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Bachelor of Science in Medicine Degree Program
End of Term Final Report

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Date: 08/04/17

Project Title: Neurocognitive changes in student athletes with and without a concussion.

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Summary (250 words max single spaced):

Background: Approximately half of all emergency department visits for concussions occur in a sport setting. ImPACT is increasingly used in concussed student athletes and professionals to measure neurocognitive changes post-concussion.

Objective: Systematically review the literature to summarize ImPACT neurocognitive findings in sport-concussed student (pediatric- and collegiate-aged) athletes and determine in healthy athletes both the proportion of below normal scores at baseline, and reliable changes on ImPACT after a season of hockey.

Materials and Methods: A systematic review of the literature identified studies that incorporated ImPACT testing on pediatric- and collegiate-aged physician-diagnosed concussed athletes. Results were summarized narratively. Additionally, a prospective cohort study of players from two female Midget hockey teams was conducted and ImPACT was administered pre-season and post-season.

Results: Overall, 11 articles were included in the systematic review, of which 3 included pediatric-aged athletes only, 7 included collegiate-aged athletes only, and 1 included both. Data is provided on ImPACT scores over time, the proportion of athletes showing reliable changes over time, correlation analyses with ImPACT, and potential neurocognitive predictors. Within the cohort study, base rates for low performance pre-season in healthy female athletes ranged from 4-12%, while 67% of healthy athletes showed at least one-reliable change in ImPACT composites scores after one season of hockey.

Conclusions: The majority of studies in the review and the prospective study noted some change in ImPACT scores but substantial clinical and methodological heterogeneity precluded making generalized conclusions. ✚

Student Signature

Primary Supervisor Signature

MD/PHD   MD/MSc.   BSc. (MED)   MED II Research Program

Joe Doupe Annual Event   Undergraduate Medical Student Research Symposium
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Introduction and Background

Concussion Definition and Epidemiology

Concussions have been defined within the most recent concussion in sport consensus statement as a "traumatic brain injury induced by biomechanical forces" (1) to the head, face, or neck, or from a transmitted force to the head from a sustained blow elsewhere on the body (2). In the literature, the definition of concussion is often inconsistent, and concussion and mild traumatic brain injury (mTBI) are frequently used interchangeably (1-3). A concussion is part of the spectrum of traumatic brain injuries and results in functional deficits (2), while mTBI can also include structural injuries (4,5). Roughly half of all concussion-related emergency department visits in the United States occur in a sport setting (6), with a yearly incidence rate between 1.6 and 3.8 million (7). The incidence of concussion is likely highest in those participating in contact sports (8-11). Additionally, certain athletic positions are associated with an increased risk of sustaining concussions (12,13), such as linebackers in American football (13).

Concussion Symptoms, Outcomes, Management

Commonly reported symptoms immediately following concussion span multiple domains (cognitive, somatic, emotional, sleep disturbances) (2) and include headaches, dizziness/unsteadiness, difficulty concentrating, confusion/disorientation (9,13) and visual disturbance/sensitivity to light (9). The presence of mediating factors, such as age, sex, or concussion history can extend the time to symptom resolution (2,8,13). Initial symptom severity (10) may also prolong recovery. In youth, most symptoms resolve within four weeks (2,9,14-17), but some youth may still be symptomatic longer, particularly if they have pre-existing comorbidities (e.g., mental health difficulties, migraine headaches) (1).

Within the return-to-play (RTP) rehabilitation strategy, neuropsychological assessment has been described as an integral part in sport-related concussion management for select individuals (1). Neuropsychological testing can objectively evaluate concussed individuals for cognitive deficits. Neuropsychologists have the specific educational and clinical expertise (1,18) to assess cognitive and emotional consequences of concussion (18). Various cognitive domains, such as memory, attention, language, and executive function, can be objectively measured to diagnose a concussion and measure recovery (1,2). This can assist in return to play decision making (1), but cognitive and symptom recoveries do not always occur simultaneously (8,19). A multifaceted objective and subjective assessment battery, including computerized and pencil-and-paper neurocognitive testing, postural testing, and symptom reporting is most sensitive to concussion consequences (20,21). The goal of RTP rehabilitation is to return athletes to full physical and cognitive activity without symptom exacerbation (1,2).

Neuropsychological Outcomes Post-concussion

Many individuals who sustain a sports-related concussion experience neuropsychological deficits in the acute period, with no long-term continuation (8,14,22-24). However, patients who suffered from mTBI were found to have more post-concussive symptoms years later compared to age- and sex-matched controls (25). Additionally, mTBI individuals had significant impairments in episodic memory (acquisition and consolidation, retention and recognition), working memory, attention, and executive functions (e.g. word fluency) when compared to healthy controls 6 years post injury (3). Furthermore, ~33% of individuals with mTBI had mild dysfunction in memory and attention 3 months after sustaining the injury (26). Thus, individuals with concussions/mTBI could be left with long-term implications.

The Immediate Post-concussion Assessment and Cognitive Test (ImPACT) is a clinical software program designed to measure several cognitive functioning domains, including attention span, working memory, reaction time, verbal and visual memory, response variability,

and non-verbal problem solving (27). Demographics and current symptoms are also collected within the software program (27). The test contains six modules (Word Discrimination, Design Memory, X's and O's, Symbol Matching, Color Matching, and Three Letters), where scores within modules contribute to five summary or composite scores, including Verbal Memory, Visual Memory, Visual Motor Speed (or Processing Speed), Reaction Time, and Impulse Control (27). The program contains reliable change index (RCI) calculations to detect changes in composite scores that exceed a predefined 80% confidence interval (CI) around baseline or normative scores while reducing measurement error effects. The RCI is a statistic used to determine if a change seen in an individual's score is statistically significant based on ImPACT's test re-test reliability. If an individual's post-season score falls outside the 80% CI of expected change due to normal variation, the ImPACT clinical report will identify the athlete as having shown a reliable change in score. Higher scores are better in Verbal Memory, Visual Memory, and Visual Motor Speed while lower scores are superior in Reaction Time and Impulse Control (27). With increased use of ImPACT in interscholastic, collegiate, and professional settings for pre-season baseline and post-concussion management (28,29), it is important to investigative this computerized neurocognitive test in pediatric- and collegiate-aged athletes.

Project A: Systematic Review
Objective
The objective was to systematically review the literature to summarize ImPACT neurocognitive findings in sport-concussed student (pediatric- and collegiate-aged) athletes.

Materials and Methods
Data Sources and Search
The PRISMA guidelines were used (30). Searches were conducted from database inception until July 8-11, 2016, using a combination of appropriate subject headings and text words. Relevant studies were identified from Ovid MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), SPORTDiscus and PsycINFO and were limited to English. Search terms included brain concussion, brain injuries, sport injuries, neuropsychological tests, and Immediate Post-concussion Assessment and Cognitive Testing. The full search strategies are available upon request. No hand-searching was conducted; however, the reference lists of articles that subsequently met the inclusion criteria were reviewed. An update of the exact searches was completed June 20-21, 2017. Duplicate results from the database searches were identified using the Bramer method (31).

Study Selection
The following inclusion criteria was used: 1) The study design must be primary research (randomized control trial, cohort study, case-control study, cross-sectional study), 2) Participants must have sustained a sport-related concussion or sport-related mTBI, 3) The concussion or mTBI must have been diagnosed by a physician, 4) The study must include data for one or more ImPACT composite scores (Verbal Memory, Visual Memory, Reaction Time, Processing Speed or Visual Motor Speed, and/or Impulse Control but excluding the subjective symptom rating scale), and 5) The study population included student athletes who were pediatric (younger than 19 years old) or collegiate/university-aged athletes. Studies must have met all five of the inclusion criteria. Studies were excluded if they were 1) Not available in English, 2) The study did not report ImPACT data, 3) The severity of the brain injury was not reported, 4) The patient sustained a moderate or severe traumatic brain injury, 5) The patient sustained a traumatic brain injury or concussion with positive neuroimaging findings, or 6) The study design was a case-series. Two reviewers independently screened titles and abstracts to identify potentially relevant articles to review. Subsequently, full articles were obtained, and each reviewer independently applied the above inclusion criteria. Discrepancies were resolved through consensus.

Data Extraction and Analysis

A structured extraction form was used for data extraction (available upon request). Relevant data included study design, recruitment method, participant characteristics (total number of participants, age, sex, number of concussions assessed), setting (inpatient or outpatient), diagnosis and diagnostic criteria used for defining the concussion or mTBI, inclusion and exclusion criteria, study duration, co-morbidities of study participants, neuropsychological tests used and assessment time points, the comparison group, neuropsychological predictors assessed, and assessment method (computerized or pencil and paper assessed in person, over the phone or through the mail). In addition, neuropsychological outcomes, group or individual administration of ImPACT, training of the individual interpreting ImPACT results, results of each ImPACT composite (p-values), and statistical methods used for each reported outcome were also extracted. The authors' conclusions about the ImPACT data were extracted as well. Data extraction was performed by one individual, and reviewed by a second for accuracy and completeness. Due to the heterogeneity of study designs, post-concussion assessment time points, and age of participants, a meta-analysis was not performed. Results of the systematic review are presented narratively.

Results

Identification of Studies

The search process yielded 1915 studies, with 608 duplicates. Overall, 55 articles were found by searching through systematic review articles identified during the initial search process, and 1 article was found by searching the references lists of the included articles. With duplicates removed, 1363 articles were assessed for relevance. Of the 1363 studies, 1013 were excluded during the initial screen. Overall, 350 full-text manuscripts were appraised for eligibility based on the above-defined inclusion/exclusion criteria and 11 studies were included (20,21,32-38). Reasons for exclusion were inappropriate study design (n=52), did not include a sport-related concussion or sport-related mTBI (n=72), concussion diagnosis was not made by a physician (n=174), no ImPACT result data (n=29), and not pediatric or collegiate-aged student population (n=9). Additionally, 3 articles could not be retrieved in a timely fashion to be assessed.

*Study Characteristics [Please see **Table I**]*

Of the studies included, 3 studies included pediatric-aged ($\leq$ 19 years) student athletes, 7 included collegiate-aged athletes, and one included middle school- to college-aged participants. Studies were published between 2007-2016, 10 of which were conducted in the USA and one was conducted in Canada. Study designs included six prospective cohort studies, one retrospective chart review with follow-up, one retrospective analysis, two retrospective cohort studies, and one cross-sectional study. The number of participants recruited into the studies ranged from 21 to 618, while the number of participants with ImPACT data ranged from 20 to 545. The proportion of male athletes ranged from 52 -100%.

*Synthesis of Results [Please see **Table II**]*
Pediatric-aged Athletes:

In a retrospective chart analysis with follow-up, an aim was to determine if impairment on ImPACT in adolescent athletes ($\leq$19 years old) existed once athletes were deemed asymptomatic on Sideline Concussion Assessment Tool 2, and if so, was neurocognitive impairment correlated with problems returning to school (35). Authors found 16 (41%) of 39 individuals who completed telephone follow-up demonstrated one ImPACT composite score in borderline range when asymptomatic before undergoing the Zurich RTP stepwise recovery progression. Borderline was defined as ImPACT scores less than the 9th percentile compared to national age group standards. When adolescents and parents were followed-up two months

after starting the RTP progression, authors found no correlation between ImPACT composite scores and difficulty in school (P > 0.05).

Post-traumatic migraine (PTM) during the first week postinjury was investigated to determine if it predicted neurocognitive impairment on ImPACT (36). In this prospective cohort study, high school male football players (<19 years old) were assessed at baseline, 1-7 days postinjury and 8-14 days postinjury. Results were stratified based on self-reported headache symptoms experienced within the first week of injury. Performance from baseline in the PTM group (headache, nausea, and photosensitivity or phonosensitiviy) was compared to headache only and no headache groups. For Visual Memory (P=0.002) and Reaction Time (P=0.001), the PTM group performed significantly worse at both 1-7 and 8-14 days post-concussion when compared to the headache and no headache groups. The PTM group scored worse on Verbal Memory (P=0.02) compared to headache only group when assessed at 8-14 days post-concussion. No differences were seen in Processing Speed between groups. Verbal Memory (P=0.001), Visual Memory (P=0.001), Processing Speed (P=0.001), and Reaction Time (P=0.001) all showed main effects for time when not stratified by headache status: all ImPACT composite scores at 1-7 days post-concussion were lower than baseline and scores at 8-14 days post-concussion were higher than 1-7 days scores. Verbal and Visual Memory composites scores remained below baseline at 8-14 days after concussion.

A chart review of 545 concussed athletes (<18 years old) was completed to correlate neurocognitive function on ImPACT with self-reported sleep quantity and sleep disturbance symptoms (37). Athletes were grouped based on self-reported sleep quantity: short (<7 hours), intermediate (7-9 hours), or long (>9 hours), and self-reported sleep disturbance symptoms (trouble falling asleep, sleeping less than normal, sleeping more than normal, or no sleep disturbance). Up to three ImPACT testing sessions were conducted when the treating physician required ImPACT results to inform clinical management and not at a priori, systematic time assessment points. They found individuals with long durations of sleep had worse scores on the Visual Motor Speed (Test 1; P<0.001) compared to short and intermediate duration groups. The long duration group scored worse on Reaction Time (Test 1; P=0.04) when compared to the short duration group. Long duration group had worse scores on the Visual Memory (Test 2; P=0.01) compared to other sleep duration groups. There were no significant differences between groups on ImPACT composites during the third testing session.

Those who endorsed self-reported sleep disturbance symptoms showed significantly worse results in one or more composite scores on ImPACT (Test 1 and Test 2) when compared to the no sleep disturbance cohort (37). Individuals who reported trouble falling asleep scored worse on Verbal Memory (Test 1, P=0.01; Test 2, P=0.01) and Visual Memory (Test 2, P=0.03), individuals who self-reported sleeping less than normal had worse performance on Visual Memory (Test 1, P=0.04) and Reaction Time (Test 2, P=0.02), and athletes who reported sleeping more than normal scored worse on Verbal Memory (Test 1, P<0.001; Test 2, P<0.001), Visual Memory (Test 2; P<0.001), Visual Motor Speed (Test 1, P=0.05; Test 2, P<0.001) and Reaction Time (Test 1, P=0.01; Test 2, P=0.01). No differences were seen between sleep disturbance groups on the third ImPACT test.

Collegiate-aged Athletes:
In university athletes, neurocognitive testing was administered preseason and within 24 hours of concussion to compare sensitivities of multiple concussion assessment tools, including ImPACT (20). Impairments identified by ImPACT were considered significant if changes in composite scores exceeded the baseline composite scores RCI 80% CI. They found 15 (63%) of 24 athletes had one or more impairments in ImPACT composite scores. Of the athletes who

completed ImPACT, 10 (42%) were impaired on Verbal Memory, 5 (21%) on Visual Memory, 5 (21%) on Visual Motor Speed, 10 (42%) on Reaction Time, and 1 (4%) on Impulse Control.

The incidence of neurocognitive impairment on ImPACT was evaluated in 21 sport-concussed athletes no longer reporting concussion symptoms (19). ImPACT was administered at several time points, including pre-season baseline, within 72 hours of injury, and when the athlete self-reported being asymptomatic. Impairments in ImPACT composite scores were identified by RCI calculations embedded within ImPACT comparing post-concussion scores to baseline. They found 15 (71%) of 21 concussed athletes had impairments on one or more ImPACT summary scores within 72 hours postinjury. Specifically, 7 (33%) athletes were impaired on Verbal Memory, 8 (38%) on Visual Memory, 5 (24%) on Visual Motor Speed, and 9 (43%) on Reaction Time. Furthermore, it was found 38% of athletes were impaired on at least one ImPACT composite score when athletes reported being asymptomatic, with 1 (5%) athlete found to have impairment on Verbal Memory, 2 (10%) on Visual Memory, 3 (14%) on Visual Motor Speed, and 4 (19%) on Reaction Time.

In a retrospective assessment of concussed athletes, 32 individuals received ImPACT testing at baseline and within 48 hours postinjury (21). The authors found 22 (69%) of 32 concussed athletes demonstrated significant declines in cognitive function on ImPACT using RCI calculations. In a correlation analysis between ImPACT change scores and cognitive symptoms, significant associations (P<0.05) between "feeling mentally foggy" and a change in Reaction Time, "difficulty concentrating" and a change in Verbal Memory, and "difficulty remembering" and changes in Verbal Memory and Reaction Time were identified.

In a study examining the effectiveness of cognitive and physical rest, 50 athletes were evaluated with ImPACT (33). Half of the athletes were prescribed one additional day of physical and cognitive rest after sustaining a concussion and 25 athletes were not given an additional rest day. ImPACT was administered at baseline and one day after concussion diagnosis, with re-administration every 2 or 3 days until baseline values were met or exceeded. There was no difference (P=0.395) in mean (SD) time to achieve baseline scores on any ImPACT composite scores when comparing the rest and no-rest groups (5.7 (5.0) days and 7.1 (6.3) days, respectively). However, the no-rest group had a significantly lower Visual Memory score (P=0.026) compared to the rest group one day after injury. When one day postinjury ImPACT scores were compared to baseline, all 4 composite scores (Verbal Memory, Visual Memory, Processing Speed, Reaction Time) of ImPACT were lower in the no-rest group, while the rest group only showed reductions in Reaction Time; however, significance was not reported.

Sex differences in 41 male and 38 female concussed athletes were investigated in a prospective cohort study (34). ImPACT was given at baseline, within 3 days of injury, and 7-10 days post-concussion. A significant decline in ImPACT scores was noted postinjury (P=0.0001), with worse performance within 3 days post-concussion and 7-10 days post-injury compared to baseline. The authors found no between-subject effect of sex (P=0.69) or a significant interaction between sex and time (P=0.59). Based on a proposed formula by Jacobson and Traux, RCI calculations identified 58% of athletes had one and 27% of athletes had two reliable declines or increases in symptom reporting up to 3 days postinjury compared to baseline. At 7-10 days postinjury, 32% had one and 8% had two reliable declines in composite scores or increase in symptom reporting. No sex differences were seen in the percentage of athletes showing one or more reliable declines 3 days postinjury and 7-10 days postinjury.

A Canadian prospective study of university athletes during one hockey season included ImPACT testing (39). Approximately 45 male and female university hockey players underwent

ImPACT testing pre-season, along with 72 hours, 2 weeks, 2 months post-concussion, and post-season. The actual number of athletes recruited was unclear. Pre-season and post-season ImPACT scores showed no significant interaction effects between concussion or time variables; however, the significance of this conclusion was not stated. Among the postinjury ImPACT scores, multivariate analysis was not significant (P>0.05); thus ImPACT composite scores did not change significantly post-concussion when compared to pre-season.

In a prospective cohort study, ImPACT was provided to 20 athletes pre-season and within 24 hours following mTBI (38). Authors found significant worsening in Verbal Memory (P=0.04), Visual Memory (P<0.01), and Reaction Time (P=0.02) following an mTBI. Visual Motor Speed and Impulse Control did not significantly change after mTBI (P>0.05).

Pediatric- and Collegiate-aged Athletes:
One retrospective study including concussed middle school- to collegiate-aged athletes compared ImPACT composite scores based on helmet status (32). Both the helmeted and non-helmeted groups (n=69 in each) completed ImPACT testing at baseline and within 10 days post-concussion. Mean ImPACT composite scores post-concussion and change from baseline scores did not significantly differ between the helmeted and non-helmeted groups (P>0.05). Twenty-two (31.9%) helmeted and 21 (30.4%) non-helmeted athletes showed change in Verbal Memory, 20 (29.0%) helmeted and 13 (18.8%) non-helmeted in Visual Memory, 15 (21.7%) helmeted and 12 (17.4%) non-helmeted athletes in Visual Motor Speed, and 21 (30.4%) helmeted and 11 (15.9%) non-helmeted in Reaction Time. No group differences were seen in the number of athletes showing one or more (68.1% in helmeted, 55.1% in non-helmeted), two or more (36.2% in helmeted, 30.4% in non-helmeted), or mean (SD) number (1.5 (1.5) for helmeted, 1.1 (1.4) for non-helmeted) of reliable changes on ImPACT composite scores (P>0.05).

Discussion
ImPACT scores over time:
Six articles were found to report changes in ImPACT scores in the post-concussion time period in pediatric- or collegiate-aged athletes (33-36,38,39). Two articles reported on ImPACT changes over time in a pediatric population. One study found a significant proportion (41%) of athletes who described themselves as asymptomatic were found to have ImPACT composite scores below the 9th percentile (35). Another another study found four ImPACT composite scores (Verbal Memory, Visual Memory, Processing Speed, and Reaction Time) were worse within a week of concussion (36). By two weeks post-concussion, Processing Speed and Reaction Time had returned to baseline limits, while Visual and Verbal Memory remained below baseline levels (36).

Four articles looked at collegiate-aged athletes and reported on changes in ImPACT scores in the post-concussion time period. One article found impairment in Verbal Memory, Visual Memory, and Reaction Time 24 hours after concussion (38). These three composite scores and Processing Speed were reportedly impaired during the same time period in a cohort of athletes who received no physical or cognitive rest, while only Reaction Time was impaired in a cohort who received a day of rest prior to testing; however, the significance of these declines was not reported (33). Another study found ImPACT performance remained below baseline up to 10 days after concussion (34). In terms of ImPACT performance pre-season and post-season in concussed athletes, one study found no significant difference between scores; however, no level of significance was reported (39).

Percentages of athletes showing change in ImPACT performance (identified by RCI):

Five articles included within the systematic review were found to use RCI calculations to identify significant changes in ImPACT performance (19-21,32,34). In four articles, collegiate-aged athletes were studied. Overall, 63% of athletes were found to show at least one reliable change in ImPACT performance within 24 hours after concussion (20), 69% demonstrated significant declines in cognitive function within 48 hours of concussion (21), and 71% showed at least one reliable change within 72 hours postinjury (19). Similarly, one study found 58% of athletes showed one while 27% of athletes showed two or more reliable declines or increases in symptom reporting within 72 hours postinjury (34). Up to 10 days after injury, 32% of athletes still continued to show at least one and 8% showed two or more reliable declines or increases in symptom reporting (34). When athletes first self-reported asymptomatic, 38% of athletes were found to show at least one reliable change (19).

One article included middle school, high school, and collegiate athletes who sustained a concussion during sport (32). Within their cohort of helmeted and non-helmeted athletes, 55 - 68% of athletes showed at least one impairment, while 30 - 36% showed two or more impairments on ImPACT composites up to 10 days postinjury.

Correlation Studies and Neurocognitive Predictors:
Two articles within the pediatric population looked at potential neurocognitive predictors (36,37), while one article looked at a correlation analysis (35). PTM was found to negatively influence ImPACT performance in one study; specifically, PTM athletes performed worse in Visual Memory and Reaction Time up to 2 weeks after a concussion compared to athletes reporting headache only or no headaches, and Verbal Memory was seen to be lower than in athletes who suffer from only a headache during the second week post-concussion (36). In terms of self-reported sleep duration, one study found ImPACT performance was negatively influenced by long durations of sleep, since athletes had worse Visual Memory, Visual Motor Speed, and Reaction Time scores post-concussion; yet, performance differences disappeared between sleep duration groups by the third ImPACT testing session (37). It was also found Verbal Memory, Visual Memory, Reaction Time, and Visual Motor Speed were all negatively influenced by the self-reported sleep disturbance complaint of sleeping more than normal, while athletes complaining of trouble falling asleep showed worsening of Verbal and Visual Memory scores, and the sleeping less than normal cohort showed performance declines in Visual Memory and Reaction Time (37). However, performance differences disappeared by the third ImPACT testing session (37). In terms of academic outcomes, one study did not find ImPACT composites scores were correlated with academic difficulty (35).

Within the collegiate studies, one study looked at a correlation analysis (21) and two articles investigated neurocognitive predictors (33,34). When one article looked to correlate changes in ImPACT performance between baseline and 48 hours post-concussion with cognitive symptoms, authors found correlations between "feeling mentally foggy" and a change in Reaction Time, "difficulty concentrating" and a change in Verbal Memory, and "difficulty remembering" and changes in both Verbal Memory and Reaction Time (21). Another study investigated whether physical and cognitive rest influenced ImPACT performance, and found the cohort of athletes who did not receive a day of rest performed significantly worse on Visual Memory 24 hours post-concussion (33). When authors set out to investigate whether sex influenced ImPACT performance, they found no sex influence on ImPACT performance between groups or over time up to 10 days post-concussion (34).

One study included middle school- to collegiate- aged athletes to investigate whether helmet status influenced ImPACT performance; however, average change scores from baseline to 10 days post-concussion did not significantly differ (32).

Overall Conclusions

As illustrated, the results obtained from each individual study are heterogeneous and no clear patterns emerged. Studies have looked at the influence of concussions on ImPACT scores over time, the proportion of athletes showing impaired composite scores at certain time points, whether changes in ImPACT score correlate with other outcomes, and if certain characteristics predict poorer performance on ImPACT. The diversity of assessment time points demonstrates a key time point to best test concussed athletes to obtain meaningful results has yet to be identified. Additionally, it has been demonstrated that one composite of ImPACT is not more likely than others to be negatively influenced by concussion. A severe limitation is seen in the pediatric population, since only three articles used ImPACT, and all are unique in how they utilized the computerized test. At this point in time, there is no compelling evidence to recommend mass ImPACT testing in pediatric- or collegiate-aged athletes in a clinical setting. The most recent consensus statement on concussions in sport also does not endorse mass baseline testing (1). This conclusion was also supported by a systematic review assessing the reliability of ImPACT in high school to collegiate students, which found poor to moderate reliability for most ImPACT scores (40).

Limitations

In terms of assessment time points, there was heterogeneity for when athletes completed ImPACT testing (e.g., baseline, 24 hours postinjury, etc) (19-21,32-34,36,38,39) and assessment time points were not always defined (35,37). As such, conclusions regarding ImPACT performance at specific time points could not be assessed. ImPACT was also used in a variety of ways, such as comparing ImPACT scores over time (33-36,38,39), correlating ImPACT scores to other measures (21,35), assessing how potential neurocognitive predictors influence ImPACT scores (32-34,36,37), and determining how many concussed individuals showed a reliable change on ImPACT (19-21,32,34). Therefore, the results could not be pooled using meta-analytic techniques. In addition, ImPACT data over time was provided in several studies but the authors did not determine the statistical significance of change over time (19-21,32,34,37,39) and this limited the interpretability of the results. One study (32) analyzed the mean score changes in composite domains, while five studies used RCI to identify reliable changes (19-21,32,34). Only three manuscripts were identified that exclusively included pediatric athletes and all of them differed in how ImPACT was utilized (35-37), significantly limiting the conclusions that could be drawn in this population. Also, the method of ImPACT administration varied between studies (individually and group settings, or not stated) and only one study (39) consulted a neuropsychologist concerning ImPACT results.

Project B: Prospective Cohort Study

Objective and Hypotheses

The primary objective was to determine if a season of hockey influenced ImPACT performance among female hockey players who did and did not sustain a concussion. The proportion of below normal scores at baseline was also investigated. It was predicted concussed athletes would perform more poorly on ImPACT composite scores immediately after concussion, compared to their baseline performance. Additionally, no difference between pre-season and post-season ImPACT testing was predicted in a single season of hockey in non-concussed athletes. Performance was predicted to fall within normal limits for all athletes at baseline.

Methods

This prospective cohort study included youth female hockey players from two Midget hockey teams in Winnipeg, Manitoba. A typical hockey season runs approximately from

September until March, followed by play-offs. All baseline testing, post-concussion, and post-season testing was conducted at the Pan Am Concussion Program in Winnipeg, Manitoba.

Pre-season, In-season, and Post-season Testing Protocol
Prior to the 2016 – 2017 and 2017 – 2018 hockey seasons, all athletes recruited into the study completed ImPACT baseline testing. ImPACT testing was conducted individually in a quiet room on a single desktop computer with a single proctor, and took approximately 20 minutes to complete. The neuropsychologist who is part of the clinical team at the Pan Am Concussion Program interpreted results.

Any athlete who was suspected of sustaining a concussion during hockey game-play within the 2016 – 2017 hockey season was seen at the Pan Am Concussion Clinic. A single neurosurgeon utilized the Zurich consensus statement (2) when rendering a concussion diagnosis. Concussed athletes completed ImPACT at their initial presentation and when medically cleared to return to play. Medical clearance was obtained when athletes were asymptomatic at rest, tolerating school full time, successfully completed the Return to Play (RTP) protocol (2), and demonstrated a normal neurological examination. If an athlete sustained a concussion outside of hockey, the athlete was excluded from analysis, but followed the same treatment protocol.

All athletes (concussed and non-concussed) were scheduled to complete ImPACT after the completion of their hockey season.

Outcomes measured
1. In the cohort of female athletes recruited during the 2016 – 2017 and 2017 – 2018 hockey seasons, the primary outcome was to determine the percentage of individuals showing below normal ImPACT composite scores at baseline. Below normal was defined as below the 9th percentile compared to normative data.
2. In the cohort of athletes recruited during the 2016 – 2017 hockey season, the primary outcome was the number of athletes who showed a reliable change in post-concussion (when applicable) and post-season scores compared to baseline, as identified using the RCI calculation embedded within the ImPACT program. Clinically meaningful changes in the composite scores were indicated on the ImPACT clinical report if the athlete's change from baseline exceeded the RCI 80% CI from pre-season results. The changes would be seen on the four summary composite scores (Verbal Memory, Visual Memory, Visual Motor Processing Speed and Reaction Time). The RCI embedded within the ImPACT program does not identify reliable changes in Impulse Control.

Statistical Analysis
Descriptive statistics will be presented, including means and standard deviations for continuous outcomes. Base rates are calculated by dividing the proportion of athletes who scored below the 9th percentile by the total number of athletes who completed pre-season ImPACT. Individuals who showed a reliable change in scores pre-season to post-season were identified within the ImPACT program utilizing an 80% CI. If an ImPACT test is flagged as "invalid" within the program, it was based on the following criteria (27):
   a) Word Memory Learning Percentage < 69%, OR
   b) Design Memory Learning Percentage < 50%, OR
   c) X's and O's Total Incorrect > 30, OR
   d) Impulse Control Composite > 30, OR
   e) Three Letters Total Letters Correct < 8.

A flagged ImPACT report was included in analysis if the treating neuropsychologist determined low scores were not reflective of suboptimal effort.

Results *[Please see **Table III**]*

Of the 10 athletes recruited in 2016, the mean age was 15.20 (1.14) years pre-season and 16.10 (1.12) years post-season. The number of athletes who reported previous concussions was 3 in pre-season testing, and 4 athletes post-season. No athlete included in analysis was diagnosed with an in-season hockey-related concussion. Prior to the 2017 hockey season, 16 of the 17 females recruited completed pre-season ImPACT testing. For the entire cohort of female hockey players who completed pre-season ImPACT testing, the mean (standard deviation) age was 15.50 (1.03) years.

1. Ten female hockey players were recruited from a single hockey team prior to the start of the 2016 – 2017 hockey season and seventeen additional female athletes were recruited from a second team prior to the 2017 – 2018 hockey season. In total, 26 athletes completed pre-season ImPACT testing. One ImPACT test pre-season was flagged as invalid (three letters total letters correct < 8); however, the neuropsychologist noted the athlete demonstrated adequate effort on paper and pencil testing, and the ImPACT profile was not otherwise indicative of poor engagement. The results were included in these analyses. The percentage of athletes who scored below the 9th percentile on each ImPACT composite varied: 3.9% on Verbal Memory, 11.5% on Visual Memory, 3.9% on Visual Motor Speed, and 7.7% on Reaction Time.
2. Of the 10 athletes recruited in 2016, one athlete did not complete post-season ImPACT testing; thus, she was excluded from RCI analysis. ImPACT test results from 9 athletes were used to determine the proportion of athletes who showed a reliable change from baseline at post-season testing. On average, post-season ImPACT testing was completed 309.78 days after baseline (range 276 – 343 days). Overall, 6 (66.7%) athletes showed at least one reliable change in the ImPACT composite scores compared to pre-season scores. In regards to specific composites, a reliable change was identified for 33% of athletes on Verbal Memory, 22% on Visual Memory, and 33% on Reaction Time. All changes identified using the RCI calculation showed post-season scores were lower that pre-season scores.

Discussion

No athlete sustained a concussion during the 2016 – 2017 hockey season; as a result, the change in ImPACT scores before and after a concussion could not be determined. In our cohort of 26 healthy athletes who completed pre-season ImPACT testing, the percentage of individuals scoring below the 9th percentile on each ImPACT composite score was 4% of athletes in Verbal Memory, 12% in Visual Memory, 4% in Visual Motor Processing Speed, and 8% in Reaction Time. Calculating base rates of below normal performance in healthy populations is essential to the interpretation of low scores following a concussive event. Base rates for a variety of neuropsychological tests in an adult normative population have been examined and low or abnormal scores were common in healthy populations (41) for the 16th percentile or 9th percentile cut-offs (42). To the best of our knowledge, our study is the first to report base rates in a healthy pediatric population, and we have found similar results to those found in adults. Low or abnormal scores are not specific to any particular battery of tests or normative sample, and are linked to individuals with lower intelligence, fewer years of education, language barriers, fluctuations in motivation and effort, fatigue, and/or minor illness (41,42). In our sample, only one individual reported a diagnosis of Attention Deficit Hyperactivity Disorder; otherwise, no other athlete reported a co-morbidity that could account for low scores.

Within the cohort of 9 healthy athletes, 6 (66.7%) showed at least one reliable decline in ImPACT performance over time: 33% declined in Verbal Memory, 33% in Reaction Time, and 22% in Visual Memory. In a systematic review including healthy high school and collegiate students, the percentage of participants showing significant change between two time points ranged from 5 – 27% for Verbal Memory, 2 – 20% for Visual Memory, 4 – 24% for Visual Motor Processing Speed, and 4 – 23% for Reaction Time (40). Reliability was also investigated, which found Visual Motor Speed was the most reliable composite score, while Verbal Memory, Visual Memory and Reaction Time show poor to moderate reliability (40). ImPACT should not be the only tool used to measure recovery, since a significant portion of athletes will show reliable changes in the absence of a concussion.

This study is not without limitations. The primary study aim to determine the effects of concussion on ImPACT performance could not be investigated. Additionally, the sample sizes utilized in both analyses were small and this may explain the different proportions of athletes showing changes on ImPACT composites scores compared to the literature. Base rates were not calculated based on the athlete's school grade due to the small sample size. Furthermore, all athletes who completed pre-season and post-season ImPACT testing took the same version of ImPACT; however, since at least 276 days passed between testing sessions, it is unlikely learning effects occurred.

In our sample, the base rates for low performance in ImPACT composite scores ranged from 4 – 12% in a sample of healthy female hockey players at preseason testing. This will assist in the interpretation of low performance rates in concussed athletes seen at our clinic. Moreover, 67% of healthy athletes showed at least one reliable change in ImPACT composites scores after one season of hockey. The utility of baseline testing in female adolescent hockey players is questionable since a majority of healthy athletes in this study demonstrated changes in composite scores without sustaining a concussion, supporting recent recommendations against mass baseline testing of athletes (1). Additionally, the reliability of ImPACT over time is poor to moderate for most composite scores (40). Research examining the utility of computerized neurocognitive measures for concussion in youth is heterogeneous and, as noted above, cross-study comparisons of findings are limited due to the variability in the administration and interpretation of ImPACT testing. Further research should investigate a larger sample of female adolescent hockey players to establish a better understanding of standard base rates of performance in the absence of concussion.

Future Directions

The systematic review and prospective cohort study provides evidence to recommend against ImPACT mass testing, or using ImPACT as the sole neuropsychological test in the management of concussed athletes. Poor performance on ImPACT post-concussion was demonstrated in the literature; however, reliable declines were also common in healthy athletes who were free from concussion. Additionally, base rates of low performance on composite scores were common in a healthy cohort of female athletes at baseline testing. In future studies, the pediatric concussed population should be investigated more extensively to determine how ImPACT scores are influenced by time postinjury and common cognitive symptoms experienced by a concussed athlete. Additionally, association studies between changes in ImPACT composites and other psychosocial outcomes besides school functioning should be studied. Furthermore, studies should use more standardized assessment time points in order to investigate which, if any, time points are most useful when testing concussed athletes with ImPACT. Finally, consulting neuropsychologists regarding ImPACT scores is warranted in future studies to help interpret change in scores in a broader clinical context.

Table I. Study characteristics of included studies stratified by age of participants.

Author, Year Country, Study Design	Sample size, Groups	Age (years) Mean (SD)	Sex (Male)	Previous Concussion Mean (SD)	ImPACT Analysis by NP (Y/N)
Pediatric (Age < 19 years)					
Darling, 2014, USA, Retrospective Chart Review & Follow-up	117 (39 with both ImPACT and follow-up data)	Total: 15.5 (1.6) Female: 15.4 (1.5) Male: 15.4 (1.6)	N: 88 (75%)	Total: N=37 1: N=24 2: N=10 3+: N=3	No
Kontos, 2013, USA, Prospective cohort	138 Posttraumatic Migraine (PTM): 56 Headache: 63 No Headache: 19	Total: 16.0 (1.2) PTM: 15.9 (1.2) Headache: 15.9 (1.2) No Headache: 16.2 (1.1)	N: 138 (100%)	Total: 0.5 (0.8) PTM: 0.4 (0.9) Headache: 0.7 (0.9) No Headache: 0.5 (0.9)	Not stated
Kostyun, 2015, USA, Cross-sectional study	545 Trouble Falling Asleep, Sleeping Less than Normal, Sleeping More than Normal, No Sleep disturbances; Short Sleep Duration, Intermediate Duration, Long Duration	Male: 14.4 Female: 14.6	N: 301 (55%)	0: N=321 1: N=148 2: N=53 3+: N=23	Not stated
Collegiate-aged Athletes					
Broglio, 2007, USA, Prospective Cohort	75 (24 with ImPACT)	Not stated	N: 62 (83%)	Not stated	No
Broglio, 2007, USA, Retrospective Analysis	21	19.8 (1.3)	N: 16 (76%)	1.8 (2.0)	Not stated
Broglio, 2009, USA, Retrospective Cohort	36 (32 in final analysis)	19.7 (1.2)	N: 24 (75%)	1.1 (1.8) N=16	Not stated

Buckley, 2016, USA, Prospective Cohort	50 Physical & Cognitive Rest: 25 No-rest: 25	Rest: 19.8 (1.2) No rest: 19.4 (1.3)	N: 31 (62%) Rest: 18 (72%) No rest: 13 (52%)	Rest: 0.6 (0.7) No-rest: 0.8 (0.9)	Not stated
Covassin, 2007, USA, Prospective Cohort	79 Males: 41 Females: 38	Not stated	N: 41 (52%)	N: 41 (51.9%) 1: 20% 2+: 32%	Not stated
Echlin, 2012, Canada, Prospective Cohort	Approx. 45* Concussed: 11 Non-concussed: 35	Not stated	N: 25 (54 - 56%)	Male: 14 (56%) Female: 4 (20%)*	Yes
Sosnoff, 2008, USA, Prospective Cohort	618 (36 concussed; 20 completed ImPACT)	Concussed: 21.2 (1.5)	N: 29 (81%)	Not stated	Not stated
Pediatric- and Collegiate-aged Athletes					
Zuckerman, 2015, USA, Retrospective Cohort	138 Helmeted: 69 Non-helmeted: 69	Helmeted: Median=16 (95% CI: 15, 16) Non-helmeted: Median=16 (95% CI: 15, 17)	N: 134 (97%) Helmeted: N: 67 (97%) Non-helmeted: N: 67 (97%)	Helmeted Sport Group: Median = 0 (95% CI: 0,0) Non-helmeted Sport Group: Median = 0 (95% CI: 0,1)	Not stated

NP: Neuropsychologist
*Uncertainty regarding whether 20 or 21 female athletes were used in analysis

Table II. A summary of results of included studies stratified by age of participants.

Author, Year, Country	Assessment Time Points	Main Conclusions
Pediatric (Age < 19 years)		
Darling 2014 USA	Athlete- reported Asymptomatic	41% of individuals had 1 ImPACT composite score in borderline range the day they passed BCTT. No ImPACT composite score significantly correlated with difficulty in school.

Kontos, 2013 USA	Baseline, Post-injury Days 1-7, Post-injury Days 8-14	PTM group performed worse in Visual memory and Reaction time 1-7 days and 8-14 days postinjury and performed worse in Verbal Memory 8-14 days postinjury. ImPACT composite scores were lower 1-7 days postinjury. All scores at 8-14 days postinjury were higher than 1-7 days postinjury scores. Verbal and Visual Memory scores remained below baseline levels 8-14 days postinjury.
Kostyun, 2015, USA	No universal time points – 3 ImPACT tests given (not all patients completed 3 ImPACT tests)	Long duration cohort performed worse on Visual Motor Speed and Reaction Time on first ImPACT testing session, and Visual Memory on second ImPACT testing session. Compared to the no sleep disturbance cohort, trouble falling asleep cohort performed worse on Verbal Memory and Visual Memory; sleeping less than normal cohort scored worse on Visual Memory and Reaction Time; and, sleeping more than normal cohort performed worse on Verbal Memory, Visual Memory, Visual Motor Speed, and Reaction Time.
Collegiate-aged Athletes		
Broglio, 2007, USA	Baseline, Post-injury Day 1	63% of athletes identified as impaired on $\geq$ 1 ImPACT composite
Broglio, 2007, USA	Baseline, within 72 hours, SRA	71% of athletes identified as impaired on $\geq$ 1 ImPACT composite within 72 hours. 38% of athletes identified as impaired on $\geq$ 1 ImPACT domain at SRA compared to baseline
Broglio, 2009, USA	Baseline, Post-injury $\leq$2 days	69% of athletes had significant declines in ImPACT performance. Significant correlations between changes in composite scores and symptoms: "feeling mentally foggy" with Reaction Time, "difficulty concentrating" with Verbal Memory, and "difficulty remembering" with Verbal Memory and Reaction Time.
Buckley, 2016, USA	Baseline, Post-injury Day 1, then every 2-3 days until baseline met or exceeded	No difference between rest and no-rest cohorts in time to reach baseline. For group differences, the no-rest group had significantly lower Visual Memory performance Day 1 postinjury. No-rest group had significant reductions in Verbal Memory, Visual Memory, Processing Speed and Reaction Time Day 1 postinjury. Rest group had a significant reduction in Reaction Time Day 1 postinjury.
Covassin, 2007, USA	Baseline, Post-injury $\leq$3 days, Post injury 7-10 days	ImPACT performance was worse within 3 days and 7-10 days postinjury. No sex differences were identified. 58% of athletes had 1 and 27% of athletes had 2 reliable declines in performance or increase in symptom reporting within 3 days postinjury. 32% had 1 and 8% had 2 reliable declines in performance or increase in symptom reporting 7-10 days postinjury,

Echlin, 2012, Canada	Pre-season, 72 hours post-injury, 2 weeks post-injury, 2 months post-injury and post-season	No significant difference between the preseason and postseason ImPACT composite scores. For post-injury analysis, no changes in ImPACT composites were identified from baseline.
Sosnoff, 2008, USA	Baseline, Post-injury ≤ 1 Day	Worse performance was seen in Verbal Memory, Visual Memory, and Reaction Time 24 hours after a mTBI.
Pediatric- and Collegiate-aged Athletes – Results not stratified by age		
Zuckerman, 2015, USA	Baseline, ≤10 days postinjury	No differences seen between helmet status groups on ImPACT composite scores, mean change scores, number of individuals showing change on specific ImPACT composites, number of individuals with ≥ 1 impaired domains, number of individuals with ≥ 2 impaired domains, or average number of impairments. 68% helmeted and 55% non-helmeted showed ≥ 1 reliable changes. 36% helmeted and 30% non-helmeted showed ≥ 2 reliable changes. The average number of changes was 1.5 ± 1.5 for helmeted and 1.1 ± 1.4 for non-helmeted.

BCTT = Buffalo Concussion Treadmill Test

Table III. Age, ImPACT values, and percentage of healthy female hockey players scoring below normal and showing reliable changes on ImPACT composite scores.

	Preseason[Ψ]		Preseason	Postseason	RCI Change from Baseline[ɫ] (%)
	Mean (SD)	**Below Normal* (%)**	**Mean (SD)**	**Mean (SD)**	
Age	15.50 (1.03)		15.20 (1.14)	16.10 (1.12)	
ImPACT Composites					
Verbal Memory	88.88 (9.04)	3.85	84.90 (11.40)[Λ]	84.44 (11.54)[ɫ]	33.33
Visual Memory	74.23 (15.28)	11.54	71.00 (16.13)[Λ]	60.67 (16.71)[ɫ]	22.22
Visual Motor Speed	38.10 (6.77)	3.85	33.64 (5.53)[Λ]	35.89 (5.99)[ɫ]	0
Reaction Time	0.60 (0.06)	7.69	0.61 (0.07)[Λ]	0.65 (0.09)[ɫ]	33.33
Impulse Control	8.46 (5.17)	N/A	9.40 (6.42)[Λ]	6.78 (5.47)[ɫ]	N/A

[Ψ] 26 athletes recruited in 2016 and 2017 included (ImPACT data missing for one athlete preseason)
*Below the 9th percentile
[Λ] 10 athletes recruited in 2016 included
[ɫ] 9 athletes recruited in 2016 included (ImPACT data missing for one athlete postseason)
N/A – Reliable change was not calculated using RCI embedded within ImPACT

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