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REVIEW ARTICLE

Systematic Review of Prognosis and Return to Play After Sport Concussion: Results of the International Collaboration on Mild Traumatic Brain Injury Prognosis

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Abstract

Objective: To synthesize the best available evidence on prognosis after sport concussion.

Data Sources: MEDLINE and other databases were searched (2001−2012) with terms including "craniocerebral trauma" and "sports." Reference lists of eligible articles were also searched.

Study Selection: Randomized controlled trials and cohort and case-control studies were selected according to predefined criteria. Studies had to have a minimum of 30 concussion cases.

Data Extraction: Eligible studies were critically appraised using a modification of the Scottish Intercollegiate Guidelines Network (SIGN) criteria. Two reviewers independently reviewed and extracted data from accepted studies into evidence tables.

Data Synthesis: Evidence was synthesized qualitatively according to modified SIGN criteria, and studies were categorized as exploratory or confirmatory based on the strength of their design and evidence. After 77,914 records were screened, 52 articles were eligible for this review, and 24 articles (representing 19 studies) with a low risk of bias were accepted. Our findings are based on exploratory studies of predominantly male football players at the high school, collegiate, and professional levels. Most athletes recover within days to a few weeks, and American and

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Australian professional football players return to play quickly after mild traumatic brain injury. Delayed recovery appears more likely in high school athletes, in those with a history of previous concussion, and in those with a higher number and duration of postconcussion symptoms.
Conclusions: The evidence concerning sports concussion course and prognosis is very preliminary, and there is no evidence on the effect of return-to-play guidelines on prognosis. Our findings have implications for further research. Well-designed, confirmatory studies are urgently needed to understand the consequences of sport concussion, including recurrent concussion, across different athletic populations and sports.
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Concussion or mild traumatic brain injury (MTBI) has been defined as a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces.[1] Concussions that result from participation in sports are a major public health issue affecting 1.6 to 3.8 million individuals in the United States annually.[2] While most persons with concussions are said to recover completely within the first 3 months in terms of cognitive function,[3] the American Academy of Neurology stated that the long-term effects of multiple concussions are unknown.[4] However, great concern remains regarding the potential for permanent cognitive and other neurologic deficits,[5,6] and permanent brain injury causing dementia or movement disorders.[7] In a large systematic review[8] of MTBI prognosis, the World Health Organization (WHO) Collaborating Centre for Neurotrauma, Prevention, Management and Rehabilitation Task Force found that athletes recover rapidly after sport concussion. However, they found very few scientifically admissible studies focused on the long-term consequences of multiple concussions and could not make any strong conclusions regarding their effects on overall health.[8] Previous research has been limited by methodological weaknesses such as small sample sizes, poor description and ascertainment of the exposure (concussion), and short follow-up periods.[8]

Understanding the course of recovery and identifying potential prognostic factors (eg, age, sex, sport) affecting recovery after sport concussion is important for effective management and return-to-play (RTP) decisions. However, expert opinions and research findings about the prognosis after sport concussion vary widely.[9] Given the controversy and uncertainty that still exists, reviewing the scientific evidence is important.

The objective of this review is to update the WHO Collaborating Centre Task Force findings by synthesizing the best available evidence on prognosis of sport concussion and RTP.[8] The terms *MTBI* and *concussion* are used interchangeably in this review.

Methods

The protocol registration, case definition, literature search, critical review strategy, and data synthesis are outlined in detail elsewhere.[10,11] Briefly, the review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[12] The electronic databases MEDLINE, PsycINFO, Embase, CINAHL, and SPORTDiscus were systematically searched from 2001 to 2012, and the reference lists of all reviews and meta-analyses related to MTBI, and articles meeting the eligibility criteria were screened for additional studies.

List of abbreviations:

CDC	**Centers for Disease Control and Prevention**
CI	**confidence interval**
LOC	**loss of consciousness**
MCI	**mild cognitive impairment**
MTBI	**mild traumatic brain injury**
RTP	**return to play**
WHO	**World Health Organization**

Articles were screened for eligibility according to predefined criteria. Inclusion criteria included original, published peer-reviewed research reports in English, French, Swedish, Norwegian, Danish, and Spanish. Studies had to have a minimum of 30 concussion cases resulting from sports participation, and had to assess outcomes such as self-rated recovery, clinical improvement, or RTP.

The definition of MTBI had to fall within the definitions provided by the WHO Collaborating Centre Task Force on MTBI and the Centers for Disease Control and Prevention (CDC).[10] The WHO Task Force defines MTBI as

> "an acute brain injury resulting from mechanical energy to the head from external physical forces. Operational criteria for clinical identification include: (i) 1 or more of the following: confusion or disorientation, loss of consciousness for 30 minutes or less, posttraumatic amnesia for less than 24 hours, and/or other transient neurologic abnormalities such as focal signs, seizure, and intracranial lesion not requiring surgery; and (ii) Glasgow Coma Scale score of 13−15 after 30 minutes postinjury or later upon presentation for healthcare. These manifestations of MTBI must not be due to drugs, alcohol, medications, caused by other injuries or treatment for other injuries (eg, systemic injuries, facial injuries, or intubation), caused by other problems (eg, psychological trauma, language barrier, or coexisting medical conditions), or caused by penetrating craniocerebral injury."[8(p115)]

Persons with fractured skulls were included if they fit this case definition. The CDC provides an additional definition that can be derived from clinical records. According to the CDC, MTBI is present if an Abbreviated Injury Severity Scale score of 2 for the head region is documented.[10] An administrative data definition for surveillance or research is also provided.[10] Specifically, cases of MTBI are recognized among persons who are assigned certain *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnostic codes.[10,11]

Eligible study designs were randomized controlled trials and cohort and case-control studies. Exclusion criteria included study designs such as cross-sectional studies, and case reports and series, as well as cadaveric, biomechanical, and laboratory studies.

Eligible articles were critically appraised using a modification of the Scottish Intercollegiate Guidelines Network criteria.[13] Two reviewers independently reviewed and extracted data from accepted articles into evidence tables. A third reviewer was consulted for disagreements. The evidence was synthesized according to the modified Scottish Intercollegiate Guidelines Network criteria, and a best-evidence synthesis was performed to provide clear and useful conclusions linked to the evidence tables. We also categorized the evidence on prognostic factors as exploratory or confirmatory, using the phases of study framework described by Côté et al.[14] Phase I studies are hypothesis-generating investigations that explore the associations between potential prognostic factors and disease outcomes in a descriptive or univariate way. Phase II studies are extensive exploratory analyses that focus on particular sets of prognostic factors, or attempt to discover which factors have the highest prognostic value. Both phase I and phase II studies provide preliminary evidence. Lastly, phase III studies are large confirmatory studies of explicit prestated hypotheses that allow for a focused examination of the strength, direction, and independence of the proposed relationship between a prognostic factor and the outcome of interest. The strongest evidence is found in phase III studies, followed by phase II. Phase I studies do not consider confounding and are weaker evidence.

Results

Of 77,914 records screened for our entire review, 121 full-text articles related to sport concussion were assessed for eligibility (fig 1).[11] There were 52 English articles that assessed sport concussion and met our eligibility criteria. About half of these (n=24) were accepted as scientifically admissible articles, represented by 19 studies (table 1). These studies form the basis of our best-evidence synthesis.

We accepted 19 cohort studies, of which 10 were phase II and 9 were phase I. Fourteen studies were conducted in the United States, 4 in Australia, and 1 in Canada. Most participants were male and played American football at the high school, collegiate, or professional level. Follow-up periods varied, with most high school and collegiate athletes being followed up for a few days to 12 weeks. Professional athletes were followed for up to 4 seasons. The findings are divided into 6 sections relating to the different outcome variables reviewed: (1) cognitive function; (2) postconcussion symptoms; (3) recurrent concussion; (4) RTP; (5) sport performance; and (6) course and predictors of recovery after sport concussion.

Cognitive function after sport concussion

We accepted 7 phase II[9,15-20] and 5 phase I[21-26] studies. The findings were inconsistent because of varied patient characteristics, study designs, follow-up periods, and assessments of exposures and outcomes. It generally appears that cognitive function is not significantly impaired, or if impaired resolves within a few days to a few weeks for most high school, collegiate, and professional athletes after concussion.

Predictors of cognitive function after sport concussion

Factors that appear to impair cognitive performance are a history of previous concussion, number and duration of postconcussion symptoms, and being a younger-aged high school athlete compared with a collegiate or professional athlete.

History of previous concussion: Five studies[9,15,21-24] assessed the effect of concussion history on cognitive function. Two phase II[9,15] and 1 phase I[21] study indicated worse cognitive function for those with a history of previous concussion compared with those without, while 2 phase I studies[22-24] found no group differences. In the first group of studies, statistically significant impairments in verbal memory and reaction time were found in college athletes approximately 1 week after a new concussion. In another study,[21] college athletes with a previous history of concussion reported more cognitive symptoms than those without ($P<.05$), with 32% endorsing 1 or more cognitive symptoms at the 1-week assessment versus 8% in those without a previous history of concussion. Additionally, professional Australian footballers with a history of concussion performed significantly worse than those without on visual motor speed ($d=-.55$; 95% confidence interval [CI], -1.02 to $-.08$), impulse control ($d=-.88$; 95% CI, $-.40$ to -1.36), and processing speed tests ($d=-.41$; 95% CI, $-.88$ to $.05$).[9] In the other group of studies, an association between concussion history and cognitive performance was not found in college or professional American football/National Football League players as assessed by traditional[22,23] and computerized tests.[24]

The amount of time between concussions is a potentially important confounding variable but was only reported in 1 of the studies[9] that suggested worse cognitive function in those with a history of previous concussion. In those with 3 or more concussions, the mean $\pm$ SD number of days since the previous concussion was reported to be 561 ± 672.[9] The amount of time between successive concussions may affect the outcome and account for some of the different findings. For instance, 2 concussions within a 6-month period may lower cognitive performance more than, say, 2 concussions within 12 months.

Postconcussion symptoms: Commonly reported postconcussion symptoms include headaches, balance problems, dizziness, fatigue, depression, anxiety, irritability, and memory and attention difficulties.[27] Six studies[16,17,20,23,25,26] examined the relationship between postconcussion symptoms and objective evidence of cognitive impairment, as assessed with neuropsychological tests within 2 weeks postinjury. Postconcussion symptoms were mainly self-reported and included cognitive symptoms (eg, memory problems) and physical symptoms (eg, headache).

Five studies (2 phase II,[16,20] 3 phase I[23,25,26]) found that the presence of postconcussion symptoms was associated with a negative effect on cognitive function, while 1 phase II study[17] did not come to the same conclusion. For instance, high school athletes who were identified as having postconcussion mental status changes on sideline assessment, such as retrograde amnesia and confusion, had impaired memory 36 hours ($d=.74$, medium-large effect size), 4 days ($d=.69$, medium-large effect size), and 7 days ($d=.34$, small effect size) postinjury compared with baseline.[26] Impaired cognitive function was found in both American and Australian professional footballers with postconcussion symptoms in 2 studies.[20,23] For example, the cognitive performance of a symptomatic group of concussed professional Australian footballers declined at the postconcussion assessment on computerized tests of simple, choice, and complex reaction times compared with the asymptomatic and control groups.[20] The magnitude of these changes, expressed in within-subjects SD, was large (simple reaction speed, $-.86$; choice reaction speed, $-.60$; complex reaction speed, $-.61$). The most common symptom experienced in the symptomatic group was headache. Of note, pain (eg, chronic pain) has been associated with lower cognitive function.[28] The use of an injured control group rather than an uninjured one might be useful in observing whether concussion-related pain affects cognitive function differently than pain from other causes such as orthopedic injuries.

One study[17] found that self-reported postconcussion symptoms did not predict poor performance on neuropsychological testing in any high school or college athlete when compared with noninjured

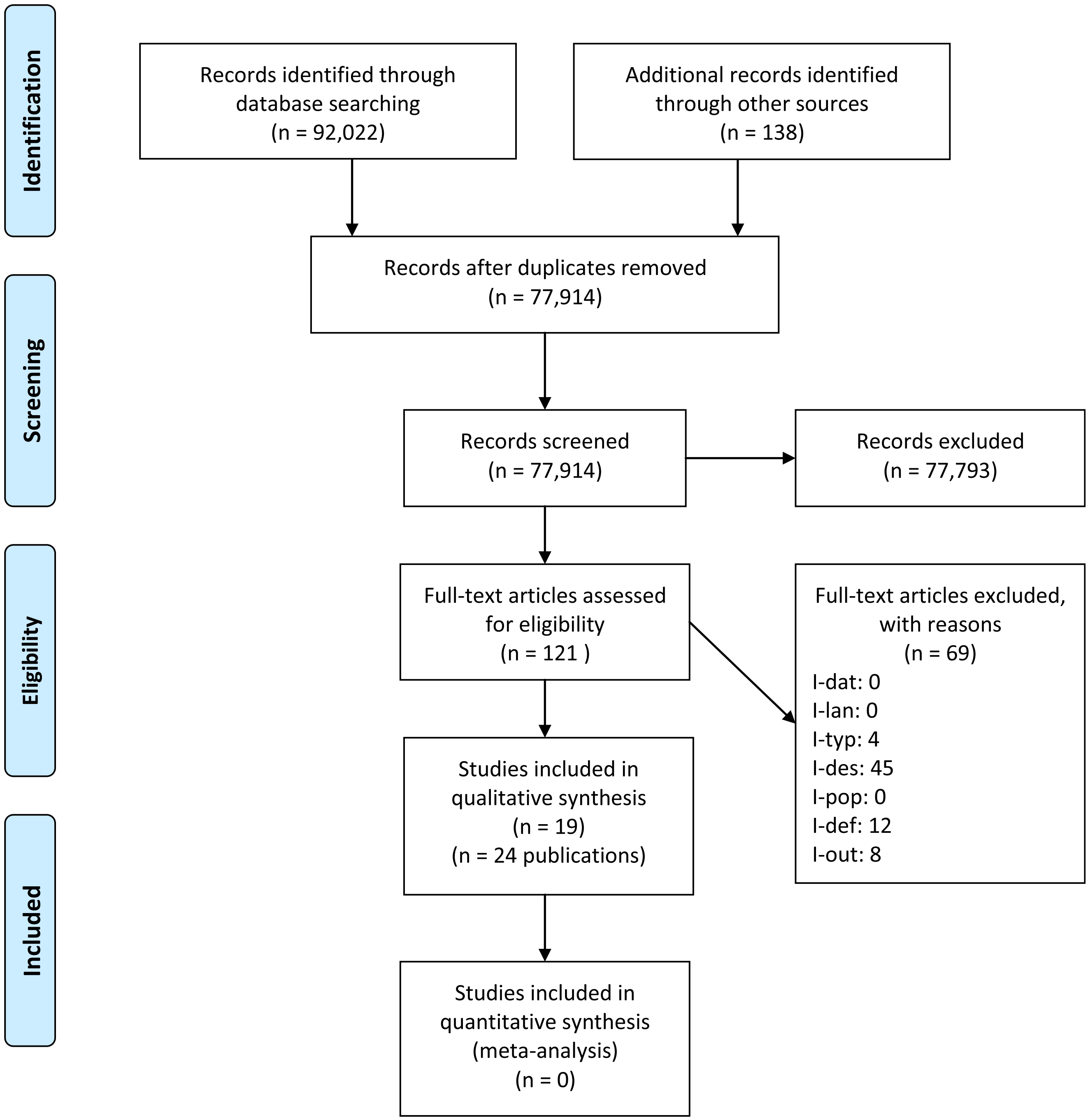

Fig 1 Flow diagram of literature search. Abbreviations: dat, date; def, definition; des, study design; I, ineligibility code; lan, language; out, outcome; pop, population; typ, publication type.

controls. However, specific symptoms were not reported. It might be the case that some symptoms, such as cognitive symptoms, are more related to cognitive performance deficits than others such as fatigue.

Athlete level/age: Four studies[17,18,23,24,26] suggest that high school athletes (ie, 13−18y of age) appear to take longer to recover cognitive function compared with older and more experienced athletes (ie, collegiate and professional athletes). To illustrate, high school athletes (aged ∼16y) took up to 21 days to return to baseline levels for reaction time after concussion[18] and had prolonged memory dysfunction compared with college athletes (aged ∼20y).[17] A comparison of these groups at 3 days postinjury indicated significantly poorer performance for the high school group for both the Hopkins Verbal Learning Test total ($P<.005$) and the Hopkins Verbal Learning Test delay ($P<.02$). However, this performance difference was no longer evident at day 5 or day 7.[17] Professional American footballers (aged ∼26y) returned to baseline performance (verbal memory, reaction time) in 1 week, with most having normal performance within 2 days postinjury; however, high school athletes (aged ∼16y) had a slower recovery.[24] When tested within 7 days of

Table 1 Evidence table of admissible studies (n = 19)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
Cohort studies					
Phase II studies					
Collie et al,[20] 2006; Australia	615 male Australian Rules footballers participated 2001–2003 (n = 61 were concussed in game play). Assigned to 2 groups: SYMP (n = 25), ASYMP (n = 36). Participants reporting any symptoms at time of cognitive assessment (within 11d postinjury) were allocated to the SYMP group; those reporting no symptoms were allocated to ASYMP group. Controls: footballers who were not concussed and were retested after the season (n = 84)	Exclusion: nonconcussive head injuries (cuts, lacerations, etc)	Head trauma resulting in alteration in mental state, the onset of clinical symptoms, or both; diagnosed on the basis of a clinical interview conducted by the medical staff of the participating clubs (followed Vienna consensus guidelines when diagnosing concussion)	Prognostic factors: symptomatic vs asymptomatic presentation at the time of assessment within 11 days of concussion, symptom duration, time to RTS, LOC, PTA Outcomes: cognitive tests (computerized CogSport; paper-and-pencil DSST and TMT)	Compared with baseline, SYMP group displayed statistically large and significant cognitive decline on computerized tests of motor function and attention (not on paper-and-pencil tests), despite reporting relatively few symptoms postinjury (mean ± SD, 1.8±0.9). ASYMP athletes had impaired divided attention only. Improvement was observed in both ASYMP and control groups with paper-and-pencil tests b/w baseline and F/U.
Covassin et al,[19] 2007; United States	79 concussed varsity athletes from 5 northeastern universities (full range of varsity sports). F/U: preseason (baseline), up to 3 days (time 2), 7–10 days postconcussion (time 3)	Inclusion: voluntary participation; varsity athletes who sustained concussions that required serial testing across all 3 periods (baseline/preseason, up to 3d, 7–10d)	AAN criteria*	Prognostic factors: sex, time Outcomes: postconcussion symptoms (postconcussion symptom checklist), neurocognitive testing (ImPACT version 2.0)	No greater likelihood of sustaining a grade 2 or 3 concussion as a function of sex (*P* = .50) No b/w-subject multivariate effect of sex (*P* = .69), and no significant sex-by-time interaction (*P* = .59) were identified.
Covassin et al,[15] 2008; United States	Multicenter analysis of concussed collegiate athletes from 5 northeastern universities (full range of varsity sports), practicing and competing during 2002–2003 and 2003–2004 academic seasons (n = 57; 36 w/o concussion history, 21 with history of ≥2 concussions). F/U: 1 and 5 days postconcussion	Exclusion: athletes with history of 1 concussion were excluded because small sample size provided inadequate data	AAN criteria*	Prognostic factors: concussion history (no history of concussion vs ≥2 concussions), time (baseline, day 1 postconcussion, or day 5 postconcussion) Outcomes: neurocognitive testing (ImPACT: verbal memory, visual memory, processing speed, reaction time, symptoms)	Athletes with a history of concussion did not have a greater likelihood of sustaining a more severe concussion (grade 2 or 3) compared with a grade 1 (*P* = .10). A within-subjects effect (time) on ImPACT performance (*P* < .001), a b/w-subjects multivariate effect of group (no concussion history vs history of ≥2 concussions) (*P* < .001), and a group-by-time interaction (*P* = .034) were noted. Multivariate assessment of symptoms across days and groups revealed no differences b/w groups (*P* = .622), within-subjects effect

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Table 1 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
					(time) (*P*=.171), or group-by-time interaction (*P*=.493).
Covassin et al,[18] 2010; United States	2000 athletes volunteered from 8 mid-Michigan area high schools (baseball, men's and women's basketball, cheerleading, football, women's gymnastics, men's ice hockey, men's and women's soccer, softball, volleyball, and wrestling). Study sample included 72 athletes who sustained a concussion over 2-year period. F/U: preseason (baseline), 2, 7, 14, 21, 30 days postconcussion	Inclusion: met case definition Exclusion: history of learning disability, color blindness, psychological disorder, brain surgery, major neurologic condition, history of TBI, LOC >5 minutes	Concussion in sport group definition: complex pathophysiological process affecting brain, induced by traumatic biomechanical forces; further described as rapid onset of short neurologic impairments and neuropathologic changes; and, graded set of clinical syndromes that may or may not involve LOC	Prognostic factors: Not applicable—descriptive prognostic study Outcomes: neurocognitive performance (ImPACT: verbal memory, visual memory, processing speed, reaction time, symptoms)	Significant effects for reaction time (F=10.01; *P*=.000), verbal memory (F=3.05; *P*=.012), motor processing speed (F=18.51; *P*=.000), and PC symptom scores (F=16.45; *P*=.000) compared with baseline. Significant decrease in reaction time up to 14 days (*P*=.001); returned to baseline at 21 days (*P*=.25). Impairments in verbal memory (*P*=.003) and motor processing speed (*P*=.000) at 7 days; returned to baseline by 14 days. Significantly more symptoms at 2 days (*P*=.000), resolved by 7 days (*P*=.06)
Fazio et al,[16] 2007; United States	Participants of the Sports Medicine Concussion Program at the University of Pittsburgh Medical Center 2001–2004 seasons (n=192 high school and collegiate athletes). 3 groups: concussed-symptomatic (n=78), concussed-asymptomatic (n=44), nonconcussed control (n=70). F/U: preinjury testing (baseline), within 7 days postconcussion	Inclusion: high school or collegiate athletes tested within 7 days of sustaining concussion; test results from athletes who completed ImPACT version 2.0 or later Exclusion: results from previous versions of ImPACT	Any observable alteration in mental status or consciousness after a blow to head or body during sport participation; and/or the presence of LOC and/or anterograde or retrograde amnesia identified in an on-field examination; and/or any self-reported symptoms such as cognitive "fogginess," headache, nausea and/or vomiting, dizziness, balance problems, and visual changes after a collision involving the head or body. Certified athletic trainers or team physicians who were present on the sideline at the time of injury made the initial diagnosis of concussion.	Prognostic factors: concussion symptom presentation Outcomes: neurocognitive testing (ImPACT: verbal memory, visual memory, processing speed, reaction time, symptoms)	Concussed-asymptomatic athletes: poorer performance vs controls on all ImPACT scores; significantly better performance than concussed-symptomatic group. Concussed athletes who denied subjective symptoms demonstrated poorer performance than control subjects on all 4 scores of ImPACT. Concussed-asymptomatic group demonstrated significantly better neurocognitive performance than did the concussed-symptomatic group.
Field et al,[17] 2003; United States	College athletes (370M/23F; mean age, 19.9y) from 4 Division 1A programs and high school athletes (183M/0F; mean age,	Inclusion: met case definition	On-field presentation of ≥1 of following symptoms after a blow to head/body: (1) any observable alteration in mental	Prognostic factors: self-reported postconcussion symptoms Outcomes: structured interview; neuropsychological tests: HVLT	High school athletes with concussion had prolonged memory dysfunction compared with college athletes with concussion. High school athletes

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Table 1 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
	15.9y) from 5 schools in Shiawassee County, Michigan, who underwent baseline neuropsychological evaluation b/w 1997 and 2000. Study sample: Athletes concussed during competition (n=54) compared with noninjured control group (n=38) matched on sport, age, high school grade point average/college board examination scores, history of diagnosed learning disability, history of previous concussion. F/U: preseason (baseline), 1, 3, 5, 7 days postconcussion		status or consciousness; (2) constellation of self-reported symptoms (eg, posttraumatic headache, "fogginess," nausea/vomiting, dizziness); and/or (3) LOC, disorientation, PTA, or retrograde amnesia. Concussions were defined and graded according to the AAN.*	(verbal learning and memory), DST (attention/concentration), SDMT (speed of information processing), TMT (visual scanning, executive functioning), COWAT (word fluency); Concussion Symptom Scale. High school athletes also given Brief Visual Spatial Memory Test-Revised (visual memory).	performed significantly worse than age-matched control subjects at 7 days after injury ($P<.005$). College athletes: had more severe concussions, but displayed similar performance as controls by 3 days postinjury. Self-reported postconcussion symptoms by any athlete did not predict poor performance on neuropsychological testing.
Gardner et al,[9] 2010; Australia	Male rugby union players aged 19–30 years during 2009 preseason (n=73). ≥3 concussions group: players with self-reported history of ≥3 concussions, but had not sustained concussion in previous 3 months, were referred to study by medical staff from 3 Sydney grade rugby union clubs (n=34). Control group (no previous concussions): recruited via identical methods as concussed group; matched on sex, age, education, number of years of participation in rugby union, level of competition played, and position (forward vs backline) (n=39)	Inclusion: met case definition. There were no participants with a positive history of epilepsy, brain surgery, meningitis, substance use, learning disorder, or hyperactivity.	Presence of at least one of: confusion or disorientation; LOC ≤30 minutes; PTA<24 hours; and/or other transient neurologic abnormalities (eg, focal signs, seizure, intracranial lesion not requiring surgery)	Prognostic factors: self-reported number of previous concussions via ImPACT (data restricted to estimates of dates for athletes' 5 most recent concussions). Outcomes: computerized neuropsychological test (ImPACT version 6.0); traditional pencil-and-paper measure of processing speed (WAIS-III PSI)	Athletes with history of multiple concussions performed significantly worse than those w/o history of concussion on: ImPACT visual motor speed ($d=-.55$; 95% CI, −1.02 to −.08; $P=.013$); ImPACT impulse control ($d=-.88$; 95% CI, −.40 to −1.36; $P=.024$); and WAIS-III PSI ($d=-.41$; 95% CI, −.88 to .05; $P=.025$).
Lau et al,[37] 2011; United States	Male high school football athletes (Pennsylvania high school football programs, 2002–2006	Inclusion: sustained concussions during preseason and regular season football activity; must	On-field presentation of ≥1 of the following after head impact: any noticeable change in	Prognostic factors: ImPACT: (verbal memory, visual memory, processing speed, reaction	Time to RTP: short-recovery group: 6.90±3.30 days; protracted group: 33.04±47.22 days. Combination of 4

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Table 1 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
	seasons). All athletes who sustained concussion were referred to sports concussion clinic (n=177). 108 were cleared to play and analyzed: 58 had short recovery (≤14d), 50 had protracted recovery (>14d). 69 athletes not cleared to play were either lost to F/U or did not return to football by 2006 season end. F/U: until RTP	have completed both ImPACT and PCSS assessment during F/U until full recovery Exclusion: athletes injured in postseason playoffs	mental status or consciousness; LOC, disorientation, PTA, or retrograde amnesia; or any self-reported symptoms (eg, headache, dizziness, balance dysfunction, or visual changes that appeared after a collision on the field)	time, symptoms) PCSS, symptom clusters (migraine, cognitive, sleep, neuropsychiatric) Outcomes: subacute recovery after sports-related concussion (protracted recovery >14d vs short recovery ≤14d)	symptom clusters and 4 neurocognitive composite scores had the highest sensitivity (65.22%), specificity (80.36%), positive predictive value (73.17%), and negative predictive value (73.80%) in predicting protracted recovery. 4 variables contributed most to classifying patients with protracted recovery: migraine symptom cluster (P=.012) (largest contributor), reaction time (P=.042), visual memory (P=.017), verbal memory (P=.047).
Lau et al,[38] 2011; United States	Male high school football players from Pennsylvania Interscholastic Athletic Association who incurred sport-related concussion during preseason or regular season 2002–2006 (n=176). 39% excluded (did not RTP, were lost to F/U, or did not return to football before end of data collection) Participants: n=107. Final sample had to meet criteria for recovery and were grouped into rapid (≤7d, n=58) or protracted recovery (≥21d, n=31) groups. F/U: until RTP	Inclusion: sustained concussions during preseason and regular season football activity, practices, and games; diagnosed concussion by trained medical personnel (ie, certified athletic trainer, team physician); documented, observed on-field SS by trained sports medicine staff at time of injury; evaluation and F/U by clinical members of research team until RTP Exclusion: injured in postseason playoffs; current or history of brain surgery, substance abuse, or other neurologic disorder (seizures, meningitis, psychiatric diagnosis, alcohol abuse); not cleared to RTP; lost to F/U; did not return to football before end of 2006 regular season	Complex pathophysiological process affecting the brain, induced by direct or indirect traumatic biomechanical forces; on-field presentation of ≥1 of the following: confusion, headache, LOC, PTA, retrograde amnesia, balance problems, dizziness, visual problems, personality changes, fatigue, sensitivity to light/noise, numbness, vomiting	Prognostic factors: on-field SS (confusion, LOC, PTA, retrograde amnesia, imbalance, dizziness, visual problems, personality changes, fatigue, sensitivity to light/noise, numbness, vomiting) Outcomes: subacute recovery after sports-related concussion (protracted recovery ≥21d vs rapid recovery ≤7d)	Dizziness at time of injury was associated with protracted recovery (OR=6.42; 95% CI, 1.39–29.7). No significant associations found b/w protracted recovery and LOC, vomiting, or any of the other factors considered (crude analysis)
Makdissi et al,[32] 2009; Australia	All elite professional football players in AFL followed up prospectively for 4 seasons (2000–2003). Players referred	Exclusion: players who played no games before their concussive injury; played no games after concussive injury (insufficient	Symptoms after traumatic injury included feeling dinged, dazed, stunned, woozy, foggy, “head full of cotton wool” or “not	Prognostic factors: concussion during study period (2000–2003)	92% RTP without missing a game (able to return to competition 6–9d postinjury); 8% RTP after missing 1 game.

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Table 1 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
	into study after sustaining concussion during AFL competition (n=158); 117 players (138 concussive injuries) analyzed. Controls: noninjured players matched for team, position, age, and size	F/U; this group included players who returned to a lesser grade competition on their recovery from injury and those who were concussed during the last game of the season); had an unrelated nonconcussive concurrent injury/illness preventing RTP	quite right," PTHA, visual disturbance, balance disturbance, vertigo, lightheadedness. Signs included confusion, LOC, disorientation, memory disturbance, unsteadiness, attention deficit, personality change.	Outcomes: performance statistics (disposals per hour match time), injury rates, recurrence of concussion	Performance (disposal rate) of concussed players was not impaired on RTP. No significant differences in injury rates b/w concussed players and controls. No player was concussed again in the first game back after injury.
Preiss-Farzanegan et al,[29] 2009; United States	Nested cohort from NIH-funded TBI registry designed to evaluate epidemiology and 3-month outcomes of concussion. Individuals who presented to a regional trauma center ED with concussion Feb 3, 2003, to Sep 20, 2003, were recruited (n=1438). 260 were admitted with a primary sport-related concussion; 215 eligible for analysis. F/U: 3 months after initial assessment	Inclusion: subset of NIH registry patients who reported their mechanism of injury involved a sport; did not report intentions to file a lawsuit as a result of their injury	American Congress of Rehabilitation Medicine: a blow to head or acceleration/deceleration movement of head resulting in ≥1 of: LOC <30 minutes or amnesia <24 hours or altered mental status at the time of injury; GCS ≥13 measured 30 minutes or more after injury	Prognostic factors: sex Adjustment factors: age, source of postconcussion symptom reporting (self, proxy, or interviewer), previous head injury or LOC, sport Outcomes: postconcussion symptoms (RPQ)	Compared with males, adult females (≥18y) are at greater risk for elevated RPQ scores (OR=2.57; 95% CI, 1.09–6.08) but not female minors (≤17y) (OR=1.07; 95% CI, .52–2.19). Adult females, compared with males, appear to have elevated risk for specific symptoms of headache (OR=4.5; 95% CI, 1.6–12.4), dizziness (OR=2.8; 95% CI, 1.0–7.9), fatigue (OR=2.8; 95% CI, 1.0–7.4), irritability (OR=2.8; 95% CI, 1.0–7.7), and concentration problems (OR=3.0; 95% CI, 1.1–8.4) at 3 months after sport-related concussion.
Phase I studies					
Bruce and Echemendia,[22] 2009; United States	3 large multisport male collegiate samples: Study 1 sample underwent computerized testing (ImPACT) (n=858; 298 reported a history of concussion); Study 2 sample underwent traditional testing (n=479; 187 reported a history of concussion); Study 3 sample underwent computerized and traditional testing (n=175; 57 reported a history of concussion)	Inclusion: no history of concussion in previous 6 months, spoke English fluently, no history of learning disability	Self-reported concussion based on questionnaires (no details provided for Studies 1 and 3). Study 2 used self-reported Previous Head Injury Questionnaire (assesses the number of concussions someone has experienced, the circumstances surrounding the concussions, symptoms, and treatment).	Prognostic factors: self-reported concussion history (Previous Head Injury Questionnaire) Outcomes—cognitive abilities: Study 1: computerized ImPACT test; Study 2: Pennsylvania State University Concussion Battery, SDMT, Stroop Color, SCWT, COWAT, TMT, HVLT; Study 3: ImPACT and Pennsylvania State University Concussion Battery	No significant association b/w concussion history and performance on either computerized or traditional neurocognitive tests

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Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
Bruce and Echemendia,[21] 2004; United States	Multisport sample of Division 1 male collegiate athletes part of a concussion management program (n=433); 57 sustained concussion during study period. PC (previous concussion history) group (n=30): 1 previous concussion (n=17), >1 previous concussion (n=13); NPC (no previous concussion history) group (n=27); Controls (n=29): noninjured athletes drawn from same sample; 1 previous concussion (n=9), >1 previous concussion (n=4). F/U: 2 hours, 48 hours, 1 week postinjury	Inclusion: met case definition. Athletes included if they were concussed. Controls could not have been concussed within past 6 months	AAN criteria*	Prognostic factors: concussion history (Previous Head Injury Questionnaire) Outcomes: PCSS (physical, emotional, and cognitive symptoms) at baseline (before concussion) and postinjury	Athletes with a history of ≥1 concussion reported more postconcussion symptoms at baseline than athletes who had never been concussed ($P<.01$). PC athletes reported significantly fewer postconcussion symptoms than NPC athletes 2 hours postinjury ($P<.05$). No significant differences at 48 hours postinjury. At 1 week, PC athletes reported more cognitive/balance symptoms than NPC athletes ($P<.05$). For number of symptoms, no significant differences b/w PC athletes and controls at 1 week, but NPC athletes reported fewer cognitive/balance and emotional symptoms than controls at 1 week ($P<.05$)
Erlanger et al,[25] 2003; United States	Baseline CRI assessments were administered to 1603 athletes in computer laboratories at 9 U.S. high schools, colleges, and sports organizations as part of an ongoing research project initiated in 2000. Majority of athletes engaged in high-risk sports (football, hockey). After concussion, athletes were administered F/U tests, typically at 1- to 2-day intervals, until symptom resolution (n=47).	Exclusion: athletes who displayed no symptoms at any given F/U examination were not evaluated further.	AAN criteria*	Prognostic factors/clinical course indicators: number of immediate symptoms, number of symptoms at initial F/U examination, duration of symptoms, history of concussion, neurocognitive testing Outcomes: Internet-based neurocognitive assessment battery (CRI), postconcussion symptoms, concussion severity	All postconcussion symptoms resolved in all participants by day 16. Mean± SD duration of symptoms was 6.02±4.82 days. 55.3% of athletes performed significantly slower on 1 or more CRI speed/error indices. Athletes reporting memory problems at 24 hours postconcussion had significantly more symptoms, longer symptom duration, and decreased scores on neurocognitive tests at 48 hours. A decline on neurocognitive testing was significantly related to symptom duration. Neither brief LOC or history of concussion predicted postconcussion symptom duration.
Guskiewicz et al,[39] 2003; United States	Collegiate football players from 19 Division I, 3 Division II, and 3 Division III schools enrolled (n=2905, 69% response rate). Data collected during 3 football	Inclusion: met case definition	Injury resulting from a blow to head that caused an alteration in mental status and ≥1 of the following symptoms: headache, nausea, vomiting, dizziness/	Prognostic factors: concussion history, LOC, PTA Outcomes: incidence of concussion and repeat concussion; type and duration	Athletes with a history of multiple concussions experienced a longer recovery ($P=.03$). Presence of LOC and amnesia tended to be associated with a slower recovery.

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Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
	seasons (1999—2001, accumulating 4251 player-seasons of F/U). F/U: Players who sustained incident concussions followed up for repeat concussions until completion of collegiate football career or end of 2001 football season		balance problems, fatigue, difficulty sleeping, drowsiness, sensitivity to light or noise, blurred vision, memory difficulty, and difficulty concentrating	of symptoms (GSC); course of recovery (concussion index)	
Guskiewicz et al,[35] 2001; United States	Division 1 collegiate athletes who sustained concussion during practice/competition (n=36). Injured players who received preseason baseline neuropsychological and postural stability testing were assessed on days 1, 3, and 5 postconcussion. Controls: recreational and collegiate athletes of the same approximate age, height, and weight who played approximately the same amount of time on the day of their matched counterparts' injuries (n=36)	Exclusion: control subjects who sustained concussion within 6 months of testing or presented with vestibular deficit or acute musculoskeletal injury that affected postural equilibrium	Injury to the brain caused by sudden acceleration or deceleration of head that resulted in any immediate, but temporary, alteration in brain functions (eg, LOC, blurred vision, dizziness, amnesia, or memory impairment)	Prognostic factors/clinical course indicators: postural stability (Sensory Organization Test on NeuroCom Smart Balance Master System and Balance Error Scoring System), neuropsychological tests (TMT-A and TMT-B, WDST, SCWT, HVLT), LOC, amnesia. Outcomes: course/rate of recovery	Injured subjects: postural stability significantly worse than baseline and control subjects' scores on day 1. Recovery back to baseline occurred b/w days 1 and 3. Injured subjects: lowered neuropsychological performance (TMT-B, WDST Backward). Significant differences b/w control and injured groups at days 1 (TMT-B, WDST) and days 3 and 5 (TMT-B), but no significant decline b/w baseline and postinjury scores. LOC and amnesia not associated with increased deficits or slowed recovery
Iverson et al,[36] 2003; Canada	Amateur high school and university athletes (90% M; median age, 16y; range, 13—22y) who sustained sports-related concussion (54% grade 1, 22% grade 2, 7% grade 3) and completed ImPACT preseason and within 72 hours of injury (n=41). F/U: 72 hours postconcussion	Inclusion: amateur athletes who sustained a sports-related concussion; completed ImPACT at the beginning of the season and were retested within 72 hours of their concussions	AAN criteria*	Prognostic factors/clinical course indicators: neuropsychological test battery (ImPACT version 2.0), reliable change parameters (80% CIs for estimating change are: verbal memory $\geq$9 points, visual memory $\geq$14 points, reaction time >.06s, processing speed $\geq$5 points, and postconcussion total scores $\geq$10 points). Outcomes: concussion recovery	Significant decline in verbal memory (d=.82, large effect size), visual memory (d=.69, medium-large effect size), processing speed (d=.49, medium effect size), reaction time (d=.95, large effect size). Large increase in symptom reporting (d=.99, large effect size)

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Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
Lovell et al,[26] 2003; United States	High school athletes from multiple sites who had concussion (n=64): East (Pennsylvania and Maine), Midwest (Illinois and Michigan), and West (Oregon). Controls: recruited from a single high school in Pennsylvania (n=24). F/U: preseason (baseline); 36 hours, 4 and 7 days postconcussion	Exclusion: history of learning disabilities, attention-deficit disorder, alcohol/drug abuse or dependence; athletes who experienced any degree of postinjury LOC	Criteria: (1) any observable alteration in mental status/ level of consciousness such as LOC, retrograde amnesia, PTA, disorientation; and/or (2) self-reported symptoms after collision such as “fogginess,” “grogginess,” headache, nausea/vomiting, dizziness, balance problems, and/or visual changes. Subgroup analysis based on duration of on-field symptoms: More severe concussion: (1) retrograde amnesia >5 minutes; (2) PTA >5 minutes; or (3) disorientation >5 minutes. Less severe concussion: mental status changes ≤5 minutes	Prognostic factors: duration of on-field mental status changes (eg, retrograde amnesia, posttraumatic confusion), self-reported postconcussion symptoms Outcomes: memory dysfunction, self-reporting of symptoms (ImPACT test battery, PCS)	Clinical course findings: Pairwise comparisons b/w memory scores among concussed athletes revealed significantly lower memory scores at 36 hours (d=.74, medium-large effect size, P<.000), at day 4 (d=.69, medium-large effect size, P<.000), and at day 7 (d=.34, small effect size, P<.017) compared with baseline. Significant decline in postconcussion symptoms only at 36 hours postinjury (d=.84, large effect size, P<.000). Prognostic findings: Significant difference in postinjury memory performance b/w athletes with on-field mental status changes (P<.024). Clinical course findings: Pairwise comparisons revealed significant declines in memory performance relative to baseline at all 3 F/U intervals for players with a longer duration of on-field mental status changes (P<.017, .004, and .037, respectively). Longer-duration group reported more postconcussion symptoms (P<.096).
Makdissi et al,[34] 2010; Australia	Male Australian Rules football players recruited from elite senior, elite junior, and community-based team competitions (n=1015: 675 elite senior players, 272 elite junior players, 68 community-level players); study conducted over 4 competitive seasons (2001—2004). All players were prospectively monitored for concussive injuries. 88 concussions observed in 78 players.	Inclusion: met case definition	Symptoms reported by players or signs observed by medical staff after traumatic injury. Symptoms included feeling dinged, dazed, stunned, woozy, foggy, “head full of cotton wool,” or “not quite right,” PTHA, visual disturbance, confusion, memory disturbance, balance disturbance, vertigo, lightheadedness. Signs included confusion, LOC, disorientation, memory disturbance, unsteadiness,	Prognostic factors/clinical course indicators: postconcussion symptoms, LOC, cognitive function (paper-and-pencil tests: DSST, TMT-B; CogSport computerized test battery), self-reported history of concussion Outcomes: clinical course of concussion in sport, time to RTS (full training or competitive playing)	Mean number of symptoms reported per concussion was 3.7 (95% CI, 3.4—4.0); duration of symptoms was 48.6 hours (95% CI, 39.5—57.7). Prognostic findings: Delayed RTS correlated with ≥4 symptoms, headache lasting ≥60 hours, or self-reported “fatigue/fogginess.” Headache lasting <24 hours associated with shorter time to RTS. No significant association b/w LOC, cognitive deficits, or history of concussion and prolonged time to RTS. Clinical course findings: Cognitive deficits using paper-and-

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Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
	F/U: preseason (baseline); until clinical features of concussion resolved		attention deficit, personality change.		pencil tests recovered concomitantly with symptoms; computerized test results recovered 2–3 days later and remained impaired in 35% of players after symptom resolution. Mean time taken to RTS was 4.8 days (95% CI, 4.3–5.3). No significant difference b/w senior, junior, and community-level athletes
Pellman et al,[30] 2004; United States	From 1996 to 2001, concussions were reported by 30 NFL teams using standardized reporting. Data were captured for 887 concussions in practices and games involving 650 players.	Inclusion: any player who met case definition	NFL Committee on MTBI, 1996: traumatically induced alteration in brain function, which is manifested by (1) alteration of awareness or consciousness, including but not limited to being dinged, dazed, stunned, woozy, foggy, amnesic, rendered unconscious, or experiencing seizure; or (2) SS commonly associated with PCS, including persistent headaches, vertigo, lightheadedness, loss of balance, unsteadiness, syncope, near syncope, cognitive dysfunction, memory disturbance, hearing loss, tinnitus, blurred vision, diplopia, visual loss, personality change, drowsiness, lethargy, fatigue, inability to perform usual daily activities	Prognostic factors: repeat injuries, player position Outcomes: SS (general, somatic, cranial nerve effects, cognition problems, memory problems, unconsciousness)	160 players (24.6%) had repeat injury; 51 had $\geq$3. Median time b/w injuries was 374.5 days; only 6 concussions occurred within 2 weeks of initial injury. Similar SS found with single and repeat concussion, except for higher prevalence of somatic complaints in players on their repeat concussions compared with their first (27.5% vs 18.8%, $P<.05$). Quarterbacks had higher odds of repeat concussion (OR=1.92; 95% CI, .99–3.74; $P<.10$); the offensive line had lower odds (OR=.54; 95% CI, .27–1.08; $P<.10$)
Pellman et al,[31] 2004; United States	From 1996 to 2001, concussions were reported by 30 NFL teams using standardized reporting. Data were captured for 887 concussions in practices and games involving 650 players.	Inclusion: any player who met case definition	Same as previous	Prognostic factors: player position, team activity Outcomes: SS (general, somatic, cranial nerve effects, cognition problems, memory problems, unconsciousness) of players who RTP within 7 days after	72 concussions (8.1%) involved 7+ days out of play; only 1.6% involved prolonged PCS. All recovered and RTP in NFL. Quarterbacks were most vulnerable of being 7+ days out (OR=2.10; 95% CI, .99–4.45; $P=.049$); running backs had lowest risk (OR=.14; 95% CI,

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Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
				concussion vs 7+ days or extended postconcussion recovery	.02–.99; P=.021). Greatest fraction of 7+ days out occurred on passing plays (36.1%) and kickoffs (22.2%). Players 7+ days out had greater frequency of SS on initial examination (average, 4.64 vs 2.58 with fewer days out). SS with highest incidence for 7+ days out: disorientation to time, retrograde amnesia, fatigue, cognition problems, LOC >1 minute
Pellman et al,[23] 2004; United States	650 NFL athletes who experienced 887 concussions during 1996– 2001 underwent neuropsychological testing voluntarily (n=143). Participating players represented a relatively homogenous group (all men, 21–35y of age in all offensive and defensive positions). F/U: initial evaluation 24–48 hours postinjury; F/U evaluation recommended 5–7 days postinjury if athlete had persistent cognitive deficits or postconcussion symptoms	No specific criteria	Same as previous	Prognostic factors: on-field memory dysfunction, ≥3 concussions, 7+ days out from practice and play Outcomes: neuropsychological function (NFL test battery: HVLT, BVMT-R, TMT parts A and B, COWAT, DST, SDMT)	No significant neuropsychological dysfunction relative to baseline within a few days of injury. Those with on-field memory dysfunction performed significantly more poorly on 2 memory tests: immediate memory (F=6.1, P<.02) and delayed memory (F=5.4, P<.03) aspects of BVMT-R. No significant difference b/w those with history of ≥3 concussions and those with <3 concussions or compared with league-wide normative data. No significant difference in performance b/w those out 7+ days vs those who RTP within 7 days or the norms
Pellman et al,[33] 2005; United States	From 1996 to 2001, concussions were reported by 30 NFL teams using standardized reporting. Data were captured for 887 concussions in practices and games involving 650 players.	Inclusion: any player who met case definition	Same as previous	Prognostic factors: SS (general, somatic, cranial nerve effects, cognition problems, memory problems, unconsciousness) Outcomes: immediate RTP vs rest and RTP in same game, subsequent concussion, more serious concussion involving 7+ days out	135 players (15.2%) RTP immediately; 304 (34.3%) rested and returned to same game after concussion. Mean number of SS progressively increased from those who RTP immediately (1.52), rested and RTP (2.07), were removed from play (3.51), or were hospitalized (6.55). Factors predictive of removal from play or hospitalization were immediate recall problems (OR=1.93; 95% CI, 1.26–2.94), memory problems (OR=1.52; 95% CI, 1.06–2.19), and number of SS (OR=1.39; 95% CI, 1.25–1.55). No association b/w RTP in same game and

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Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
					subsequent concussion in same game or a more serious concussion during season
Pellman et al,[24] 2006; United States	Convenience sample of consecutive injured athletes in 2002–2004 seasons: 48 NFL athletes and 37 high school athletes completed 1 postinjury evaluation; 30 NFL and 28 high school athletes completed second evaluation (those with normal performance after first evaluation were not evaluated a second time). Evaluated a second time: 63% of NFL athletes, 75% of high school athletes. Participation was voluntary. Preseason baseline test data collected on separate groups of professional and high school football players (n=68 NFL athletes, n=125 high school athletes). Baseline and postconcussion samples were very similar in age, education level, and percentage of athletes in each position group. F/U: 2–3 days for high school sample, 1 day after injury for NFL	Inclusion: only professional and high school athletes who had completed ImPACT 2.0 or 3.0. High school baseline group: male football players in grades 9–12 who had completed baseline testing. Postconcussion group: only athletes who completed 2 postinjury F/U evaluations. Exclusion: athletes who had completed earlier version of ImPACT (version 1.0) from 2000 to 2002	NFL: Same as above High school: concussions were witnessed and diagnosed by physicians and certified athletic trainers. Criteria were very similar as above; based on the presence of mental status changes or player symptoms after a collision or blow to the head	Prognostic factors: age, concussion history Outcomes: recovery assessed by computerized neurocognitive testing (ImPACT)	NFL athletes returned to baseline performance in 1 week; majority had normal performance 2 days postinjury. High school athletes had a slower recovery than NFL athletes. History of concussion was not related to neurocognitive test performance.

Abbreviations: AAN, American Academy of Neurology; AFL, Australian Football League; ASYMP, asymptomatic; b/w, between; BVMT-R, Brief Visuospatial Memory Test—Revised; COWAT, Controlled Oral Word Association Test; CRI, Concussion Resolution Index; *d*, effect size; DSST, Digit Symbol Substitution Test; DST, Digit Span Test; ED, emergency department; F, female; F/U, follow-up; GCS, Glasgow Coma Scale; GSC, Graded Symptom Checklist; HVLT, Hopkins Verbal Learning Test; ImPACT, Immediate Postconcussion Assessment and Cognitive Testing; M, male; NFL, National Football League; NIH, National Institutes of Health; OR, odds ratio; PC, previous concussion; PCS, postconcussion syndrome; PCSS, Postconcussion Symptom Scale; PSI, Processing Speed Index; PTA, posttraumatic amnesia; PTHA, posttraumatic headache; RPQ, Rivermead Postconcussion Symptoms Questionnaire; SCWT, Stroop Color Word Test; SDMT, Symbol Digit Modalities Test; SS, signs and symptoms; SYMP, symptomatic; TBI, traumatic brain injury; TMT, Trail Making Test; RTS, return-to-sport; WAIS-III, Wechsler Adult Intelligence Scale—3rd Edition; WDST, Wechsler Digit Span Test; w/o, without.

* American Academy of Neurology concussion grading scale criteria: grade 1, transient confusion, no LOC, concussion symptoms/mental status change resolves in ≤15 minutes; grade 2, transient confusion, no LOC, concussion symptoms/mental status change resolves in >15 minutes; grade 3, brief or prolonged LOC.

injury, high school athletes had a drop of approximately 0.4 SD units in verbal memory and a .83 SD change in reaction time relative to preseason performance.[24]

The sex of concussed collegiate athletes (phase II)[19] and time out of play after concussion in professional American footballers (phase I)[23] did not predict performance on neuropsychological tests.

Postconcussion symptoms after sport concussion

Five studies[21,25,26,29-31] suggest that postconcussion symptoms and sequelae, if any, appear to be short-lived (a few days to a few weeks) in athletes.

Predictors of postconcussion symptoms

There is only limited evidence that the following factors increase postconcussion symptoms in the short-term: being an adult female, having a longer duration of postinjury memory problems and on-field mental status changes, and showing decreased cognitive function postinjury.

Sex: Only 1 accepted phase II study assessed sex as a prognostic factor for the development of postconcussion symptoms after sport concussion.[29] In adults and minors presenting to an emergency department, compared with males, adult females (≥18y) were at greater risk of postconcussion symptoms (odds ratio, 2.57; 95% CI, 1.09−6.08), but not female minors (≤17y).[29] Compared with adult males, adult females appeared to have an elevated risk for headache, dizziness, fatigue, irritability, and concentration problems at 3 months postinjury.[29] Differences in reporting styles between males and females may exist and may partially account for this finding.

Presence and duration of memory problems and on-field mental status changes: Two phase I studies[25,26] assessed these factors in a total of 111 participants with concussion. In high school and college athletes, all postconcussion symptoms resolved in all participants within 16 days after the injury.[25] The mean ± SD duration of symptoms was 6.0±4.8 days.[25] Athletes reporting memory problems at 24 hours postinjury had more symptoms and longer symptom duration (P=.003).[25] In another study[26] comprising high school athletes, those with a longer duration (>5min) of on-field mental status changes (retrograde amnesia, anterograde amnesia, or disorientation) reported more postconcussion symptoms (P<.096) compared with the shorter-duration group (ie, <5min of on-field mental status changes). Pairwise comparisons revealed a significant increase in symptoms from baseline to 36 hours for athletes whose on-field mental status changes were of longer duration (d=1.37, very large effect size; P<.003).[26] In athletes with a shorter duration of on-field mental status changes, pairwise within-group comparisons revealed significantly greater symptoms from baseline to 36 hours (d=.73, large effect size; P<.000). By days 4 and 7, there were no significant differences compared with baseline in either group.

Decline on neurocognitive testing: One phase I study[25] found that a decline on neurocognitive testing 1 to 2 days postinjury was significantly related to symptom duration in high school and college athletes participating in high-risk sports such as football and hockey (P=.005).

Factors that did not appear to significantly contribute to postconcussion symptoms included sport characteristics in adults and minors (1 phase II study)[29]; a history of previous concussion in high school, collegiate, and professional athletes (3 phase I studies)[21,25,30]; and a loss of consciousness (LOC) in high school and collegiate athletes (1 phase I study).[25]

Recurrent concussion after sport concussion

Recurrent concussion was examined in 2 studies of adult professional athletes. One phase II study[32] revealed no differences in reinjury rates between concussed Australian Football League players and controls. In this single study, no players were concussed again in their first game back after injury. One phase I study[33] found that in American football/National Football League players, there was no association between RTP in the same game and subsequent concussion in the same game or a more serious concussion during the season.

RTP after sport concussion

Preliminary evidence from 1 phase II[32] and 2 phase I[33,34] studies suggests that most athletes RTP within the same game or a few days after concussion. Two studies assessed professional footballers, while the third studied elite and community-level football players. In a study[32] of 117 Australian footballers, more than 90% returned to play without missing a game (ie, 6−9d postinjury). Most of the remainder returned to play after missing only 1 game. Pellman et al[33] found that of 650 injured American football players, 15% returned to play immediately, while 34% rested and returned in the same game. Factors predictive of removal from play or hospitalization were immediate recall problems, memory problems, and the number of signs and symptoms postinjury.[33] Among Australian elite senior and junior football players and community-level football players (median age, 22y), delayed RTP correlated with having 4 or more symptoms, headache lasting greater than 60 hours, or self-reported "fatigue/fogginess."[34] Headache lasting less than 24 hours was associated with a shorter time to RTP. There was no association between LOC, cognitive deficits, or history of concussion and prolonged time to RTP. The mean time taken to RTP was 4.8 days (95% CI, 4.3−5.3d). No differences were found between senior, junior, and community-level athletes.[34]

Sport performance after sport concussion

Only 1 phase II study[32] addressed this issue and found that the football performance of professional Australian footballers was not impaired on RTP from a sport concussion.

Course and predictors of recovery after sport concussion

Three studies assessed the course of recovery within a few days postinjury. One study[35] found that athletes returned to pre-injury status within a few days, while the other 2[34,36] did not. In collegiate athletes, postural stability, as measured by the Sensory Organization Test and the Balance Error Scoring System, returned to baseline levels between 1 and 3 days postinjury.[35] There was no significant decline between baseline and postinjury scores at 1, 3, and 5 days postinjury on traditional neuropsychological tests. Additionally, LOC and amnesia were not associated with increased deficits or slowed postural stability and neurocognitive recovery. Conversely, in amateur high school and collegiate athletes, there was a significant decline on the Immediate Postconcussion Assessment and Cognitive Testing computerized neuropsychological test battery and a large increase in symptom reporting at 72 hours postinjury.[36] In Australian footballers (ie, elite senior and junior, and community-level players), cognitive deficits, measured using paper-and-pencil tests, recovered concomitantly with symptoms.[34] However, computerized test performance recovered 2 to 3 days later and remained impaired (lower scores in psychomotor and attention tasks) in 35% of players after symptom resolution. Different modes of testing, such as computer-based tests versus traditional neuropsychological tests, may produce different results since they measure different neurocognitive constructs.[22] Traditional tests typically rely more on free recall assessment of memory, such as recalling previously presented word lists, and computer-based tests assess less demanding forced-choice recognition memory paradigms.[22] As reported by Bruce and Echemendia,[22] the literature suggests that free recall tasks are more difficult than recognition tasks.

One phase II[37,38] and 1 phase I[39] study suggested certain predictors of longer recovery. Four variables contributed the most to classifying high school footballers with protracted recovery (>14d): the migraine symptom cluster (largest contributor), reaction time, visual memory, and verbal memory.[37] Dizziness at the time of injury was also associated with protracted recovery.[38] However, there were no significant associations between protracted recovery and LOC, vomiting, confusion, posttraumatic amnesia, retrograde amnesia, imbalance, visual problems, personality changes, fatigue, sensitivity to light/noise, or numbness.[38] A history of multiple concussions was also found to predict longer recovery in collegiate football players.[39] In this group, Guskiewicz et al[39] found that the presence of LOC and amnesia also tended to be associated with a slower recovery.

Discussion

The best available evidence on prognosis after sport concussion suggests that most athletes recover within days to a few weeks to preinjury levels in terms of cognitive performance (as measured by objective traditional and computerized neuropsychological tests) and postconcussion symptoms (as measured by self-report). Our findings indicate that younger players (average age, 16y) have a slightly longer recovery (about 21d) than adults. Our limited findings on RTP after concussion, based mainly on adult professional American and Australian footballers assessed by team physicians, suggest that concussed players who RTP are not likely to sustain a more serious concussion during the respective game or season. Factors that appear to delay recovery are a history of previous concussion, number and duration of postconcussion symptoms (eg, memory problems and headache), and being a younger-aged/high school athlete compared with a collegiate or professional athlete. Most studies assessed short-term prognosis, and most of the participants were male football players at the high school, collegiate, or professional level. Most high school athletes studied were approximately 16 years of age; therefore, information is still lacking on younger male athletes aged 13 to 15 years, and in female athletes of all ages.

Our findings are consistent with the last review conducted by the WHO Collaborating Centre Task Force on MTBI,[8] which found that self-reported postconcussion symptoms usually resolve quickly in athletes. Two other recent meta-analyses assessed the effects of sport concussion, 1 of which reached similar conclusions. Belanger et al[40] concluded that the effect of multiple concussions on neuropsychological functioning (attention, executive functioning, fluency, memory acquisition, delayed memory, motor abilities), as measured by traditional and computerized neuropsychological tests, was minimal and not significant. Of note, the quality of the analyzed studies was not reported. Their analysis was also based on some studies that we excluded because of small sample size, design issues, and publication date, or judged as scientifically inadmissible because of risk of bias.

Broglio and Puetz,[41] on the other hand, concluded that sport concussion had a large negative effect on neurocognitive functioning and postural control even at 14 days after the initial assessment. Their results differed somewhat from ours. Our findings were inconsistent but suggest that cognitive function is not significantly impaired, or if impaired resolves within a few days to a few weeks. A number of reasons could explain some of the discrepancies between their findings and ours. Many studies in their review were not eligible for ours based on our inclusion criteria. For example, some of their eligible studies had publication dates before 2001, sample sizes of less than 30 participants, and case series and cross-sectional study designs. These designs were ineligible for our review because they cannot demonstrate causality, and a sample size of less than 30 is too small, in our view, to support valid conclusions.[11] Furthermore, the International Collaboration on MTBI Prognosis and the WHO Collaborating Centre Task Force[8] rejected certain studies that they accepted, based on methodological quality.[41] These groups used different methods for assessing study quality than Broglio and Puetz,[40] which could have contributed to some discordant findings.[11]

Debates still exist about whether there is a link between repetitive concussion in athletes and late-life depression and mild cognitive impairment (MCI), chronic traumatic encephalopathy, and other dementia-related neurodegenerative disorders.[42-46] There is insufficient high-quality evidence at this time to suggest these associations. Well-designed, controlled studies are needed to address these important issues in lieu of more case reports and cross-sectional studies.

Two highly cited studies by Guskiewicz et al[44,45] were reviewed by members of the International Collaboration on MTBI Prognosis but were deemed to have a high risk of bias. These studies indicated an association between recurrent concussion and both clinically diagnosed MCI[45] and an increased risk of clinical depression[44] in retired professional football players with an average age $\pm$ SD of 53.8$\pm$13.4 years and an average $\pm$ SD professional football playing career of 6.6$\pm$3.6 years. Besides having cross-sectional designs, a number of methodological weaknesses exist in these studies. The response rate was only 55%, and selection bias is a threat since it is unknown whether respondents differed from nonrespondents. Other weaknesses include the lack of control for potential confounders (eg, chronic pain and substance abuse) and the risk of information bias (ie, self-reported memory problems might not indicate real or objective memory problems). A significant limitation of these studies was the use of a self-reported history of concussion, since imperfect recall can generate differential recall bias.[47] Kerr et al[47] assessed the reliability of concussion history in this same cohort of retired professional football players and found that those who reported more concussions had worse physical and mental health at follow-up. This differential recall bias would result in an overestimation of the risk of MCI[45] and depression[44] resulting from concussions. In other words, those with MCI or depression, as well as their spouses, might have overreported their concussions, while those without these conditions might have underreported their concussions. Furthermore, Kerr et al demonstrated that the reliability of concussion reporting was moderate (weighted Cohen $\kappa = .48$).[47] This would result in a significant amount of misclassification of exposure status. Thus, the associations observed by Guskiewicz linking recurrent concussion with late-life MCI and depression may be misleading because of differential recall bias and other study weaknesses.

Injury prevention and evidence-based management should remain a high priority for amateur and professional athletes alike regardless of these possible negative associations, since most would agree that repeated head trauma is undesirable. However, ongoing publicity about "brain damage" after sport concussion might have a deleterious effect on recovery. Iverson and Gaetz[48] state that it is important to avoid over-pathologizing neuropsychological test scores and postconcussion symptoms because this can inadvertently cause athletes to feel undue stress, anxiety, and depression. Athletes who worry and focus on their symptoms are at increased risk for protracted recovery patterns.[48]

We found no acceptable phase III studies that investigated prognosis after sport concussion. Of the 19 acceptable studies, approximately half were phase II, with the remainder being phase I; all provided exploratory evidence for potential associations between prognostic factors and recovery from sport concussion. Overall, there is a great need for well-designed, long-term confirmatory studies that take into consideration potential confounders to better understand prognosis after sport concussion. Potential confounding factors include age, sex, concussion history, years of education, medication, and alcohol use, as well as comorbidities and premorbidities (eg, migraine, depression or other mental health disorders, attention-deficit/hyperactivity disorder, learning disabilities, and sleep disorders).[1,49] Experience, level of competition (ie, amateur vs professional), and type of sport should also be taken into account in future studies. The use of appropriate comparison groups is also recommended.[49] A comparison group of uninjured athletes drawn from the same source population would help to deal with issues related to repeat test administration (ie, practice effects and motivation/response bias).[36,50] Additionally, comparison groups consisting of participants with musculoskeletal or orthopedic injuries are recommended. This would help address whether postconcussion sequelae are actually due to MTBI, and not to other factors common to other injuries such as pain, stress, and removal from play.[51] Considerable research is also needed to improve the reliability, validity, and accuracy of serial assessments of athletes in the domains of subjectively experienced and reported symptoms, and measured cognitive abilities.[48] Lastly, consensus guidelines have been developed and are widely implemented,[1,52] but they need to be scientifically tested, preferably with randomized controlled trials.

Study limitations

While our review has several strengths, such as the use of a comprehensive and sensitive search strategy, and a best-evidence synthesis based on studies of higher methodological quality, important limitations also exist. The strength of our findings is limited by the lack of high-quality and confirmatory (phase III) studies available in the literature. Comper et al[49] also concluded that the methodological quality of neuropsychological sport concussion studies is highly variable, with many lacking proper scientific rigor. Many of the same biases and issues of confounding found in the previous WHO review[8] still exist in the studies we reviewed for our best-evidence synthesis. Examples of selection bias include small sample sizes, unknown response rates, poorly described sample selection, the use of voluntary or convenience samples, insufficient description of nonparticipants, nonreporting of reasons for attrition, and the inappropriate selection of controls (eg, from different sports than cases).[53] Information bias was also problematic. Different studies used varying definitions of concussion, or concussion was not always well defined. The exposures (concussions) were not consistently ascertained. For example, with respect to concussion history, in many cases, either the information was not collected or it was given via athlete self-report. Thus, the potential for recall bias also exists. For cases where concussion history was given, the periods between concussions were largely unknown or unreported. All of these factors could influence outcomes and should be carefully considered in future studies in order to gain a better understanding of prognosis after sport concussion.

Conclusions

The best evidence, all of which is exploratory at this time, indicates that most concussed athletes recover to preinjury levels, with those at the professional level recovering the most quickly. Additionally, we found that decrements in cognitive performance and postconcussion symptoms are largely resolved within days to a few weeks of the injury, and most athletes RTP soon after sport concussion. Although only 2 studies on the risk of recurrent concussion were admitted in our review, these studies indicate that professional athletes may not be at significant risk of recurrent concussions, especially during the same game or during the same season. Possible predictors of delayed recovery were suggested in certain studies; however, none have been conclusively studied. Despite the proliferation of research on sport concussion over the past 10 to 15 years, studies are very heterogeneous in design and outcomes, and contain a number of methodological weaknesses and biases. The lack of confirmatory studies (phase III)[14] limits our ability to make firm conclusions. Future research needs to be well designed and executed to reduce the risk of bias. A better understanding of prognosis after sport concussion will help to inform evidence-based guidelines for management and RTP.

Keywords

Athletic injuries; Brain concussion; Prognosis; Rehabilitation; Sports

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