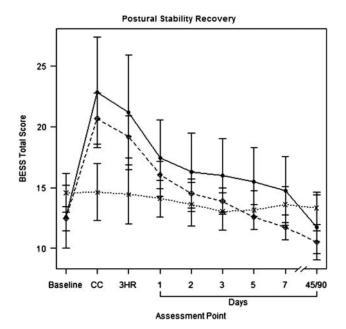


Fig. 3. Postural stability recovery curve comparing typical recovery (open circles), prolonged recovery (filled circles), and normal control (Xs) groups. Group x time interaction, p < .001. Higher scores indicate poorer balance test performance on the BESS. BESS = Balance Error Scoring System; CC = time of concussion; 3 HR = = 3 hours postinjury. Error bars indicate 95% confidence interval.

Table 2. Estimated differences among typical recovery group, prolonged recovery group, and control group on GSC, SAC, and BESS

		Symptoms (GSC score)			Cognitive function (SAC score)				Postural stability (BESS score)				
Time	Comparison	Estimate	95% CI	Effect size	P value	Estimate	95% CI	Effect size	p value	Estimate	95% CI	Effect size	p value
BL	Typical vs. Control	0.38	(-0.95, 1.71)	0.05	.5747	0.06	(-0.31, 0.43)	0.03	.7376	-2.12	(-4.01, -0.23)	-0.29	.031
	Prolonged vs. Typical	-1.04	(-3.1, 1.02)	-0.15	.1607	0.05	(-0.6, 0.7)	0.03	.8741	0.15	(-2.66, 2.96)	0.03	.9155
	Prolonged vs. Control	-0.66	(-2.91, 1.59)	-0.10	.5699	0.12	(-0.57, 0.81)	0.06	.7384	-1.97	(-4.81, 0.88)	-0.30	.1763
CC	Typical vs. Control	13.03	(10.25, 15.81)	1.08	<.0001	-2.07	(-2.93, -1.21)	-0.57	<.0001	6.07	(2.95, 9.19)	0.53	.0002
	Prolonged vs. Typical	15.27	(11.06, 19.48)	0.95	<.0001	-0.93	(-2.52, 0.66)	-0.22	.2531	2.17	(-2.85, 7.19)	0.18	.3979
	Prolonged vs. Control	28.29	(23.45, 33.13)	1.93	<.0001	-3.01	(-4.72, -1.3)	-0.79	.0007	8.24	(3.16, 13.32)	0.79	.0017
3HR	Typical vs. Control	10.75	(8.22, 13.28)	0.95	<.0001	-1.27	(-1.88, -0.66)	-0.47	<.0001	4.74	(1.77, 7.7)	0.42	.0023
	Prolonged vs. Typical	18.05	(13.99, 22.11)	1.11	<.0001	-0.24	(-1.38, 0.9)	-0.08	.6775	2.00	(-2.86, 6.87)	0.18	.4208
	Prolonged vs. Control	28.80	(24.21, 33.39)	2.01	<.0001	-1.51	(-2.67, -0.35)	-0.55	.0115	6.74	(1.48, 12)	0.64	.0135
D1	Typical vs. Control	9.72	(7.62, 11.82)	1.03	<.0001	-1.09	(-1.58, -0.6)	-0.48	<.0001	1.95	(0.08, 3.82)	0.21	.0418
	Prolonged vs. Typical	21.35	(17.88, 24.82)	1.45	<.0001	-0.68	(-1.56, 0.2)	-0.23	.1333	1.38	(-1.92, 4.68)	0.16	.4129
	Prolonged vs. Control	31.07	(27.19, 34.95)	2.46	<.0001	-1.77	(-2.69, -0.85)	-0.66	.0002	3.33	(-0.17, 6.84)	0.39	.063
D2	Typical vs. Control	4.94	(3.2, 6.68)	0.64	<.0001	-0.72	(-1.17, -0.27)	-0.35	.0024	0.90	(-1.31, 3.1)	0.09	.4258
	Prolonged vs. Typical	21.81	(19.07, 24.55)	1.64	<.0001	-0.68	(-1.5, 0.14)	-0.27	.1095	1.74	(-1.6, 5.08)	0.22	.3069
	Prolonged vs. Control	26.74	(23.72, 29.76)	2.20	<.0001	-1.39	(-2.25, -0.53)	-0.59	.0018	2.64	(-1.07, 6.36)	0.31	.1646
D3	Typical vs. Control	3.51	(1.82, 5.2)	0.47	<.0001	-0.37	(-0.8, 0.06)	-0.19	.095	0.85	(-1.03, 2.73)	0.10	.3777
	Prolonged vs. Typical	21.70	(19.03, 24.37)	1.68	<.0001	-1.58	(-2.36, -0.8)	-0.57	<.0001	2.13	(-1.07, 5.33)	0.26	.1933
	Prolonged vs. Control	25.21	(22.29, 28.13)	2.13	<.0001	-1.96	(-2.78, -1.14)	-0.72	<.0001	2.98	(-0.46, 6.41)	0.39	.0904
D5	Typical vs. Control	0.97	(-0.19, 2.13)	0.21	.1027	-0.27	(-0.72, 0.18)	-0.13	.2284	-0.57	(-2.49, 1.34)	-0.07	.5582
	Prolonged vs. Typical	21.51	(19.75, 23.27)	1.94	<.0001	-0.94	(-1.74, -0.14)	-0.35	.0224	2.91	(-0.1, 5.92)	0.38	.0591
	Prolonged vs. Control	22.48	(20.52, 24.44)	2.05	<.0001	-1.21	(-2.05, -0.37)	-0.49	.0049	2.33	(-0.92, 5.59)	0.30	.1611
D7	Typical vs. Control	-0.79	(-1.63, 0.05)	-0.24	.0714	0.01	(-0.4, 0.42)	0.01	.9499	-1.89	(-3.67, -0.1)	-0.22	.0385
	Prolonged vs. Typical	19.45	(18.2, 20.7)	2.07	<.0001	-1.34	(-2.01, -0.67)	-0.62	<.0001	3.00	(0, 5.99)	0.37	.0505
	Prolonged vs. Control	18.67	(17.26, 20.08)	1.94	<.0001	-1.33	(-2.04, -0.62)	-0.59	.0003	1.11	(-2.07, 4.3)	0.13	.4945
D45/90	Typical vs. Control	-0.86	(-1.88, 0.16)	-0.16	.098	0.24	(-0.13, 0.61)	0.14	.1986	-2.81	(-4.47, -1.15)	-0.34	.001
	Prolonged vs. Typical	5.21	(3.62, 6.8)	0.65	<.0001	-0.57	(-1.2, 0.06)	-0.31	.0799	1.20	(-1.64, 4.04)	0.18	.4063
	Prolonged vs. Control	4.35	(2.59, 6.11)	0.50	<.0001	-0.32	(-1.01, 0.37)	-0.16	.3506	-1.61	(-4.61, 1.4)	-0.21	.2953

Note. Bold p values < .002.

GSC = Graded Symptom Checklist; SAC = Standardized Assessment of Concussion; BESS = Balance Error Scoring System; BL = Baseline (pre-injury); CC = time of concussion; 3 HR = 3 hours post-injury; D1 = Day 1 post-injury; D2 = Day 2 post-injury; D3 = Day 3 post-injury; D45/90 = Day 45/90 post-injury; 95% CI = 95% confidence interval of estimate.

Table 3. Estimated differences among typical recovery group, prolonged recovery group, and control group on neuropsychological tests

		HVLT Immediate Memory			HVLT Delayed Recall			HVLT Recognition					
Assessment point	Comparison	Estimate	95% CI	Effect size	p value	Estimate	95% CI	Effect size	p value	Estimate	95% CI	Effect size	p value
BL	Typical vs. Control	0.11	(-1.07, 1.29)	0.03	.8594	-0.04	(-0.59, 0.52)	-0.02	.9023	0.02	(-0.39, 0.44)	0.01	.9167
	Prolonged vs. Typical	-1.72	(-3.98, 0.54)	-0.41	.1382	-0.46	(-1.58, 0.66)	-0.21	.4233	-0.28	(-1.09, 0.53)	-0.18	.5006
	Prolonged vs. Control	-1.61	(-3.93, 0.71)	-0.4	.1754	-0.49	(-1.58, 0.59)	-0.23	.3719	-0.26	(-1.04, 0.52)	-0.18	.5192
D1-2	Typical vs. Control	-1.1	(-2.18, -0.03)	-0.25	.0449	-0.49	(-1.06, 0.09)	-0.2	.0968	-0.52	(-0.96, -0.07)	-0.28	.0238
	Prolonged vs. Typical	-1.29	(-3.26, 0.68)	-0.29	.1997	-0.78	(-1.84, 0.28)	-0.32	.1497	0	(-0.81, 0.82)	0	.9968
	Prolonged vs. Control	-2.39	(-4.44, -0.35)	-0.57	.0222	-1.27	(-2.36, -0.18)	-0.55	.0233	-0.51	(-1.36, 0.33)	-0.32	.2327
D6-7	Typical vs. Control	0.45	(-0.58, 1.47)	0.1	.3927	0.16	(-0.49, 0.82)	0.06	.6271	0.35	(-0.11, 0.82)	0.19	.1375
	Prolonged vs. Typical	-2.88	(-4.76, -1.00)	-0.65	.0028	-1.35	(-2.53, -0.16)	-0.46	.0261	-0.79	(-1.61, 0.03)	-0.44	.06
	Prolonged vs. Control	-2.43	(-4.37, -0.5)	-0.54	.0141	-1.19	(-2.41, 0.04)	-0.39	.0591	-0.43	(-1.3, 0.43)	-0.21	.3236
D45/90	Typical vs. Control	-0.21	(-1.16, 0.73)	-0.05	.6578	0.1	(-0.46, 0.67)	0.04	.7208	0.16	(-0.27, 0.59)	0.09	.4699
	Prolonged vs. Typical	-2.03	(-3.89, -0.18)	-0.45	.0321	-0.58	(-1.66, 0.49)	-0.25	.2857	-0.62	(-1.44, 0.19)	-0.33	.1337
	Prolonged vs. Control	-2.25	(-4.16, -0.34)	-0.49	.0213	-0.48	(-1.58, 0.61)	-0.21	.3896	-0.47	(-1.29, 0.36)	-0.29	.2709
			Symbol Digit Mod	dalities Test			Trail Marking Test – Part B			Stroop Color-Word Test			
Assessment point	Comparison	Estimate	95% CI	Effect size	p Value	Estimate	95% CI	Effect size	p value	Estimate	95% CI	Effect size	p value
BL	Typical vs. Control	-1.22	(-4.35, 1.91)	-0.1	.4463	5.15	(-0.76, 11.06)	0.25	.091	-0.43	(-2.85, 2)	-0.05	.7306
	Prolonged vs. Typical	-2.3	(-8.31, 3.71)	-0.19	.4543	3.99	(-8.09, 16.07)	0.18	.5194	0.46	(-4.1, 5.03)	0.05	.8423
	Prolonged vs. Control	-3.52	(-9.49, 2.45)	-0.29	.2492	9.14	(-2.65, 20.93)	0.43	.1318	0.04	(-4.53, 4.61)	0	.9874
D1-2	Typical vs. Control	-2.85	(-5.65, -0.05)	-0.25	.0474	4.98	(0, 9.95)	0.25	.0514	-1.3	(-3.63, 1.03)	-0.14	.2766
	Prolonged vs. Typical	-2.96	(-7.96, 2.05)	-0.27	.2474	-3.04	(-11.66, 5.59)	-0.17	.4902	1.77	(-2.6, 6.13)	0.17	.4284
	Prolonged vs. Control	-5.81	(-10.92, -0.69)	-0.54	.0265	1.94	(-7.08, 10.96)	0.12	.674	0.47	(-4.02, 4.96)	0.05	.8374
D6-7	Typical vs. Control	-0.26	(-3.05, 2.52)	-0.02	.8526	5.35	(1.32, 9.38)	0.32	.0097	0.13	(-2.31, 2.58)	0.01	.9142
	Prolonged vs. Typical	-3.71	(-8.43, 1.01)	-0.36	.1236	2.29	(-5.14, 9.72)	0.13	.5465	0.37	(-4.19, 4.92)	0.04	.8746
	Prolonged vs. Control	-3.97	(-8.96, 1.01)	-0.36	.1185	7.64	(-0.04, 15.31)	0.44	.0515	0.5	(-4.2, 5.21)	0.05	.8344
D45/90	Typical vs. Control	0.49	(-2.15, 3.13)	0.04	.7138	3.91	(-0.15, 7.97)	0.24	.0597	-0.42	(-2.8, 1.95)	-0.04	.7289
	Prolonged vs. Typical	-5.97	(-11.14, -0.8)	-0.58	.024	4.65	(-3.02, 12.31)	0.24	.2351	0.73	(-3.91, 5.36)	0.06	.7591
	Prolonged vs. Control	-5.47	(-10.75, -0.19)	-0.52	.0426	8.56	(0.76, 16.36)	0.45	.0319	0.31	(-4.43, 5.04)	0.02	.8995

Note. Bold p values < .004.

HVLT = Hopkins Verbal Learning Test; BL = Baseline (pre-injury); CC = time of concussion; 3 HR = 3 hours post-injury; D1 = Day 1 post-injury; D2 = Day 2 post-injury; D3 = Day 3 post-injury; Day 5 = Day 5 post-injury; D7 = Day 7 post-injury; D45/90 = Day 45/90 post-injury. 95% CI = 95% confidence interval of estimate.

Table 4. Results of univariate logistic regression on factors associated with prolonged recovery

Category	Categorical variables	Odds 1	p		
Demographics	Gender (male)	1.736	(0.83, 3.63)	.1422	
Participation	Sport				
-	Soccer (reference)	1.000			
	Football	0.872	(0.36, 2.11)	.1342	
	Hockey	2.960	(0.27, 31.91)	.4543	
	Lacrosse	2.130	(0.67, 6.74)	.4737	
	Level of competition				
	College (reference)	1.000			
	High school	1.318	(0.73, 2.37)	.3565	
	Sport orientation				
	Offense (reference)	1.000			
	Defense	1.217	(0.47, 3.13)	.6825	
Mechanism of injury	Being tackled by opponent	0.584	(0.23, 1.51)	.2684	
integration of injury	Tackling opponent	1.696	(0.92, 3.12)	.0897	
	Collision with opponent	0.752	(0.42, 1.35)	.3376	
	Contact with ground	2.008	(0.92, 4.38)	.0792	
	Contact with barrier (e.g., goal)	0.509	(0.07, 3.9)	.5158	
	Contact with ball	2.143	(0.67, 6.82)	.1966	
		0.556	(0.19, 1.59)	.2748	
Acute injury characteristics	Loss of consciousness	4.152	(2.12, 8.15)	<.0001	
Acute injury characteristics	Posttraumatic amnesia	1.814	(1.00, 3.28)	.0489	
	Retrograde amnesia	2.190	` ' '	.0469	
Concussion history	Same season repeat concussion	1.141	(1.18, 4.06) (0.57, 2.31)	.7133	
Category	Continuous variables	Estimate (95% CI)			
		0.124	(0.20, 0.01)	0651	
Demographics		-0.134	(-0.28, 0.01)	.0651	
	-	-0.018	(-0.07, 0.03)	.5035	
and	_	-0.001	(-0.01, 0.01)	.6453	
Sport of Offer Defermance Defermance Defermance Defermance Defermance Defermance Defermance Defermance Demographics GSC scores Sport of Offer Defermance Defermance Demographics Demographics Age Height Weight Weight Demographics Demograp		-0.022	(-0.07, 0.02)	.3311	
	Time of concussion	0.047	(0.03, 0.06)	<.0001	
	2–3 hours post	0.053	(0.04, 0.07)	<.0001	
	Day 1 post	0.071	(0.05, 0.09)	<.0001	
SAC scores		0.001	(-0.17, 0.17)	.9904	
	Time of concussion	-0.042	(-0.12, 0.03)	.2819	
	2–3 hours post	-0.055	(-0.18, 0.07)	.3853	
	Day 1 post	-0.086	(-0.20, 0.03)	.1507	
BESS scores	Baseline	0.004	(-0.05, 0.06)	.8939	
	Time of concussion	0.012	(-0.02, 0.05)	.5256	
	2-3 hours post	0.016	(-0.02, 0.05)	.4087	
	Day 1 post	0.017	(-0.02, 0.05)	.3726	
Injury management	Total time symptom free before return	0.005	(0.001, 0.009)	.0007	
	Total time withheld from competition	0.024	(0.008, 0.040)	.0016	
Concussion history	Total number of prior concussions	-0.167	(-0.59, 0.26)	.4435	

Note. Bold p values < .05.

GSC = Graded Symptom Checklist; SAC = Standardized Assessment of Concussion; BESS = Balance Error Scoring System; 95% CI = 95 percent confidence interval of odds ratio or estimate.

point, but there were no statistically significant residual impairments on performance based measures of cognitive functioning or balance 45/90 days post-injury.

Factors Associated With Prolonged Recovery

Acute injury characteristics of unconsciousness (p < .0001), posttraumatic amnesia (p = .049), retrograde amnesia (p = .013) and symptom severity within the first 24 hr of injury (p < .0001)

were the factors most strongly associated with prolonged recovery (see Table 4). When present, the period of unconsciousness had a maximum of a few seconds and the period of amnesia had a maximum of several minutes. Demographic variables, level of competition, player position, mechanism of injury, concussion history, and acute scores on the SAC and BESS were not predictive of prolonged recovery time.

Athletes who were rendered unconscious had 4.15 times (95% CI, 2.12 to 8.15) higher odds of prolonged recovery

than those with no loss of consciousness. Retrograde amnesia was associated with 2.19 times (95% CI, 1.18 to 4.06) higher odds and posttraumatic amnesia 1.81 times (95% CI, 1.00 to 3.28) higher odds for prolonged recovery.

Based on symptom severity at the most acute time point immediately following concussion, individuals with an increase of 20 points or more over baseline on the GSC had 2.56 times (95% CI, 1.80 to 3.64; p < .0001) greater risk of prolonged recovery at day 7. Individuals with an increase of 20 points or higher on the GSC at the 2–3 hr assessment point and on day 1, respectively, had 2.89 (95% CI, 2.03 to 4.11; p < .0001) and 4.14 (95% CI, 2.80 to 6.11; p < .0001) times higher risk of prolonged recovery at day 7.

The total length of time a player was withheld from competition (p = .0016) and the duration of a symptom free waiting period (p = .0007) after concussion were inversely associated with a reduced risk of prolonged recovery. That is, the longer a player was withheld from competition and allowed a symptom free waiting period, the lower their risks of prolonged recovery.

At 45/90 days post-injury, 23% (n = 13) of the prolonged recovery group continued to report symptom scores higher than the normative-based criterion for recovery (outside the 95th percentile of the control group change score from baseline to day 45/90). This figure compares to just 5% of the typical recovery group (n = 26), which is equivalent to the "false positive" rate in the control group. The difference in frequency of persistent symptoms between the typical recovery group and prolonged recovery group at day 45/90 was statistically significant ($\chi^2 = 21.08$; p < .001).

None of the specific variables reached statistical significance in the second logistic regression on factors associated with continued definition of prolonged recovery at day 45/90.

DISCUSSION

This study reports major findings from the largest prospectively collected dataset to appear in the literature on the incidence, course, and predictors of prolonged recovery time following sport related concussion. In our study sample, 10% of injured athletes exhibited postconcussive symptoms that persisted beyond the typical seven day window of recovery commonly reported in group studies. The prolonged recovery group demonstrated a different pattern and course of recovery than the typical recovery group, evidenced by symptoms and cognitive dysfunction that were more pronounced during the acute period and persisted over a lengthier period of time than that observed in the typical recovery group. Nearly a quarter of those athletes who failed to meet the criteria of recovery within 1 week (2.3% of the total injured sample) continued to report elevated symptoms 6 to 12 weeks post-injury.

Despite the report of persistent symptoms 45–90 days post-injury in the prolonged recovery group, there were no statistically significant deficits that persisted on objective neuropsychological or postural stability testing, suggesting that functional impairment 2–3 months following concussion

is likely minimal. The differences between the two groups on measures of balance acutely were relatively small, with no group differences evident by day 6–7, and the two groups differed on only 2 of 7 cognitive measures at day 6–7, with no evidence of residual impairments on performance based measures of cognitive functioning and balance 45–90 days after concussion.

Results from the current study have potential public health implications when applied in the context of concussion as a common injury in many organized sports and recreational activities. Our methodology involved the use of a 95% oneway confidence interval using self-reported symptoms in a control sample to define prolonged recovery, so it is important to recognize that we have a defined 5% false positive rate in our prolonged recovery group. If we conservatively apply our current findings of a 5% "true" prolonged recovery incidence to previous epidemiologic estimates of 300,000 concussions occurring annually in organized sports in the United States (Thurman, Branche, & Sniezek, 1998), that would suggest that 15,000 young athletes continue to experience symptoms and functional impairments beyond 1 week after concussion, and that 3750 athletes continue to experience persistent symptoms for at least several weeks after concussion. If we apply our findings to larger estimates of 3.8 million concussions due to sport and recreational activities each year (Langlois et al., 2006), those figures expand to 190,000 individuals experiencing symptoms and other postconcussive problems beyond 1 week and nearly 50,000 individuals still affected by symptoms several weeks after their injury.

In addition to our findings on the frequency and time course of prolonged recovery, this study identified certain predictive factors associated with persistent symptoms. Our findings suggest acute injury severity, marked by unconsciousness, amnesia and elevated initial symptom severity significantly increases an athlete's risk of prolonged recovery time. The presence of acute injury characteristics of unconsciousness and amnesia significantly increased the risk of an athlete requiring longer than the typical seven day window to achieve a full recovery. Thus, more severe injuries were associated with more severe and longer lasting symptoms, as well as deficits in cognitive functioning and postural stability. Our findings are consistent with a recent study reporting that persistent symptom increases in children one year after mTBI were more common among children who had a period of unconsciousness and abnormalities on neuroimaging associated with their mTBI (Yeates et al., 2012).

Of interest, an athlete's risk of prolonged recovery following concussion was not predicted on the basis of variables relevant to their level or type of participation (e.g., high school vs. college), the mechanism of their concussion, or their prior concussion history. With regard to the influence of specific injury management strategies, the directionality of our findings (i.e., lengthier time withheld from competition in the prolonged recovery group) suggests that prolonged recovery predicted how long a clinician withheld the athlete from returning to competition, rather than vice versa.

This dampens speculation of a reverse finding that prematurely returning to participation accounted for worsening or extended symptoms in our study sample. Beyond the large set of variables included in our regression analysis, we are unable to determine the association between certain non-injury (e.g., psychological factors, other etiologies) and prolonged symptom reporting in our sample, which represents an important question for future studies to address.

These findings move forward the existing evidence base for clinical management of sport related concussion. One of the greatest challenges faced by sports medicine clinicians is determining an athlete's expected course of recovery, which has implications for clinical management and return to play decision making. Our findings suggest that acute injury characteristics, symptom severity, and performance on functional assessments during the acute period are predictive of an athlete's eventual recovery time. In addition to recognizing the importance of acute injury characteristics of unconsciousness and amnesia, our findings also support the call for greater emphasis on methods for assessing the severity of symptoms, cognitive dysfunction, postural instability, and other functional impairments during the acute phase that will assist the clinician in monitoring an athlete's level of recovery and fitness to safely return to competition. Ideally, future research will produce algorithms that effectively predict for clinicians an athlete's likely risk of prolonged recovery and guide clinical decision making to improve safety in return to play.

For the current study, we specifically elected to stratify athletes into the typical recovery group or the prolonged recovery group based on their symptom recovery time because we were directly interested in the indicator relied on most commonly in the setting of clinicians monitoring an athlete's level of recovery and fitness to return to play. This stratification then allowed us to compare recovery on performance based measures of cognitive function and balance in athletes with typical and prolonged symptom recovery. While it is commonly thought that athletes are inclined to under-report their symptoms in hopes of more quickly being cleared to return to competition, results from the current study indicate significant overlap in the time course of self-reported and performance based metrics of recovery in the overwhelming majority of athletes. Furthermore, our results also indicate a higher likelihood of persistent subjective symptoms further out from injury (e.g., 45-90 days postinjury), in the absence of impairments on cognitive or balance testing, which is counter to the common stereotype.

Several limitations of the current study require consideration. First, our findings speak only to the lingering effects from a single, uncomplicated concussion during a period of several weeks. The larger public health concern is whether exposure to recurrent concussion may predispose athletes to risks of chronic symptoms, cumulative cognitive impairment or premature onset of degenerative dementia syndromes. We concur with the call for large prospective studies on the true incidence, risk factors, mechanism and underlying pathophysiology of possible late-life effects of recurrent trauma, whether this is due to recurrent concussion or to

exposure to recurrent sub-concussive head trauma. It should also be acknowledged that nearly 90% of the sample included in this study was male and approximately 80% of the injuries studied were in American football. There is a clear need for larger scale studies looking at the effects of gender on recovery, as well as the complexion of concussion across a broader array of sports other than American football. It should also be recognized that the figure of 10% of athletes with prolonged recovery includes a known 5% "false positive" rate, as prolonged recovery was defined as symptom elevation greater than 95% of uninjured control levels. We elected this methodology based on what we considered to be empirically appropriate to define "typical recovery" based on GSC score, while also allowing for the modest psychometric variability of the scale even among normal, non-concussed athletes. Further study is required to determine if educational and policy making initiatives to raise awareness about sportrelated concussion over the last 10 years would influence the results of our study now (e.g., result in a higher rate of prolonged recovery due to influences on symptom reporting vs. result in lower rate of prolonged recovery due to improved injury management strategies).

Additionally, studies of this type are often not, from an ethical and human safety standpoint, able to be carried out as truly randomized, controlled trials (RTCs). Because an athlete's assignment to the typical or prolonged recovery group was based on our empirically-derived criteria and did not involve any stratified intervention, random group assignment was not readily applicable in this study. We were prohibited by the authorizing human protection boards from prescribing injury management strategies that dictated how long an athlete was withheld from competition after injury, though prolonged recovery did not appear to be associated with athletes being prematurely returned to competition after concussion. Although the control group in this study was not randomly selected in the true sense, our approach to control sampling resulted in very tight matching of the three study groups. We achieved a matched control group sample that provided us adequate power for statistical analysis, so amassing 570 controls was not necessary.

Despite these limitations, several factors contribute to the utility of this study in expanding the existing knowledge base on the true natural history of concussion. First, previous studies have been significantly limited in their scope, sample size, or methodology. Many studies have not included preinjury baseline assessments, a control group, standardized outcome measures beyond self-reported symptoms, or longitudinal follow-up of injured athletes. Our protocol involved extensive, multi-dimensional assessments at pre-injury baseline and numerous post-injury time points to establish a continuous time course of recovery. Including a large control group allowed us to examine the frequency and variability of postconcussive symptoms among non-injured athletes and factor in the incidence of "false positives" in the current study. Furthermore, we collected an exhaustive information base on hundreds of variables relevant to the acute injury, athlete, environment, and outcome that allowed us to prospectively investigate the factors associated with recovery, which prior studies have not been able to do on a comprehensive scale.

CONCLUSION

In conclusion, findings from this study of a large sample of high school and collegiate athletes affected by sport related concussion suggest that a subset of athletes experience symptoms and other functional impairments that persist beyond the typical 7-day window of recovery and may extend out at least several weeks in a small percentage of athletes. Although prolonged recovery was associated with the report of elevated symptoms 45 to 90 days post-injury, there was no evidence of residual impairments on performancebased measures of cognitive functioning and balance. Prolonged symptom reporting was associated with markers of acute injury severity. Further study is required to clarify the lengthier course of persistent symptoms in this subset of athletes beyond the three month point, and to identifying other factors that may contribute to prolonged symptom reporting. This may help guide interventional strategies for those athletes who fail to make the typical rapid recovery from sport-related concussion.

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