Evidence-Based Practice Group Answers to Clinical Questions

Concussion Recovery Path and Past Head Traumas

By

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About this report

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About the Evidence-Based Practice Group

The Evidence-Based Practice Group was established to address the many medical and policy issues that WorkSafeBC officers deal with on a regular basis. Members apply established techniques of critical appraisal and evidence-based review of topics solicited from both WorkSafeBC staff and other interested parties such as surgeons, medical specialists, and rehabilitation providers.

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Objective

This review explores factors affecting natural recovery path in concussions/ mTBIs, with a specific focus on past head traumas.

Background

Concussion is a pathophysiological process caused by biomechanical forces that affect the brain and lead to clinical symptoms. It is a subset of traumatic brain injury (TBI). Commonly occurring after a shake to the brain, concussion leads to injury at the cellular and behavioral levels. [1] Since the term 'concussion' is used interchangeably with 'mild traumatic brain injury (mTBI)' [2] we included both terms when conducting our literature search.

In general, 70 to 90% of all patients treated for head traumas are classified as mTBIs and often the symptoms are temporary. [3] The World Health Organization (WHO) Collaborating Centre Task Force defines mTBI as "an acute brain injury resulting from mechanical energy to the head from external physical forces" [4] and the overarching case definition has been the Glasgow Coma Scale (GCS) score of 13-15, loss of consciousness (LOC) <30 minutes, and post-traumatic amnesia (PTA) up to 24 hours. [5-7] Whether from a diffuse or focal trauma, shake, blow, jolt to the head resulting in concussion, contusion, and/or with delayed, prolonged symptoms; prognosis of mTBI is usually promising. The first 0-7 days after injury is referred to as 'immediate period', the following 1-6 weeks is the 'acute period' and 7-12 weeks is frequently termed the 'post-acute period'. If symptoms persist after 12 weeks, they are commonly referred to as 'chronic'. [7] The majority of patients fully recover from symptoms in less than 12 weeks, and 80–90% of concussion symptoms resolve in 7 to 10 days. [2] When individuals have persisting nonspecific symptoms, ruling out other health conditions (e.g., psychological distress, drug/alcohol abuse, pain from musculoskeletal injuries, regular medication use) may be clinically useful. Typically, most mTBI patients progressively return to their normal daily activities.

The length of the recovery period after mTBI varies and depends on the trauma sustained and/or patient characteristics. Some of the factors suggested in the literature are age, education, pre-injury mental health status, early stage emotional distress and maladaptive coping following concussion, number of initial symptoms (including unconsciousness, posttraumatic amnesia), findings of perfusion deficit, early participation in physical activity after the injury, chronic or repeated head injury, number of preceding concussions, as well as the force of impact and injury severity. [6, 8-18]

Some studies suggest that in poorer cognitive/adaptive outcome situations (e.g., in speed of processing, intellectual ability and executive functions) injury related factors (e.g., severe injury) are found to be more pronounced. [15] Others suggest that severe childhood TBI can be associated with poorer emotion perception, and further with "reduced volume of the posterior corpus callosum, presence of frontal pathology, lower SES [socioeconomic status], and a less-intimate family environment". [13] A parent-reported mTBI study found that children with multiple mTBIs were 2.24 times more likely to have higher levels of anxiety/depression symptoms at the age of six. Aggressive behaviours and internalizing and externalizing behavioral problems were also significant. [19] Complexity and longer recovery period of cognitive symptoms after TBIs were also mentioned. [20, 21] It is stated that with persisting cognitive symptoms and affected community participation, societal and personal burden from mTBIs was larger than anticipated. [22]

There is no consensus on the effect of past concussions (single or multiple) on recovery, or on likelihood of new concussions. [8, 23] For example, O'Connor et al. stated that the cumulative magnitude of head trauma was not related to the likelihood of a new concussion, and also the 'multitude of head traumas' concept had misleadingly presumed the brain as a static structure, incapable of self-repair. [8] On the other hand, a number of case-control studies demonstrated that the percentage of past head traumas was higher in concussion patients compared to demographically matched control subjects with other conditions. [10, 24]

Evaluation of post-concussion clinical sequelae and estimation of the recovery period is clinically challenging. In their systematic review on sports concussions Foley et al. found that immediate recovery for adolescent athletes was somewhat slower compared to older ones; but did not find prolonged recovery for them in the long term (>4 weeks). [25] When Kamins et al. systematically reviewed the physiological outcomes after sports-related concussions, they stated that "physiological dysfunction may outlast current clinical measures of recovery". [26] However, due to varying measurement modalities (e.g., functional MRI, magnetic resonance spectroscopy, cerebral blood flow, electrophysiology, heart rate, exercise, fluid biomarkers) and different time courses, designs and outcomes used in different studies, it was not possible to define a single 'physiological time window' for recovery. [26] Another study, by Xu et al. found that patients with mTBI may experience difficulties in inhibiting 'unwanted actions or interfering information' when they face situations involving response conflicts. [27] In another systematic review, Emery et al. included a study which found an increased prevalence of oppositional defiant disorder (ODD) in adolescents who had sustained a mTBI when they were less than 6 years old. [28] Although the severity of head trauma was not specified, Corrigan et al. found that some patient characteristics were associated with poorer cognitive function at the 9-month follow-up. These were older age, lack of high school diploma, and not being capable of driving pre-injury. [29]

In focusing on sports related concussions, Echemendia et al. concluded that "The dynamic, evolving nature of this injury coupled with a lack of objective biomarkers creates a challenging management issue for the sports medicine team" and they emphasized that the athletes returning to play after a concussion were at higher risk for new brain injuries and called for an 'informed' return to play (RTP) process. [3] However, after an observational study, Grool et al. concluded that early (within a week) participation in physical activity after injury may improve symptom recovery in children and adolescents (e.g., decreased occurrence of persistent postconcussive symptoms). [18] In the evaluation and management of patients with a prior mTBI history and persistent symptoms, the US Veteran Affairs suggests "considering, and offering as appropriate, a primary care, symptom-driven approach." [7]

When mTBI cases are work-related, they strain the worker compensation systems; both with prolonged recovery for the worker and with the increased cost of ongoing health care services use. Kristman et al. found an increase in health care service utilization for accidents, poisoning, violence, nervous system diseases, and mental disorders two years after an mTBI related claim. They also observed an elevated health care usage for comorbidities such as neoplasms, musculoskeletal disorders, and cardiovascular diseases. [30]

With this review we searched for predictive factors that might have an effect on the natural recovery path of concussion/mTBI. We focused on the effect of 'past concussions/mTBIs' on recovery from a recent traumatic brain injury.

Methods

The literature search was conducted on September 24, 2018 on Ovid SP databases (Cochrane Central Register of Controlled Trials <August 2018>, Cochrane Database of Systematic Reviews <2005 to September 19, 2018>, Embase <1974 to 2018 September 21>, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily <1946 to September 21, 2018>)

Search Strategy

[initial OR early OR first OR previous, prior, past , childhood, multiple, repeated, latest, current] **AND** [mild traumatic brain injury/mTBI/concussion/traumatic brain injury]
AND
[(prolonged, delayed, belated, quick, time, period, trajectory) AND recovery]
OR [pre-existing condition]

Our inclusion/exclusion criteria is outlined below.

<u>Included articles</u>

- on mild traumatic brain injuries (mTBIs) and concussions
- on outcomes related with recovery (e.g., neuropsychological, cognitive, return to work, return to sports outcomes)
- on clinical prediction rules
- with at least one year follow up (for primary studies)
- published in English
- published in the last five years
- which are systematic reviews/meta-analysis, observational studies, controlled clinical trials

<u>Excluded articles</u>

- on general traumas
- on pathophysiological mechanisms of concussions/mTBIs
- on treatments/therapies for concussions/mTBIs
- including solely pediatric patients (≤12 years)
- published in languages other than English
- published prior to the last five years
- in the publication formats of single case reports, conference abstracts, narrative reviews, study protocols, letters to editors

Findings:

Out of 20 full text screened Ovid SP search articles, seven were selected for this review. [6, 28, 31-35] Of these, four were systematic reviews of primary studies [28, 32-34] and one was a systematic review of meta-analyses. [35] The remaining two were cohort studies. [6, 31, 36]

In addition, we reviewed three more articles [13, 30, 36] identified through hand-searches. These were noted to be observational studies.

We listed eight more articles as a recommendation, which were outside of our inclusion/exclusion criteria; but thought worthwhile to be highlighted. [15, 24, 37-41]

Selected Articles from Ovid SP Search

From 'miserable minority' to the 'fortunate few': the other end of the mild traumatic brain injury spectrum (De Koning, 2018) [31]

The authors studied a specific group of patients from an observational cohort study (UPFRONT), whom reported zero complaints two weeks after a mild traumatic brain injury (mTBI). This group was only about 10% of the total study population (119 out of 1151) and 49 of them (significantly younger ones) were lost to follow up over a year. The patients were recruited for the UPFRONT study from emergency departments of three trauma centres in the Netherlands and were aged 16 years and older; with a Glasgow Coma Scale score of 13–15, loss of consciousness (<30 minutes) and/or post-traumatic amnesia <24 hours. All patients received questionnaires (on posttraumatic complaints, mood, and other outcomes) at four time points during the follow up period (2 weeks, and 3, 6 and 12 months after the injury). The objective of the study was to find out if this specific group of patients (with zero complaints in the first two weeks after injury) remained asymptomatic throughout the first year after injury. The authors were also interested in secondary outcomes, especially anxiety and depression. Secondly, they were interested in the quality of life of these patients at the end of the 12-month period. There were 30 patients that were asymptomatic from two weeks onward (PnC group), whereas 40 patients developed secondary complaints (SC group). The PnC group was younger and had a higher educational level than the SC group. Compared to the PnC group the SC group developed anxiety and depression at significantly higher rates throughout the year and had lower quality of life at the end of one year following the injury. The authors stated that the high dropout rate was a limitation.

Early predictors of outcome after mild traumatic brain injury (UPFRONT): an observational cohort study (van der Naalt J, 2017) [6]

As part of an observational cohort study (UPFRONT) the authors developed a prognostic model taking into account demographics, injury severity and psychological factors with the aim to identify mTBI patients at risk of incomplete recovery. The study was undertaken in three trauma centre emergency departments in the Netherlands, and included mTBI patients with a Glasgow Coma Scale score of 13-15 and also either with amnesia less than 24 hours or loss of consciousness less than 30 minutes. In a period of two years, 910 mTBI patients with psychological data available at 2-weeks after the head injury were entered in to the study. This data was in addition to the emergency department data (demographics and injury related) collected at the initial visit. Participants were followed up at the 6th month mark and 671 of them were available for data collection. The outcome was measured using Glasgow Outcome Scale Extended (GOSE). They dichotomised the outcome measure as complete (GOSE score=8) or incomplete (GOSE score≤7) recovery. At the end of six months 44% of the participants had incomplete recovery. The authors studied multiple variables in relation to recovery (e.g., age, gender, education, mental health, alcohol use, headache, dizziness, neck pain, anxiety, depression, post-traumatic stress). <u>'Previous TBI' did not make it through the univariate analysis and was not included in the 'emergency department' and 'emergency department-plus' (including the psychological data from 2nd week of injury) multivariate models</u>. The model including 'emergency department' variables only led to a U-shaped association between age and full recovery, with the lowest recovery rates being observed in the age range 40–60. There was also an interaction between age and education (i.e., with higher education, the probability of recovery became more strongly related to age). The 'emergency department-plus' model found that <u>higher depression, post-traumatic complaints, and passive coping style were significantly associated with incomplete recovery</u>. The authors reported that high anxiety levels and use of an avoidant coping style had a protective effect. In the long-term, recovery was not related to age, sex or injury severity; hence, the authors concluded that "<u>measures of emotional distress and coping style had a higher and more specific predictive power for recovery</u>". The authors also noted that the presence of alcohol intoxication during the incident was associated with better outcomes and could be considered as a protective factor that blurs the memory of the traumatic event.

A Systematic Review of Psychiatric, Psychological, and Behavioural Outcomes following Mild Traumatic Brain Injury in Children and Adolescents (Emery, 2016) [28]

Emery et al. studied psychiatric, psychological, and behavioral outcomes following mTBI in children and adolescents. They selected 30 studies for their systematic review; however were not able to undertake a meta-analysis due to diverse methodology and outcome measures used in the primary studies. Included studies were randomized controlled trials, quasi-experiments, cohort studies, case-control studies, or cross-sectional studies that employed a control group. Study subjects were under the age of 19, with a mTBI history (traditional definition being: Glasgow Coma Scale score: 13 to 15, posttraumatic amnesia period: shorter than 24 hours, duration of loss of consciousness: shorter than 30 minutes). The authors grouped the studies based on the psychiatric, psychological, and behavioral outcomes studied (i.e., attention problems and hyperactivity, depression/withdrawal/mood problems, anxiety, oppositional defiant disorder (ODD)/conduct disorder/disruptive behaviours, post-traumatic stress disorder (PTSD), autism/pervasive developmental disorder, schizophrenia, substance abuse). They found some evidence supporting an increased prevalence of psychiatric symptoms, psychological and behavioral problems <u>if the mTBI patient was hospitalized, was younger than 6 years old when mTBI happened, had multiple previous mTBIs, if outcomes were assessed in the early period, outcomes were based on recall, the comparison group was children with no injuries (rather than children with injuries, but not mTBIs)</u>. The authors concluded that "children at risk for longer-term problems are those with multiple previous mTBI or pre-existing psychiatric illness." They also highlighted the limitation of the questionnaire- and score-based measurement (rather than a diagnostic assessment employing interviews) and mentioned limitations with self-report; selection bias with articles in English only, as well as non-randomized recruitment of patients in many primary studies.

Systematic Review of Prognosis and Return to Play After Sport Concussion: Results of the International Collaboration on Mild Traumatic Brain Injury Prognosis (Cancelliere, 2014) [32]

As part of the International Collaboration on Mild Traumatic Brain Injury Prognosis, Cancelliere et al. focused on prognosis and return to play (RTP) after sport concussions. After starting off screening with 77,914 records, they selected 19 cohort studies for their systematic review. Out of these, ten were phase II (extensive exploratory analyses of prognostic factors) and nine were phase I (descriptive or univariate analysis which explored associations between potential prognostic factors and disease outcomes) studies. The authors reported their findings classified in six different outcome variables: cognitive function, postconcussion symptoms, recurrent concussion, return to play (RTP), sport performance, and course and predictors of recovery after sport concussion. The 'history of previous concussion' was explored under the 'cognitive function' section. The selected studies were inconclusive on this matter as <u>three studies found worse cognitive function with history of previous concussion compared to without, and two studies found no difference.</u> Nonetheless, the authors included 'history of a previous concussion' along with being a high school athlete (younger age) or having higher number/duration of postconcussion symptoms when referring to delayed recovery. These three factors, including a previous concussion, seemed to impair cognitive performance of the athletes after a concussion. The authors listed the limitations of their systematic review as lack of level III confirmatory studies, small sample sizes, unknown response rates, improper sample and/or control subject selection (e.g., convenience samples), inconsistency in definitions used, self-report, and recall bias. They concluded that with these limitations and with lack of phase three confirmatory studies they were not able to offer a firm conclusion which might help 'inform evidence-based guidelines' for management of sport concussions and return to play.

Systematic Review of the Prognosis after Mild Traumatic Brain Injury in Adults: Cognitive, Psychiatric, and Mortality Outcomes: Results of the International Collaboration on Mild Traumatic Brain Injury Prognosis (Carroll, 2014) [33]

Carroll et al. undertook a systematic review of studies on cognitive, psychiatric and other objectively assessed outcomes and mortality in none-sports and non-military mild traumatic brain injuries (mTBIs) in adults. Out of 299 relevant publications (RCTs, cohort and case-control studies) 21 were selected; 12 reported on neuropsychological, three on psychiatric (including suicide), three on objectively assessed outcomes (ocular motor, upper limb visuomotor, and health care use), and three on mortality. The authors expanded the 2004 review and best evidence synthesis of the WHO Collaborating Task Force on course of recovery and prognostic factors for mTBI. They used the Scottish Intercollegiate Guidelines Network (SIGN) criteria when evaluating the methodological strength of studies. Even if the definitions used were not consistent and confirmatory studies were missing, the majority of the <u>primary studies pointed to 'presence of initial cognitive deficits' after mTBIs, in the first two weeks. However, there was no consistency about 'persistence' of these deficits</u> (e.g., up to a year to recovery, increase in risk of psychiatric illnesses and suicide). Also, the role of both initial injury severity, and pain or psychological distress in cognitive deficits were uncertain. The evidence for predicting cognitive deficit after mTBI with biological markers was limited; as well as for mTBI being a risk factor for affective/psychotic disorders and suicide. The authors stated there were limitations of this review as it included mostly exploratory phase-1, phase-2 studies, which also did not report on any mTBI-related interventions which might have had an effect on recovery outcomes. They also stated that "Large, confirmatory studies tracking recovery over an extended period of time are needed to reach firm conclusions on usual time to recovery and to identify if any subgroups are at risk for persistent post-MTBI cognitive deficits". Even if the authors reviewed the studies on "whether mTBI is a risk factor for psychiatric illness or mortality", they did not explicitly focus on the effect of prior mTBIs on recovery path for recent mTBIs.

Systematic Review of Self-Reported Prognosis in Adults After Mild Traumatic Brain Injury: Results of the International Collaboration on Mild Traumatic Brain Injury Prognosis (Cassidy, 2014) [34]

This was a systematic review as part of a set of reviews from the International Collaboration on Mild Traumatic Brain Injury Prognosis (ICoMP). Cassidy et al. focused on self-reported prognosis in adults after mTBI. They followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Out of 173 studies they selected 21 with self-reported outcomes on prognosis of mTBI. They included two other original studies by the ICoMP members. In total 23 publications were reviewed. One was a nonrandomized experimental study, one was a phase III study which measured postinjury fatigue as the outcome, and the rest were phase I and phase II cohort studies. The authors reported their findings based on the follow up period; as 1-, 3-, 6-, 12-months, or more than 12 months. Only two of the phase II cohort studies had over a year follow up. One included an uninjured control group and studied prognostic values of S100B36 and apolipoprotein E (APOE) ε4 genotypes. The mTBI cases with APOE ε4 experienced postinjury fatigue more commonly compared to the ones without. The second study compared students with 'diagnosis threat' (knowing what they were being tested for) scenario to 'neutral' (not knowing what they were being tested for) scenario. Results from this study suggested that expectations influenced self-reported cognitive and memory results. The authors of the review stated that at acute stages of injuries, self-reported symptoms (e.g., headache, fatigue, self-perceived cognitive deficits and other so-called postconcussion symptoms) were common; however, these were not specific to mTBI. In terms of clinical prediction rules, the authors cited the one described by Stulemeijer et al., "absence of comorbid physical problems, low levels of early posttraumatic symptoms, and low levels of early posttraumatic stress". This particular set of factors was able to predict a good outcome at 6 months with a probability of 90%. The authors stated the limitations of their systematic review. They referred to weak and heterogeneous primary studies (e.g., only one phase

III study) and limited number of prognostic studies (generally, not taking into account the confounding effects of various treatments on prognosis). The authors concluded that symptoms defined as 'postconcussion symptoms' are not specific to mTBI and may occur following other traumas (not involving the head) as well. They also concluded that psychosocial determinants of recovery are important, and more intervention research focusing on modifiable prognostic factors are needed. In addition, they called for more studies on clinical prediction rules.

The Neuropsychological Outcomes of Concussion: A Systematic Review of Meta-Analyses on the Cognitive Sequelae of Mild Traumatic Brain Injury (Karr, 2014) [35]

The authors undertook a systematic review of past meta-analyses to assess neuropsychological outcomes of mTBI. They aimed to identify an overall cognitive effect, as well as potential variables that may modify the cognitive effects. They chose to use a qualitative approach in synthesizing these meta-analyses; as some original/primary studies were repeatedly used in multiple meta analyses, and the statistical approach was not consistent in all (e.g., random vs. fixed effects models, metaregression, categorizing the effects or not, and varying significance tests for estimates). The authors selected 11 meta-analyses for their review. None of these included a list of excluded studies or explored confounding/moderator factors (e.g., the mechanism of mTBI, physical fitness and willingness to return to play, gender, time since injury, past head injuries; and interactions between factors, such as gender by cognitive domain, education by time since injury). Other methodological shortcomings were inadequate clinical definitions of mTBI, merely self-report, sampling bias, and lack of exploration/reporting of publication bias. This systematic review of meta-analyses touched upon 'cognitive domain', 'cumulative effects', 'time since injury', and 'persistent postacute symptoms' in relation to mTBIs. In the cognitive domain, the highest quality systematic review found strongest effects for 'fluency' and 'delayed memory'. The cumulative effects domain included mixed results, potentially pointing to more worrisome cognitive outcomes, especially in 'delayed memory'. The authors also referred to the relation between head injury in sports and neurodegeneration. Time since injury and recovery had mixed results. In general, the first 90 days after injury was treated as the acute phase and after that, it was considered the postacute phase. Recovery appeared to be quick in the acute phase of injury (by 7 days postinjury in sports related mTBIs) and full cognitive recovery expected after 90 days. When the 'time since injury' was treated as a continuum, some studies demonstrated that cognitive recovery improved by time across the acute phase (<90 days post-mTBI); however, did not hold through the postacute phase. The authors were not able to locate good quality meta-analyses on ‘persistent postacute symptoms’. However, they stated that the subgroup of mTBI patients with longlasting impairment usually presented with “a higher likelihood of having a past brain injury, neurological or psychiatric problem, or injury related to a motor vehicle accident”. They also highlighted the potential higher compensation-seeking behaviour in the persistent symptoms subgroup. The authors found that “the overall effect of mTBI ranged across meta-analyses (i.e., [Hedge’s] g=.07 to [Cohen’s] d= .61 for mixed-mechanism mTBI and d= .40 to g= .81 for sports-related mTBI)”. They pointed to moderating variables such as ‘cognitive domain’ and ‘time since injury’ possibly to account for the heterogeneity observed in outcomes.

Additional Articles – Reviewed

Health Care Utilization of Workers’ Compensation Claimants Associated With Mild Traumatic Brain Injury: A Historical Population-Based Cohort Study of Workers Injured in 1997-1998 (Kristman, 2014) [30]

Kristman et al. conducted a hypothesis-generating study of 907 workers who initiated an incident loss-time mTBI claim with the Ontario Workplace Safety and Insurance Board (WSIB) in 1997 and 1998. The cases were defined based on the ‘part of body’ and ‘nature of injury’ codes. After constructing the historical cohort from the WSIB administrative data, they linked it (first name, last name, date of birth and sex) with the Ontario Health Insurance Plan (OHIP) data, also including the period one year before and two years after the incident mTBI WSIB claim. Health care utilization was determined using the services reimbursed by OHIP for any consultation with a health care provider. The authors first assessed if their sample was representative of all WSIB mTBI claimants. They compared age, sex, and cumulative duration of WSIB benefits for 728 workers with data linkage and 179 without. They found that there were more female claimants in the group without data linkage. Health care utilization rates were computed using 7-day moving averages for health care services per 1000 claimants per day (not only mTBI related services, but all health care services). Throughout the year preceding the incident claim the mean cumulative rate for health care utilization was 67.6 services/1000 claimants per day. The rate peeked in the period following the incident and stayed higher thought the first year postclaim (average of 99.2 services/1000 claimants per day). During the second year of the study, the health care utilization rate by the study cohort remained 11% higher than the pre-claim utilization rate. Services related to diseases of the nervous system and accidents remained higher through the second year of follow-up compared to the pre-claim year, and there was a continued increase in services for neoplasms and mental disorders. The authors concluded that "workers' compensation claims involving MTBI are associated with a long-term increase in health care utilization". They suggested that the overall increase in health care utilization (e.g., in microbiology, internal medicine, neurology and diagnostic radiology) was generally related to accidents, poisoning, violence, diseases of the nervous system, and mental disorders, as well as with other comorbidities (e.g., neoplasms, musculoskeletal disorders, and diseases of the circulatory system). They suggested that this might be due to increased contact with health care services initiated by the WSIB mTBI claim.

Predictors of Very-Long-Term Sociocognitive Function after Pediatric Traumatic Brain Injury: Evidence for the Vulnerability of the Immature ''Social Brain'' (Ryan, 2014) [13]

The authors studied a sample of 34 young adults who had survived early-childhood TBI and compared their 'emotion perception' (EP) with a group of 16 healthy peers (who had a typical development). Originally recruited from consecutive admissions to an emergency department immediately after a TBI, the sample was followed-up and was revisited at year 16. The group included eight mild, 16 moderate and 10 severe TBI patients and the mean age for the 34 study subjects was 20.62 years. They were compared to the group of 16 age-, gender- and socioeconomic status-matched controls based on recognition and interpretation of facial and prosodic emotional cues dependant tasks. The authors studied sociocognitive capacity with the outcomes of emotion perception (i.e., affect naming, prosody-face matching, prosody-pair matching), intelligence quotient, and general cognitive abilities. The initial neuropsychological and psychiatric assessments were conducted by a qualified child psychologist during the follow up period. The Advanced Clinical Solutions (ACS) Social Perception subtest 40 was administered. The accuracy of TBI survivors in labeling and interpreting emotion cues that were incongruent with the semantic meaning of the statement was significantly reduced compared to the control group (effect size (d)= 0.72). However, when studying the injury severity subgroups they found no significant difference between the mild-to-moderate TBI group and controls for the three outcome variables (naming, prosody-face matching, and emotion perception total). The authors concluded that "severe childhood TBI may disrupt interregional connectivity and thus interfere with the functional refinement of areas within the distributed social brain network" and that in their study sample emotion perception was associated with injury-related risk factors (e.g., injury severity, posterior CC volume, and frontal pathology) and environmental factors (SES and family intimacy – resilience resources for the recovery from an early-childhood TBI.

Prior history of traumatic brain injury among persons in the Traumatic Brain Injury Model Systems National Database (Corrigan, 2013) [36]

The authors conducted a secondary data analysis using the TBI [traumatic brain injury] Model System data to examine the effect of prior traumatic brain injuries on the latest (index) injury sequelae. They expected that early childhood injuries would lead to worse post-Index injury outcomes. The data included information on demographic, preinjury, injury, and acute care rehabilitation characteristics of 4464 participants. Eighty percent of the pre-Index TBI were mild TBIs. The participants (or their proxies) were available to be interviewed on any of the following time points (1, 2, 5, 10, 15, or 20 years). The follow up outcomes were functional capacity, depression, anxiety, drug and alcohol abuse as measured using the Functional Independence Measure (FIM), Generalized Anxiety Disorder 7-Item Scale (GAD-7), Glasgow Outcome Score-Extended (GOS-E), Patient Health Questionnaire-9 (PHQ-9). The authors compared the pre-Index TBI group with the group without a TBI (reference group). They used Cohen d for examining mean differences and Cohen h for comparing proportions. They found that previous head injury affected the anxiety and depression scores after the index-TBI, and the age at pre-Index TBI was also important. The largest (substantial) effects were observed in the group with first injury occurring between 6 and 10 years of age. Problematic alcohol and/or drug use after Index TBI was around 33% for the ones with previous head trauma, whereas it was around 19% for the group without one. The ones who were younger age at their first head injury demonstrated more problems with substance abuse both before and after the Index-TBI. The authors suggested that post-Index TBI depression, anxiety and substance abuse displayed large and consistent associations (also showed dose-response and temporal relations) with pre-Index TBIs. Interestingly, with regards to severity of Index-TBI and attached rehabilitation and functional scores, the authors found that patients with pre-Index TBIs had less severe Index TBIs, and displayed higher levels of function both entering and leaving rehabilitation than those without a pre-Index injury. The authors concluded that <u>pre-Index TBIs were frequent (i.e., 20% in their study sample) and were significantly associated with Index injury rehabilitation response and post-Index injury outcomes; especially presenting important associations with anxiety, depression, substance misuse.</u> They emphasized that "relations observed between early life TBIs and adult consequences underscore the necessity for eliminating discontinuities between pediatric and adult TBI research."

Additional Articles – Recommended

- 10 years outcome from childhood traumatic brain injury (Anderson, 2012) [15]
- Prognosis for mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on mild traumatic brain injury (Carroll, 2004) [37]
- Reduced processing speed in rugby union players reporting three or more previous concussions (Gardner, 2010) [38]
- Cumulative effects associated with recurrent concussion in collegiate football players – The NCAA Concussion Study (Guskiewicz, 2003) [39]
- Clinical, cognitive, and genetic predictors of change in job status following traumatic brain injury in a military population (Han, 2009) [40]
- Impact of prior concussions on health-related quality of life in collegiate athletes (Kuehl, 2010) [41]
- Concussion history predicts self-reported symptoms before and following a concussive event (Bruce, 2004) [24]
- Childhood head injury and expression of schizophrenia in multiply affected families (AbdelMalik, 2003)[42]

Summary

- There is a limited number of studies on predictive factors affecting the natural recovery path from concussion/mTBI
- Quality research studying past head trauma(s) as a predictive factor for recovery from a current concussion/mTBI are few
- Technologically captured brain changes (e.g., using advanced imaging technologies) following repeated head traumas need to be studied closely to determine vulnerability, resiliency and clinical significance.
- Studying any possible association between the pathophysiology of concussion/mTBI and future risk of chronic cognitive or degenerative brain diseases is difficult, as it requires lengthy follow-up with prospective, longitudinal study design, which is inherently expensive
- In concussions, physiological recovery may take longer than clinical symptom recovery. Therefore, it will be important to develop physiological parameters and study their potential relationship with repeat concussions or prolonged/severe clinical symptoms.
- Currently, there are no standard biomarkers available to measure bio-physiological dysfunction in humans after concussion
- Concussion/mTBI is diagnosed clinically. However, there is no complete consensus on its clinical definition, nor that of 'full recovery' from concussion.
- Small sample sizes, lack of control groups, niche study populations, and a scarce number of longitudinal cohort studies limit the generalizability of the findings to larger populations that might be at risk
- In most concussion/mTBI studies, concurrent or pre-existing conditions (e.g., psychological distress, musculoskeletal injury), medications, pre-injury characteristics have not been studied
- Concussion/mTBI management should be individualized; because pre-concussion risk factors (individual characteristics), injury related factors, as well as post-concussion individual clinical response vary from person to person
- Longitudinal studies are important to assess subclinical findings overtime and to watch for clinical significance with ageing in terms of repeated head traumas, new musculoskeletal injuries, prolonged recovery, cognitive impairment or neurodegenerative conditions

Conclusion

Concussion diagnosis and clinical management requires a multidisciplinary, but individualized approach. Personal biopsychosocial characteristics, risk factors, injury characteristics, and medical interventions all play a role in the patient's recovery. Even if most clinical symptoms resolve over time, cognitive symptoms can become persistent and may have an impact on future psychosocial wellbeing of the individual.

Identifying predictive factors for an unfavorable concussion recovery would help streamline clinical management and enhance patient care. Researchers are actively exploring factors potentially affecting postconcussion sequelae and concussion recovery.

Past/multiple/repeated concussions are one of the factors explored by many researchers. The current literature is inconclusive on the relationship between multiple/repeated concussions and an extended recovery time. Younger age during past concussions, severity of the head injury, hospitalization, emotional distress and coping style are also explored. However, for any conclusive statement prospective confirmatory studies on 'recovery' with long-term follow up are needed.

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Appendix 1

WorkSafeBC - Evidence-Based Practice Group Levels of Evidence

(adapted from 1,2,3,4)

1	Evidence from at least 1 properly randomized controlled trial (RCT) or systematic review of RCTs.
2	Evidence from well-designed controlled trials without randomization or systematic reviews of observational studies.
3	Evidence from well-designed cohort or case-control analytic studies, preferably from more than 1 centre or research group.
4	Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled
5	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

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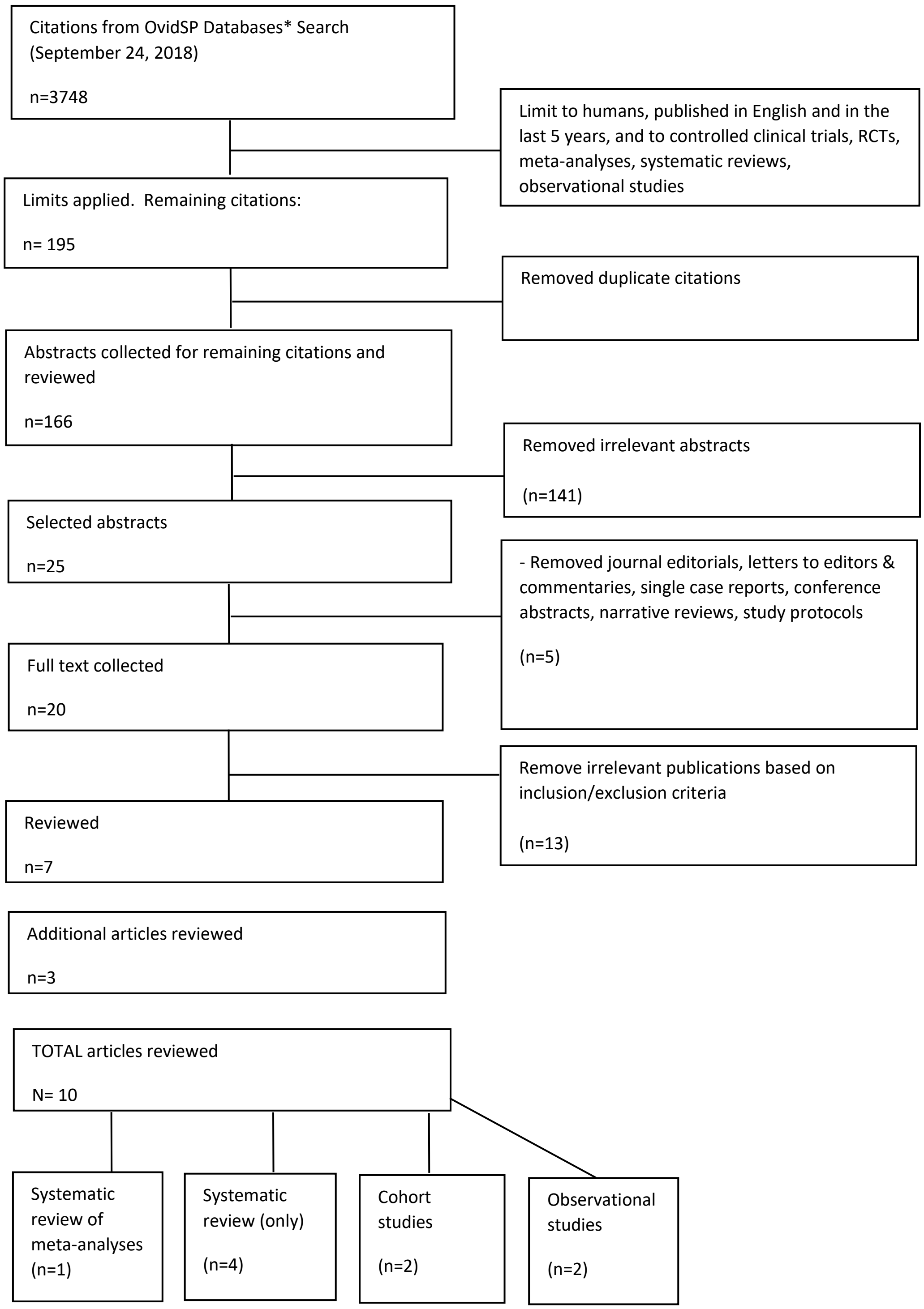
Appendix 2
List of Abbreviations

ACEs	Adverse Childhood Events
APOE	Apolipoprotein E
CI	Confidence Interval
CTE	Chronic Traumatic Encepholopathy
CNS	Central Nervous System
FIM	Functional Independence Measure
GAD	Generalized Anxiety Disorder
GOS	Glasgow Outcome Score
HR	Hazard Ratio
ICoMP	International Collaboration on Mild Traumatic Brain Injury Prognosis
LOC	Loss of Consciousness
mTBI	Mild traumatic brain injury
NDD	Neurodegenerative disease
ODD	Oppositional defiant disorder
OR	Odds Ratio
PHQ	Patient Health Questionnaire
PTA	Post-traumatic amnesia
PTSD	Posttraumatic Stress Disorder
RTP	Return to play
RTW	Return to Work
TBI	Traumatic brain injury

Appendix 3
Flow Chart (Study Selection)



* ***OvidSP Databases searched:*** *Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, EMBASE, MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, and MEDLINE Daily Update*