Exercise for concussion management in youth:

clinician use, evaluation, timing, and safety

Danielle M. Dobney

B.A. (Kinesiology), CAT(C) M.Sc. (Rehabilitation Sciences)

School of Physical and Occupational Therapy Faculty of Medicine

McGill University Montreal, Quebec, Canada April 2018

A thesis submitted to McGill University in partial fulfillment of the requirements of the degree of

Doctor of Philosophy (Rehabilitation Sciences)

Table of Contents

List of Figures

List of Tables

Abstract

Background: A concussion is a type of traumatic brain injury.[1] Approximately 30% of youth experiencing a concussion will have symptoms lasting upwards of 1 month,[2] which prevents the resumption of regular activities. Typical management strategies have involved rest and removal from physical, academic, and, social activities.[3] The most recent expert-consensus guidelines advocate early re-introduction of physical activity,[4] though little data exists to support this recommendation. While preliminary studies to date have shown promising potential, they have been hindered by methodological limitations. Exercise-based interventions for youth following concussion are not well understood as most research has focused on adult populations.

Objective: The global objective of this thesis was to contribute evidence towards an innovative approach using an exercise-based intervention for concussion management in youth with persisting symptoms. To achieve this objective two broad lines of inquiry were pursued. First, an environmental scan of exercise-based interventions; (manuscripts I and II). Second, estimating the effectiveness of an exercise-based intervention in decreasing post-concussion symptoms. (manuscripts III, IV, and V).

Methods and Results: The environmental scan consisted of two studies, a scoping review (manuscript I) and a survey of Canadian Athletic, Physical, and Occupational Therapists (manuscript II).

In the <u>first study</u> we explored the literature for non-pharmacological rehabilitation interventions for concussion in children. We retrieved 1988 articles from 5 databases (MedLine, Pubmed, CINAHL, SportDiscus, PsychInfo) between 1987 - October 24, 2017. Full-text screening was applied to 152 articles, and 26 studies met the inclusion criteria. A wide variety of intervention types were found including; rest, active rehabilitation, aerobic exercise, physical exertion, full-body stretching, vestibular, oculomotor, cervical spine manual therapy, education, telephone counselling, mobile health application, web-based self-management activity-restriction and relaxation training program, multimodal impairment based physical therapy, cognitive behavioral therapy, transcranial direct current stimulation, and acupuncture. Interventions including an exercise-based component were most abundant (12/26 studies). While most studies reported

positive findings, few were of ‘good’ quality (9/26 studies) and none were of ‘excellent’ quality. Methodological challenges limit generalizability of findings. Higher quality studies are needed.

In the second study we estimated the clinical practice habits of Canadian Athletic, Occupational, and Physical Therapists providing care for youth experiencing persisting symptoms from a concussion. This online survey featured two clinical vignettes and a series of questions regarding the type of treatment therapists would prescribe. Due to our interest in exercise-based interventions, we outlined several branching questions about exercise type, frequency, duration, and intensity. While various treatment types were prescribed, the most reported types included education-based strategies. Approximately 1/3 of clinicians reported they would prescribe aerobic exercise as part of their clinical management.

To estimate the effectiveness of an exercise-based intervention in decreasing post-concussion symptoms we conducted three studies. We evaluated an on-going intervention (Active Rehabilitation for Concussion Management) at the Montreal Children’s Hospital (manuscript III), we estimated the impact of time to initiate this intervention (manuscript IV) and assessed the feasibility of early Active Rehabilitation (manuscript V).

In the third study we used an existing database from the Montreal Children’s Hospital mTBI/Concussion Clinic to evaluate how participating in the Active Rehabilitation Intervention influenced post-concussion symptoms. The Active Rehabilitation Intervention consists of: aerobic exercise, coordination drills, visualization, and education. We included patients based on specific start times (3-4 weeks post-injury) and follow-up (4-8 weeks post-injury) appointments. This strategy allowed us to evaluate a homogenous group of patients (n=277). We found that participating in the Active Rehabilitation Intervention was associated with statistically significant, and clinically meaningful, improvements in post-concussion symptoms.

In the fourth study we conducted another examination of the existing database from the Montreal Children’s Hospital mTBI/Concussion Clinic. We explored the timing component of the Active Rehabilitation Intervention. To estimate if there was an optimal time to initiate the intervention we looked at all patients over a 3-year period (n=677) and categorized them based on the time they started the intervention (<2, 2, 3, 4, 5, 6+ weeks post-concussion). We found that, irrespective of the start time, statistically significant, and clinically meaningful, improvements were observed in post-concussion symptoms in all groups.

In the fifth study we evaluated the feasibility of early Active Rehabilitation starting 2-weeks post-injury (n=10) compared to usual care (n=10) (4-weeks post-injury). In this randomized clinical trial, patients in both groups received the same intervention, only the start time differed (2 or 4 weeks post-injury). Post-concussion symptoms decreased for participants in both groups.

Conclusion: Our environmental scan revealed that while most interventional studies from our scoping review contained an exercise-based component, few clinicians are incorporating exercise as a concussion management strategy. In estimating the effectiveness of an exercise-based intervention in decreasing post-concussion symptoms, we revealed important findings about the influence on outcomes, timing, and safety. While our work shows positive results, there are barriers preventing clinicians from adopting and utilizing exercise-based strategies as a component of concussion management in youth.

Resumé

Contexte: Une commotion cérébrale est un type de traumatisme craniocérébral léger. Environ 30% des enfants qui subissent une commotion cérébrale auront des symptômes qui dureront plus d'un mois, ce qui empêchera la reprise de leurs activités habituelles. Les stratégies de gestion couramment utilisées consistent à se reposer et à limiter les activités physiques, scolaires et sociales. Les lignes directrices les plus récentes préconisent une réintroduction plus rapide de l'activité physique, bien que peu de données existent pour appuyer cette recommandation. Alors que les études préliminaires à ce jour sont prometteuses, elles sont entravées par des limitations méthodologiques. Les interventions axées sur l'exercice pour les enfants après une commotion cérébrale ne sont pas bien comprises, car la plupart des recherches à ce jour ont porté sur les populations adultes.

Objectif: L'objectif général de cette thèse était de contribuer aux connaissances sur les interventions basées sur l'exercice pour la prise en charge des commotions cérébrales chez les enfants et adolescents présentant des symptômes persistants. Pour atteindre cet objectif, deux avenues de recherche ont été poursuivies. Tout d'abord, une analyse environnementale des interventions basées sur l'exercice; (manuscrits I et II), et deuxièmement, estimer l'efficacité d'une intervention basée sur l'exercice pour réduire les symptômes post-commotion; (manuscrits III, IV et V).

Méthodes et résultats: L'analyse environnementale comprenait deux études, une étude de la portée (manuscrit I) sur les interventions existantes, et une enquête auprès des ergothérapeutes, physiothérapeutes et thérapeutes du sport canadiens (manuscrit II).

Dans la <u>première étude</u>, nous avons exploré la littérature portant sur les interventions de réadaptation non-pharmacologiques proposées pour la gestion des commotions cérébrales chez les enfants. Nous avons identifié 1988 articles à l’aide de 5 bases de données (MedLine, Pubmed, CINAHL, SportDiscus, PsychInfo) entre 1987 – et octobre 2017. Vingt-six études répondaient aux critères d'inclusion. Une grande variété de types d'intervention fût trouvée, y compris; le repos, la réadaptation active, l’exercice aérobique, l’effort physique, les étirements complet du corps, la réadaptation vestibulaire ou oculomotrice, la thérapie manuelle du rachis cervical, l’éducation, le

counselling téléphonique, les applications mobile de santé, les programmes d'auto-gestion et de relaxation, la physiothérapie multimodale, la thérapie cognitivo-comportementale, la stimulation transcrânienne à courant continu et l’acupuncture. Les interventions incluant une composante basée sur l'exercice étaient les plus abondantes (12/26 études). Alors que la plupart des études rapportaient des résultats positifs, peu étaient de bonne qualité (9/26 études) et aucune n'était d'excellente qualité. Les défis méthodologiques limitent la généralisation des résultats. Des études de qualité supérieure sont nécessaires.

Dans la deuxième étude, nous avons estimé les habitudes de pratique clinique des physiothérapeutes, ergothérapeutes et thérapeutes du sport canadiens qui prodiguent des soins aux jeunes présentant des symptômes persistants après une commotion cérébrale. Ce sondage en ligne comportait deux vignettes cliniques et une série de questions sur le type de traitement que les thérapeutes prescriraient. En raison de notre intérêt pour les interventions basées sur l'exercice, nous avons défini plusieurs questions découlant sur le type d'exercice, la fréquence, la durée et l'intensité. Bien que divers types de traitement aient été prescrits, les types les plus souvent signalés comprenaient des stratégies basées sur l'éducation. Environ le tiers des cliniciens ont déclaré qu'ils prescrivaient des exercices aérobiques dans le cadre de leur prise en charge clinique.

Pour estimer l'efficacité d'une intervention basée sur l'exercice pour réduire les symptômes post-commotion, nous avons ensuite mené trois études disctinctes. Nous avons évalué une intervention présentement utilisée (réadaptation active pour la prise en charge des commotions cérébrales) à l'Hôpital de Montréal pour enfants (manuscrit III), évalué l'impact du temps pour initier cette intervention avec cette même population (manuscrit IV) et évalué la faisabilité d’initier l’intervention de manière plus précoce (manuscrit V).

Dans la troisième étude, nous avons utilisé une base de données existante de la Clinique de commotion cérébrale de l'Hôpital de Montréal pour enfants pour évaluer comment la participation à l'intervention de réadaptation active influençait les symptômes post-commotionnels. L'intervention de réadaptation active consiste en: des exercices aérobiques, des exercices de coordination, de la visualisation et de l’éducation. Nous avons inclus les patients en fonction du moment spécifique de l’initiation de l’intervention (3 à 4 semaines après la blessure) et du suivi (4 à 8 semaines après la blessure). Cette stratégie nous a permis d'évaluer un groupe homogène de patients (n = 277). Nous avons constaté que la participation à l'intervention de réadaptation active était associée à des améliorations statistiquement significatives et cliniquement significatives des symptômes post-commotion.

Dans la quatrième étude, nous avons effectué un autre examen de la base de données existante de la Clinique de commotion cérébrale de l'Hôpital de Montréal pour enfants. Nous avons exploré la composante temporelle de l'intervention de réadaptation active. Pour estimer s'il y avait un délai optimal pour initier l'intervention, nous avons examiné tous les patients se présentant sur une période de 3 ans (n = 677) et les avons catégorisés en fonction du moment où ils ont débuté l'intervention (<2, 2, 3, 4, 5, 6+ semaines après la commotion cérébrale). Nous avons constaté que, quel que soit l'heure le moment d'initiation, des améliorations statistiquement et cliniquement significatives, ont été observées au niveau des symptômes post-commotionnels dans tous les groupes.

Finalement, dans la cinquième étude, nous avons évalué la faisabilité de la réadaptation active précoce débutée deux semaines après la blessure (n = 10) par rapport aux soins habituels (n = 10) (quatre semaines après la blessure). Dans cet essai clinique randomisé exploratoire, les patients des deux groupes ont reçu la même intervention, seul le moment d'initiation différait (2 ou 4 semaines après la lésion). Les symptômes post-commotionnels ont diminué chez les participants des deux groupes. Aucun obstacle à la mise en œuvre n'a été identifié.

Conclusion: Notre analyse environnementale a révélé que même si la plupart des études interventionnelles de notre étude de la portée contenaient une composante axée sur l'exercice, peu de cliniciens intègrent l'exercice comme stratégie de gestion des commotions cérébrales. En estimant l'efficacité d'une intervention basée sur l'exercice pour réduire les symptômes post-commotion, nous avons révélé des résultats importants concernant les résultats, le moment d'initiation et la sécurité de l'intervention précoce. Bien que notre travail montre des résultats positifs, il existe des obstacles qui empêchent les cliniciens d'adopter et d'utiliser des stratégies axées sur l'exercice comme élément de la gestion des commotions chez les jeunes.

Acknowledgements

I gratefully acknowledge the support and guidance of my supervisor Dr. Isabelle Gagnon. Your mentoring has allowed me to grow as a clinician-scientist. I can't thank you enough for supporting my clinical endeavors during my PhD. I appreciate how you encouraged me to be independent and explore research ideas that excited me. You are an exceptional mentor, you are a master at giving just enough guidance so that I could learn and grow as a researcher. I came to McGill to work with you and you exceeded my expectations at every turn. Merci beaucoup!

Thank you to my supervisory committee members; Ms. Lisa Grilli, Dr. Marc Roig, Dr. Kathryn Schneider, and Dr. Nick Reed. Your expertise in clinical-research has guided my thinking. Thank you for critically reviewing my work. I appreciate our discussions and your thoughtful questions.

To the clinical team at the Montreal Children's Hospital (MCH) Concussion Clinic; Ms. Lisa Grilli, Christine Beaulieu, Meghan Straub, Carlo Galli, Fara Bahrpeyma, and Debbie Friedman, many thanks for generating and maintaining a clinical database that was the starting point for this thesis. As a clinician, I have a deep appreciation for how you welcomed me into your clinic. I appreciate having the opportunity to collaborate with you. This experience has been the epitome of a successful clinical research project!

This research would not be possible without the generous volunteers who participated. Many thanks to the patients and families from the MCH Concussion clinic, and clinicians across the country for participating.

I would like to acknowledge the financial support from the Canadian Institutes of Health Research, The Fonds de recherche du Québec – Santé, and McGill University School of Physical and Occupational Therapy – Graduate Excellence Award. Additionally, thank you to McGill University School of Physical and Occupational Therapy.

Thank you to my lab (the row); Eda Cinar, Laurie-Ann Corbin-Berrigan, Dr. Shihka Saxena, Dr. Jerome Gauvin-Lepage, Dr. Scott Holmes, Adrienne Crampton, Dr. Liz Teel, Guido Guberman and Christophe Alarie. You were always there for questions, fun conversation, French translations, statistical help, and lab lunches!

To the McGill Martlets Women's basketball team and coach Ryan Thorne, you welcomed me with open arms into the family – it made me feel at home in Montreal.

Thank you to my family, for your love and support. Mom and Dad, you've proofread my work, visited me in Montreal, encouraged via skype, and helped me through difficult times. Thank you for having a genuine interest in the work I'm doing.

To my partner Fiona, thank you for your unwavering support. On the tough days you nudged, on the great days you celebrated the small successes, and when it was time you were there to bring me home! ~ Plenty

Preface

Statement of Originality

This thesis adds to the existing body of knowledge regarding exercise interventions for concussion management in youth. Original scholarship in this thesis includes;

i. Conducting quality assessment of post-concussion rehabilitation interventions for youth in our scoping review;
ii. Identifying clinician practice habits for concussion management in youth;
iii. Identifying gaps between research and clinical practice relating to the use of exercise post-concussion;
iv. Estimating the impact of time to initiate exercise in symptomatic youth post-concussion;
v. Conducting feasibility testing for early active rehabilitation in youth
vi. Developing and testing a system to track safety of a home, exercise-based intervention post-concussion;
vii. Presenting preliminary data on exercise characteristics (frequency, intensity, duration) of a home program for post-concussion youth;

The studies were designed and conducted by the doctoral student to answer questions not previously addressed, or from limitations in the literature.

Contribution of Authors

The manuscripts included in this thesis are the work of Danielle Dobney with extensive guidance from Dr. Isabelle Gagnon and support from the members of the supervisory committee. Data collection, statistical analyses and writing of manuscripts were conducted by the doctoral candidate under the direct supervision of Dr. Isabelle Gagnon. Dr. Gagnon oversaw all aspects of the thesis and provided guidance related to methodology, statistical analyses, and interpretation.

<u>Manuscript I</u>: Co-Authors Matthew Miller and Emily Tufts

Matthew Miller screened titles, abstracts, and full text for inclusion. He conducted quality assessments and assisted with drafting and revising the manuscript. Emily Tufts developed the search strategy, consulted on procedures for conducting the search, and reviewed the manuscript.

Dr. Gagnon assisted with conceptualizing the study, consulted on interpretation and reviewed the final manuscript.

Manuscript II: Co-author Dr. Gagnon assisted with study design, reviewed the outcome used in the study, provided guidance on analyses and interpretation.

Manuscripts III and IV: Co-authors Lisa Grilli, Helen Kocilowicz, Christine Beaulieu, Meghan Straub, Debbie Friedman, and Dr. Isabelle Gagnon

Lisa Grilli, Helen Kocilowicz, Christine Beaulieu, Meghan Straub, Debbie Friedman provided the database, and assisted with contextualizing the data. Dr Gagnon provided extensive guidance on methods, statistical analyses and interpretation.

Manuscript V: Co-authors Lisa Grilli, Christine Beaulieu, Meghan Straub, Carlo Galli, Mitchell Saklas, Debbie Friedman, Alexander Sasha Dubrovsky and Isabelle J. Gagnon

Lisa Grilli assisted with study design, recruited participants, and data acquisition. Christine Beaulieu, Meghan Straub, and Carlo Galli assisted with study design, and data acquisition. Mitchell Saklas recruited participants, coordinated and supervised data acquisition. Debbie Friedman assisted with study design. Dr. Alexander Sasha Dubrovsky assisted with study conceptualization and reviewed the manuscript. Dr. Isabelle Gagnon assisted with conceptualizing and designing the study, assisted with analysis and interpretation of results, reviewed and revised the manuscript.

Chapter 1 - Introduction

Approximately one-third of children who sustain a concussion will experience a prolonged recovery from concussion extending beyond the initial 4-week period.[2] The presence of persisting symptoms and impairments interferes with children's involvement in sport, academic and social activities,[5] yet we still know very little about how to best help them. While promising early work has demonstrated the potential of using exercise-based interventions to promote recovery from concussion,[6,7] significant limitations exist within the current literature, making it difficult for the clinician to implement evidence-informed strategies to help children with persisting symptoms.[8] Proper management and timely care has the potential to reduce the burden of injury and the number of youth experiencing persisting symptoms following a concussion. Together, these outcomes have benefit to the individual, family, and health care system.

The overarching goal of the work presented in this thesis is to add to our current understanding of how exercise can play a role in concussion management in the pediatric population. Specifically, we first wanted to present an environmental scan focussing on how exercise was currently reported as a mode of intervention in the scientific literature and complement this by exploring how clinicians currently use exercise in their practice with children after concussion. Then we wanted to examine the effectiveness of using exercise-based interventions from three different perspectives. First, we used existing clinical data from the Montreal Children's Hospital Concussion Clinic to examine how participating in an exercise-based intervention influenced post-concussion symptoms. Second, we estimated how the timing of initiating an exercise-based intervention influenced symptom evolution. Finally, using our learnings from the previous two studies, we assessed the feasibility of starting an exercise intervention 2-weeks post-concussion.

The thesis is organized in three main parts. First a general literature review on the topic of concussion will set the stage for the experimental work which will then be presented in five separate manuscripts. Finally, the third part will consist of a general discussion of the impact of the results obtained during this work. It is articulated around the strengths and limitations of the thesis, and implications for future research and clinical practice. Specifically, we discuss how the thesis fits into the broader concussion context and propose logical progressions to build on this work. From a clinical perspective we discuss the challenges of providing care for youth with concussion and orient these barriers in the context of our findings.

Chapter 1 is a general introduction to our work, chapter 2 is a literature review on concussion in youth and exercise-based interventions. Chapter 3 outlines the objectives of the thesis. Chapters 4 to 13 present the 5 studies we have conducted in the context of my doctoral training. Integration chapters explain how findings from each study informed the next one. The findings from the 5 studies are presented in distinct manuscripts summarized below.

Chapter	Manuscript	Title
5	I	*Non-pharmacological rehabilitation interventions for concussion in children: A scoping review*
7	II	*Concussion management practices of Canadian rehabilitation therapists*
9	III	*Evaluation of an Active Rehabilitation Program for Concussion Management in Children and Adolescents*
11	IV	*Is there an optimal time to initiate an active rehabilitation protocol for concussion management in children? A case series.*
13	V	*Feasibility of early active rehabilitation for concussion recovery in youth: a randomized trial*

Finally, chapter 14 provides a general discussion integrating the entirety of our findings, the strengths and limitations of the work, and implications for future research and clinical practice. Chapter 15 is a brief concluding chapter.

Chapter 2 – Literature Review

Concussion definition

A concussion is a traumatic brain injury induced by a direct or impulsive biomechanical force.[4,9] The biomechanical force is thought to produce a chain of events resulting in both immediate and delayed impairments.[10] A range of clinical signs, symptoms, and neurological impairments are observed, and generally resolve spontaneously.[4,9]

Incidence of concussion in youth

Concussion in children and adolescents is among the top two causes of hospital visits in Canada.[11] It has been estimated that the incidence rate in Canadian children under age 14 is approximately 200 per 100,000 per year.[12] The prevalence of concussive injury is highest among adolescents with estimates as high as 600 per 100,000.[13] There is good reason to believe that the actual rate of injury is greater given that many concussions go unrecognized, unreported, and many children do not receive medical attention.[14]

Approximately one-third of children and adolescents will experience persisting impairments after a concussion.[2,15,16] *This thesis will focus on the subgroup of children and adolescents who experience persisting symptoms following a concussion*.

Concussion signs and symptoms

Children report the presence of clinical signs and symptoms following a concussion.[17-19] Symptoms can be classified into four broad categories; somatic, cognitive, emotional, and sleep related.[20] The most commonly reported signs and symptoms at initial examination include; headache, dizziness, fatigue, and cognitive complaints.[21] Impairments in cognitive function,[22,23] visual processing,[24] balance,[25] visuomotor performance,[26] strength[27] and psychosocial function,[28-31] have been observed following concussion in children.

Pathophysiology of Concussion

The biomechanical force of a concussion causes deformation of neural tissue induced by the rotational acceleration-deceleration of brain tissue.[32,33] This neural deformation causes a sequential effect altering several neurophysiological processes.[10,34] Neural deformation can include diffuse axonal injury defined as the "occurrence of diffuse damage to axons in the cerebral hemispheres,…corpus callosum,…brainstem,…and cerebellum resulting from a head injury".[35] Neural deformation and diffuse axonal injury cause disruption to the neuronal membranes resulting in widespread neuronal depolarization. This depolarization results in extracellular potassium, altered amino acid release,[10,32] and impaired mitochondrial function.[36] Together, these changes lead to altered cellular metabolism.[36] The presence of brain metabolites such as glutamate and N-acetylsparate reflect this altered neurometabolic state.[37] Evidence of neuronal depolarization following concussion have been found both acutely (< 1 week)[37] and in the subacute phase (>2 weeks).[38,39] As a result of altered neural activity and indiscriminate neural depolarization there are changes in cerebral metabolism.[32] In an effort to restore neural homeostasis, the cerebral metabolic process accelerates resulting in increased glucose usage. This process is hindered by impaired mitochondrial function, furthering the cellular energy crisis.[10] The neurometabolic changes and cerebral metabolism dysfunction results in decreased cerebral blood flow.[34] Cerebral blood flow velocity[40-42] and cerebrovascular reactivity have been found to be altered post-concussion.[43,44] These alterations in cerebral blood flow have been observed both acutely[42] and sub-acutely following concussion.[40] Alterations in the cerebral blood flow mechanisms are also demonstrated by autonomic dysfunction.[45,46] This autonomic dysfunction has been observed via heart rate variability. Heart rate variability (HRV) is used as an indirect measure of autonomic status. Higher HRV is indicative of a good balance between the sympathetic and parasympathetic systems.[47] A few studies have shown that patients recently recovered from concussion had lower heart rate variability measures compared to healthy controls.[48,49]

Recovery

The current definition of recovery is characterized by being symptom-free (at rest and with physical/cognitive exertion) and by the resolution of cognitive, physical, or psychosocial impairments,[28-31] whether compared to a pre-injury baseline or normative data.[30] The expected recovery time from a concussion in children is up to 4 weeks.[4]

Approximately 30% of children will experience persisting symptoms lasting 4 weeks or more following a concussion.[2] While it is not clear why some youth experience persisting impairments after a concussion, a number of factors have been identified that seem to predispose individuals to prolonged recovery.[50] Both injury and personal characteristics are associated with persisting symptoms. Injury factors like the severity of symptoms,[51] poor reaction time,[52] and impaired balance[2] following concussion are associated with persisting symptoms. Personal characteristics including history of concussion,[53] psychiatric conditions, anxiety, depression,[54] migraine headaches,[52] and older adolescent age,[16] have been found to predict persisting symptoms. Contradicting evidence exists for characteristics such as loss of consciousness,[50,51] female sex, and age.[2,51] While some studies have identified these three factors (loss of consciousness, female sex, and age) as contributors to prolonged recovery, other studies have found no influence on length of recovery. Further, there may be a relationship between history of concussion and length of recovery. Some studies have identified longer recovery following a second concussion,[55] while others identified no difference in recovery length between first and second concussive injuries.[23] It is acknowledged that factors unrelated to the injury can also influence length of recovery (ex. access to care,[56] co-existing injuries, conservative management[57]).

Current guidelines for management

One of the dominant forms in which concussion knowledge is generated and disseminated is through expert consensus. In 2001 the Concussion in Sport Group (CISG) was created and met for the first time to "provide recommendations for the improvement of safety and health of athletes who suffer concussive injuries in ice hockey, rugby, football (soccer) as well as other sports."[58] Since that time there have been four subsequent international conferences[4,9,59,60] intended to build on the principles from previous consensus meetings. Following each consensus meeting, publications are disseminated as a means of knowledge translation. These consensus documents are intended for use by physicians and healthcare providers for the care and management of individuals with a concussion.[4] The CISG provides information on all aspects of concussion management from immediate assessment to return to activity. In line with the evolving nature of concussion knowledge and best-practice, management strategies have changed as well. The most dramatic change that has occurred since the first consensus meeting in 2001 concerns the use of physical exercise post-concussion. The first four consensus documents clearly stated that individuals should be asymptomatic before engaging in return to activity protocols.[9,58-60] In the most recent consensus document[4] this recommendation has been revised to encourage 24-48 hours of *relative* rest. The term relative rest is purposefully used to discourage bed rest. Following 24-48 hours (of relative rest) expert consensus recommends symptom-limited activity that does not provoke symptoms.[4] This strategy differs from previous consensus statements in which activity was not recommended until an individual was asymptomatic.

There is agreement regarding the acute management of concussion.[4,61,62] The need for immediate removal from sport, preventing secondary impacts, acute physical and cognitive rest are widely acknowledged.[4,9,59,60] Because most youth recover within 4-weeks[2] this strategy is effective for most youth following concussion. Where there is limited consensus or evidence is what is the best course of action when youth experience persisting symptoms beyond the typical timeframe.

Rest

The initial approach to managing patients experiencing persisting post-concussion symptoms was to continue or re-introduce physical and cognitive rest. Rest after a concussion generally refers to restricted physical activity, mental activity (ex. school, homework) and social activity (ex. visiting with friends). From a clinical perspective, rest has been described as avoiding or limiting activities that aggravate concussion symptoms.[63]

Prolonged physical rest often means the removal from meaningful activities for children and adolescents. Further, delayed recovery and persisting deficits in youth may influence psychological outcomes.[64] Mental health symptoms can appear in the later stages of recovery which can become misattributed to the concussion itself.[65,66] As physical rest continues, physical deconditioning occurs, especially in active individuals.[67] Physical deconditioning from bed rest has been shown to induce feelings of fatigue, headache, restlessness, difficulty sleeping, mood changes, and vestibular sensitivity[68] all of which are symptoms of a concussion.[18,69] Together, prolonged rest from concussion causes removal from meaningful activity, possible increased risk of psychological outcomes, and physical deconditioning, which can increase the risk of prolonging recovery. It is possible to see how prolonged rest can perpetuate, rather than alleviate, persisting symptoms.

Theoretical rationale for acute rest

Several catalysts have triggered the recommendation for rest in the acute period. A condition called Second Impact Syndrome may have been the initial event.[70] Second Impact Syndrome is a fatal condition that can occur following two concussive blows within a short time-frame. Specifically, with the second injury occurring before recovering from the initial concussive injury.[71,72] This syndrome, although extremely rare, has been most often reported in boxing.[71] The potential for a concussion to lead to mortality caused dramatic changes in the immediate management process. Strong recommendations were made indicating that any individual suspected of a concussion should be immediately removed from sport.[4,9,59,60,71] While preventing poor outcomes was a stimulus to recommending rest, support was also gleaned from the animal model.

Evidence from the animal model demonstrated that a period of rest was needed before introducing physical activity. After an experimental injury, rats were housed in one of two conditions. One group was given access to a running wheel immediately, while the other was delayed 14 days. Those rats who exercised immediately following injury demonstrated a delayed recovery. The group with a period of rest prior to physical activity demonstrated better cognitive performance and better molecular response compared to the acute exercise group.[73] This period of rest prior to physical activity was reinforced with evidence that the severity of injury influenced the amount of time needed before exercise.[74] While the animal model demonstrated guidelines about the timing of rest before exercise, evidence in humans is less clear.

Several studies have evaluated the influence of rest on concussion recovery in humans. Studies generally define rest as restricted school, extracurricular, and physical activity.[19,75] The length of rest varied between studies ranging from 1-2 days[75,76] to as much as one week.[77,78] Rest has been prescribed in both the acute phase,[19,75,76] and sub-acutely when symptoms persisted.[77,78] Results are conflicting regarding the effectiveness of rest on concussion recovery. It is difficult to consider the studies together with the amount of variability that exists between studies (ex. time since injury, length of rest, severity of injury). A significant improvement in symptoms and cognitive function was found following 1 week of prescribed rest.[77,78] All other studies have found rest to either have mixed results,[19] no effect,[30] or to have a detrimental influence.[75,76]

Most studies evaluating rest have used a retrospective design.[30,77,78] Only one study has used a randomized trial design.[75] The initial analyses found that patients who engaged in cognitive and physical rest for five days had slower symptom resolution compared to those that rested for one to two days.[75] A secondary analyses revealed that the influence of rest was dependent on the type of signs and symptoms present at the time of injury. Those patients who showed signs of injury (ex. Loss of consciousness, post-traumatic amnesia, confusion/disorientation) benefited from rest while those with predominantly symptoms did not.[19]

The most challenging aspect of understanding if rest has an impact on concussion recovery is compliance to the intervention. In most studies it is not possible to know the extent to which participants rested due to the retrospective design.[30,77,78] In a randomized trial by Thomas et al., activity diaries were used to measure daily energy expenditure. This study identified that the intervention and control groups did not actually differ in physical activity energy expenditure. There was however a difference in mental activity. Despite the intervention group receiving instruction for strict rest, participants may have self-managed and rested as they felt was needed.[75]

Theoretical rationale for exercise

It is proposed that exercise has a positive impact on concussion recovery (in the sub-acute phase) through i) physiological mechanisms and ii) their influence on symptoms.

Exercise and concussion physiology

Diffuse axonal injury, from concussion, results in impaired mitochondrial function.[10,34,36] Aerobic exercise has been found to increase mitochondriogenesis,[79,80] the process by which new mitochondria are formed.[81] Evidence in the animal model has demonstrated that there is a beneficial effect of exercise on mitochondria in the brain as well.[82,83] Eight weeks of treadmill running in rats increased mitochondriogenesis, evidenced by the presence of greater mitochondrial DNA in several brain regions compared to controls. Exercise also influences brain neurotransmission.[84] It has been proposed that the physiological systems in the body are self-regulating in that they self-correct through feedback.[80]

Autonomic dysfunction, indicated by decreased parasympathetic and increased sympathetic activity, has been observed following concussion.[45] Acute aerobic exercise has been found to produce an opposite effect, increasing parasympathetic and decreasing sympathetic activity.[85,86] In a study of sedentary male adults (n=7), steady state cycling exercise for five minutes at 21% of maximum HR demonstrated a significant increase in low frequency HRV,[87] which has been found to be decreased during cycling exercise following concussion.[45] Both a single bout of exercise[85] and recovery from acute exercise have shown a beneficial influence on autonomic function.[87] Autonomic nervous system function is influenced by acute exercise, during recovery from exercise, and is intensity dependent.[88] These are important considerations when determining the appropriate duration and intensity of aerobic exercise for concussion interventions.

The influence of exercise following concussion may be related to its impact on cerebrovascular reactivity and cerebral blood flow. Aerobic exercise has been shown to increase cerebral blood flow.[89] A study of eleven healthy males (mean age: 34 years) identified increases in blood flow velocity in the middle cerebral artery following six minutes of supine cycling exercise. Significant increases in blood flow velocity occurred with workloads between 20% and 60% of maximum capacity. This study also revealed that blood flow velocity decreased below the level of pre-exercise following strenuous exercise (80-90% of maximum).[90] This finding (reflexive decrease in blood flow) may shed light on why moderate/vigorous exercise appears to aggravate recovery from concussion. The recovery rate of cerebral blood flow to pre-exercise levels was not determined in this study but this is an important factor to consider ensuring an appropriate workload. In a study of 14 adults (mean age: 26 years) a statistically significant increase in mean blood flow velocity in the middle cerebral artery was observed after ten minutes of cycling exercise compared to rest.[91] Aerobic exercise has also been found to induce angiogenesis, the development of new blood vessels, which has a positive impact on cerebrovascular reactivity.[80] Exercise induces acute and chronic influences on cerebrovascular reactivity that could positively influence recovery from concussion.

Exercise and concussion symptoms

As previously outlined, concussion symptoms can be classified into four categories; somatic, cognitive, emotional, and sleep related.[20] Because exercise has been found to positively influence a number of systems,[92] it is well suited as a treatment for concussion symptoms, which are broad in nature.

Somatic symptoms can include; headache, dizziness, nausea, sensitivity to light and noise, balance and visual problems. Many somatic symptoms (dizziness, balance and visual problems) are attributed to vestibular dysfunction.[93,94] While the cause of somatic symptoms is open for debate, some theorists propose that physiological changes underpin symptoms of headache, sensitivity to light and noise.[10,95] Regarding headaches, there is evidence to suggest that aerobic exercise is associated with improvements in migraine intensity, frequency, and duration.[96-98]

Cognitive symptoms following a concussion can include; difficulty concentrating, difficulty remembering, getting confused with directions or tasks, answering questions more slowly, and feeling mentally "foggy".[99] A systematic review found that aerobic exercise in youth was positively associated with cognition.[100] A meta-analysis revealed that acute physical exercise enhances executive functioning.[101] Improved cognitive function has been observed after an individual session of 20 minutes of stationary cycling. This cycling session also produced significant elevations in brain derived neurotrophic factor (BDNF), a substance that plays a central role in the health of neurons.[102] Elevations in BDNF have been found following treadmill running in rodent studies. Increased BDNF levels positively influence brain plasticity, which is linked to improved cognitive function.[103] The short-term effect of aerobic exercise has also been demonstrated following 40 minutes of treadmill running, which induced improvements in decision making.[104]

Emotional symptoms after concussion can include; irritability, sadness, nervousness, and feeling more emotional.[99] Patient-reported depressive symptoms have been reported in athletes with persisting concussion symptoms. The severity of those symptoms correlated with imaging findings in areas implicated in depression.[105] Exercise positively influences emotion by reducing symptoms of anxiety, depression, and stress.[80] A meta-analysis revealed that both state and trait anxiety are improved with acute aerobic exercise.[106] Increased positive mood (vigor and exhilaration) has been reported after only eight minutes of low-intensity exercise.[107]

Sleep related disturbances following concussion include; difficulty falling asleep, sleeping more than usual, drowsiness, and fatigue. Adolescents who are more active report higher sleep quality, less daytime tiredness, and increased concentration during the day.[108] Exercise performed 4-8 hours prior to bedtime has the ability to improve sleep onset and decrease nighttime waking.[109] Similarly, 30-60 minutes of treadmill running performed 2 hours before bedtime improved sleep efficiency.[110]

While the beneficial effects of exercise are well known, there remains a great deal to understand about the effect of exercise following concussive injury. Some have proposed that exercise facilitates endogenous repair mechanisms[111] or that external activation stimulates recovery.[112] Initial studies using exercise-based interventions have suggested various mechanisms to aid recovery.

Exercise-based interventions for concussion management

In 2009 the first study using an exercise-based intervention for youth with persisting post-concussion symptoms was published. The exercise-based intervention was coined "Active Rehabilitation" which included aerobic exercise, coordination drills, visualization, and education.[7] This concussion management strategy was significant for two reasons. First, it was the initial study to use physical activity for patients who were symptomatic, which had been discouraged by expert consensus groups.[59,60] Second, the study addressed a specific subgroup of patients who were experiencing persisting symptoms beyond what would be considered a typical recovery period.

Around the same time similar work was being conducted in adults.[113] Although both models targeted similar populations (patients experiencing persisting symptoms) with similar approaches (exercise-based), their underlying principles differed. Broadly, Gagnon et al., identified the beneficial effect of exercise on mental health related symptoms compared to a more physiological based rationale presented by Leddy et al.[113] Gagnon et al., highlight the non-specificity of concussion symptoms, the impact of withdrawal from physical activity, and the influence of physical exercise on mental health, as guiding principles for their intervention.[7] Leddy et al., propose that persisting symptoms result from physiological dysfunction thus impairing cerebral regulation. As a result, they propose that aerobic exercise increases parasympathetic activity, reduces sympathetic activation, and improves cerebral blood flow.[113] In spite of gaps in our understanding of the mechanism by which exercise may aid concussion recovery, both theories provide support for an innovative approach to concussion management for patients with persisting symptoms.

Thus far, results have been positive for the use of exercise-based strategies for concussion management.[114,115] Significant improvements in post-concussion symptoms have been observed.[7,31,116-118] In studies with safety objectives, no safety concerns were reported,[119] or equal numbers of adverse events were found.[120] Limitations arising from exercise-based interventions for concussion stem from the methodology. Lack of a control group is the most common limitation. It is not clear if studies were adequately powered for statistical testing given that only one study cited a sample size calculation.[117] Few retrospective studies were able to establish consistent assessment time points, nor did they account for time from injury until the time of the intervention in their analyses.[7,118,119] Although one study collected objective data for participants activity level using actigraphy,[121] no study has examined the influence of exercise characteristics on recovery. Few studies have reported the level of adherence to prescribed exercise.[118,121] Only two studies have included outcomes related to safety and tolerability.[119,120] Although safety is commonly discussed regarding exercise-based interventions, few have outlined strategies to measure safety or reported on safety objectives.

Chapter 3 – Objectives

The global objective of this PhD thesis was to contribute evidence towards an exercise-based concussion management approach for youth with persisting symptoms. Two broad lines of inquiry were pursued to achieve this global objective:

1. To understand current practice in the use of exercise-based interventions. The main purpose was to explore interventions in the scholarly literature and estimate if and how clinicians use these interventions in practice. This line of inquiry was undertaken to provide foundational knowledge, determine the clinical applicability of available interventions, and identify possible knowledge translation needs.
    a. To summarize the extent, nature, and quality of current evidence for the use of non-pharmacological rehabilitation interventions following concussion or mild traumatic brain injury in children.
    b. To identify clinical practice habits of Canadian Athletic, Occupational, and Physical Therapists when providing care for youth experiencing persisting symptoms from a concussion.

2. To estimate the effectiveness of an exercise-based intervention in decreasing post-concussion symptoms. The main purpose was to address limitations specific to previous work using exercise-based interventions. This line of inquiry was undertaken to estimate the clinical reproducibility of previous findings and generate new knowledge regarding the timing of implementation
    a. To estimate the extent to which post-concussion symptoms were influenced by participation in an Active Rehabilitation intervention for children and adolescents who are slow to recover from concussion.
    b. To estimate the time frame upon which initiating an active rehabilitation protocol post-concussion contributed to a greater decrease in symptoms at follow-up.
    c. To estimate the feasibility, safety, and acceptability of active rehabilitation starting 2-weeks post-concussion compared to 4-weeks (usual care).

Chapter 4 – Introduction to Manuscript I

The purpose of the first study in this doctoral thesis was to gain an understanding of the current state of the scholarly literature. Specifically, to summarize the extent, nature, and quality of studies using rehabilitation interventions for youth following concussion. The scoping review, presented in chapter 5, was undertaken as a starting place to inform our work.

To date, rehabilitation reviews have focused on adult populations,[122] and those limited to youth have lacked comprehensive search strategies.[123] Specifying the age group of our search was important because research has shown that children and youth differ in how they experience and recover from concussion compared to adults.[124]

Because rehabilitation interventions are an emerging area of concussion research we felt it was necessary to take a broad approach to the research question. This approach allowed us to understand the methodological approaches that have been used and explore trends in the literature. By extending beyond exercise-based interventions, we were able to explore limitations in the field with the aim of addressing them in future studies. Further, there was clarity regarding how other interventions influenced concussion recovery, allowing us to contextualize the research specific to exercise interventions.

Chapter 5 – Manuscript I

Title: Non-pharmacological rehabilitation interventions for concussion in children: A scoping review

Danielle Dobney[1], Matthew Miller[2], MSc., Emily Tufts[3]

1. School of Physical and Occupational Therapy, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.
2. Department of Exercise Science, Faculty of Arts and Science, Concordia University, Montreal, Quebec, Canada
3. Centennial College Libraries, Toronto, Ontario, Canada

Running Head: Concussion interventions scoping review

Article Category: Review

Declaration of Interest: The authors report no conflicts of interest.

Corresponding Author:

Danielle Dobney
Danielle.dobney@mail.mcgill.ca
3654 Prom Sir-William-Osler
Montréal, Québec H3G 1Y5
Fax: 514-398-6360

Published in: Disability and Rehabilitation 2017: 1-13

Abstract

Purpose: The purpose of this scoping review was to summarize the extent, nature and quality of current scholarly literature related to non-pharmacological, rehabilitation interventions following concussion or mild traumatic brain injury in children.

Methods: A scoping review of primary research was performed. An electronic literature search was conducted from the following databases from 1987 - October 24, 2017 MEDLINE, CINAHL, Psych Info, and SPORTdiscus. Studies were included if they met the following criteria; 1) full text, peer reviewed and written in English, 2) reported on original research, 3) a diagnosis of concussion or mild traumatic brain injury, 4) described the evaluation of a treatment or intervention, 5) the primary outcome was a concussion impairment, and 6) the mean or median age of participants in the study was under 19. Studies were also identified through hand searching the reference list of included articles. The review process involved five steps: 1) identifying the research question; 2) identifying relevant studies; 3) study selection; 4) charting the data; and 5) collating, summarizing and reporting results. Quality assessment using the Down's and Black criteria was conducted.

Results: Twenty-six studies published between 2001 and 2017 were identified and met inclusion criteria for the scoping review. Study designs included randomized trials, retrospective case series and chart reviews, cohort, prospective pre-post, and cross sectional. Articles reported on both concussion and mild traumatic brain injury using the following interventions; rest, active rehabilitation, aerobic exercise, physical exertion, full-body stretching, vestibular, oculomotor, cervicospinal therapy, education, early intervention, telephone counselling, mobile health application, Web-based Self-Management Activity-restriction and Relaxation Training program, multimodal impairment based physical therapy, cognitive behavioral therapy, transcranial direct current stimulation, and acupuncture.

Conclusions: The literature describing non-pharmacological interventions following concussion in children is scarce. While both positive and negative results were obtained, there were methodological concerns in most studies limiting the ability to draw conclusions. Interventions incorporating aerobic exercise show promise as an effective concussion management strategy. There is a need to conduct more high-quality studies (ex. Randomized controlled trials) in this area to understand which rehabilitation interventions offer benefit over usual care.

Keywords: brain concussion, mild traumatic brain injury, rehabilitation, scoping review

Introduction

Concussion is "a brain injury…defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces".[125] As the most under-reported type of brain injury,[14] the approximate incidence rate in Canadian children under age 14 is estimated at 200 per 100,000.[12] Even though many people do not seek treatment in the hospital setting,[56] this injury is among the top two causes of hospitalization among Canadian children ages 5-19.[11]

This complex injury results in an equally complex set of impairments. The causal pathway of the acute and chronic effects of concussion are not clear.[10] The most agreed upon and established acute impact of concussion is the presence of a set of clinical symptoms.[17,18] However, symptom endorsement varies between individuals based on injury severity, patient, and injury characteristics.[126] Research specific to children has revealed impairments in neurocognition,[22] working memory,[23] visual processing,[24] balance,[25] visuomotor performance,[26] and strength[27] following concussion.

The long-term consequences of concussion are not clearly understood.[127-129] Children and adolescents do not experience or recover from concussion in the same way as adults.[130,131] Much of the preliminary research on this topic was conducted in university athletes or in professional sport. As a result, there is limited information on children, and how a concussive injury during a period of significant growth and development may be influenced.[130] An array of structural and functional changes may be influenced by concussion.[10] The young brain, which undergoes structural changes during this time, may be more susceptible to injury due to the immaturity of the nervous system.[132] From a cognitive perspective, important functions like concentration, problem solving and memory patterns are developing in a non-linear fashion in children and adolescents.[133] Injury during a pivotal period of growth could have deleterious long term effects.[133] There is evidence to suggest that concussion during this time may have long term implications for learning and mental health.[134] Initially, similar tools and procedures were used to assess children and adults. The full extent of the consequences of a concussive injury during childhood may not yet be known.

There is no mutually agreed upon definition of what constitutes recovery from concussion. In general, recovery is characterized by being symptom-free, as well as by the resolution of neuropsychological impairments,[28-31] whether compared to an existing baseline or normative data.[30] Although the majority (80-90%) of people recover from concussion within 7-10 days, there is evidence to suggest that this timeframe may be longer in children.[59] The rate of resolution of concussion impairments (e.g. symptoms, neuropsychological performance, balance) varies between individuals and even subsequent injuries.[55]

There are few evidence based guidelines for the treatment of concussion-related impairments in children or adolescents.[135] Research to date has been impeded by several factors; 1) a lack of a causal pathway regarding concussion impairments,[136,137] 2) the vulnerability of the brain post-concussion and potential risk of prolonging recovery with improper care,[138] and that 3) this population is difficult to study given that most concussions resolve relatively quickly.[29] Even though some rehabilitation or treatment interventions have been modeled after those in traumatic brain injury, they may not be applicable.[122] Establishing interventions that could benefit from further study is important in developing areas of research.

Methods

The approach for this scoping review was guided by the framework of Arksey and O'Malley; 1) Identifying the research question, 2) Identifying relevant studies, 3) Study selection, 4) Charting the data, and 5) Collating, summarizing, and reporting the results.[139] Recommendations based on the work of Levac, Colquhoun and O'Brien were used to clarify the scope and purpose of inquiry.[140,141] Quality assessment is not a component of the Arksey and O'Malley framework.[139] Recent investigations regarding scoping reviews suggest the inclusion of a quality assessment with a validated instrument.[141,142] The inclusion of a quality assessment was conducted to provide adequate information for future research recommendations.[142] Each study was independently assessed for methodological quality by the first and second authors per criteria outlined by Downs and Black. These criteria are suited to randomized and non-randomized studies of health care interventions.[143] Each study was rated on the total score, out of a possible 28 points, as excellent (24–28 points), good (19–23 points), fair (14–18 points), or poor (<14).[144] The first and second author met to discuss the quality assessment scores. When the quality assessment rating of an article differed based on category ratings (e.g. Poor, fair, good, excellent), the quality assessment was reviewed, and consensus was reached.

Stage 1: Identifying the Research Question

The purpose of this scoping review was to summarize the extent, nature and quality of current evidence to identify future research priorities. The research question addressed in this scoping review was; Among children and adolescents with a diagnosed concussion or mild traumatic brain injury (mTBI), what is the current evidence supporting the use of non-pharmacological rehabilitation interventions for the resolution of concussion/mTBI impairments?

For the purpose of this study children/adolescents were classified as under the age of 19, which is consistent with the definition proposed by the World Health Organization.[145] Non-pharmacological interventions excluded the administration of any drug or medication. Concussion impairment was defined as any negative impact from concussion or mTBI including, but not limited to, symptoms, cognitive function, neuropsychological function, motor function/performance, and/or balance. Concussion impairments were considered impaired by comparison to the individual or a normative sample. These broad definitions allowed for flexibility upon which to undertake the scoping review.

Stage 2: Identifying Relevant Studies

An electronic literature search was conducted to identify studies for scoping review from the following databases; MEDLINE (1996 – October 24, 2017), EMBASE (1996 – October 24, 2017), CINAHL (1987 – October 24, 2017), Psych Info (1987 – October 24, 2017), and SPORTdiscus (1970 – October 24, 2017). A research librarian (ET) was consulted to develop the search terminology and search strategy. To search for articles evaluating non-pharmacological interventions for the resolution of concussion impairments in children/adolescents, the following search terms were used: (‘brain concussion’ [MeSH] or ‘post-concussion syndrome’ [MeSH] or ‘concussion’ [tw] or ‘mild traumatic brain injury [tw]) and (‘rehabilitation’ [MeSH] or ‘physical therapy modalities’ [MeSH] or ‘exercise therapy [MeSH] or ‘rehabilitation’ [tw] or ‘physical therapy' [tw] or 'physiotherapy' or 'exercise therapy' [tw]) and (child* or boy or boys or girl or girls or school-age* or youth* or preteen* or pre-teen* or teenage* or teen-age* or adolesc* or prepubescen* or pre-pubescen* or pubescen* [tw]). Rehabilitation and therapy subheadings were used when available. The age range was limited to zero to 18 years. Table 1 provides the MEDLINE search strategy used for this review. References of selected articles were hand searched for relevant studies. Citations from each database search were imported into Endnote X7.7 and duplicate references were removed.

Table 1: Medline Search Strategy

#	Search Statement
1	Brain Concussion/
2	Post-Concussion Syndrome/
3	concuss*.tw.
4	mild traumatic brain injur*.tw.
5	1 or 2 or 3 or 4
6	(rh or th).fs.
7	exp Physical Therapy Modalities/
8	exp Exercise Therapy/
9	Rehabilitation/
10	rehabilit*.tw.
11	(physical therap* or physiotherap* or exercise therap*).tw.
12	6 or 7 or 8 or 9 or 10 or 11
13	5 and 12
14	(child* or boy or boys or girl or girls or school-age* or youth* or preteen* or pre-teen* or teenage* or teen-age* or adolesc* or prepubescen* or pre-pubescen* or pubescen*).tw.
15	13 and 14
16	limit 13 to "all child (0 to 18 years)"
17	15 or 16

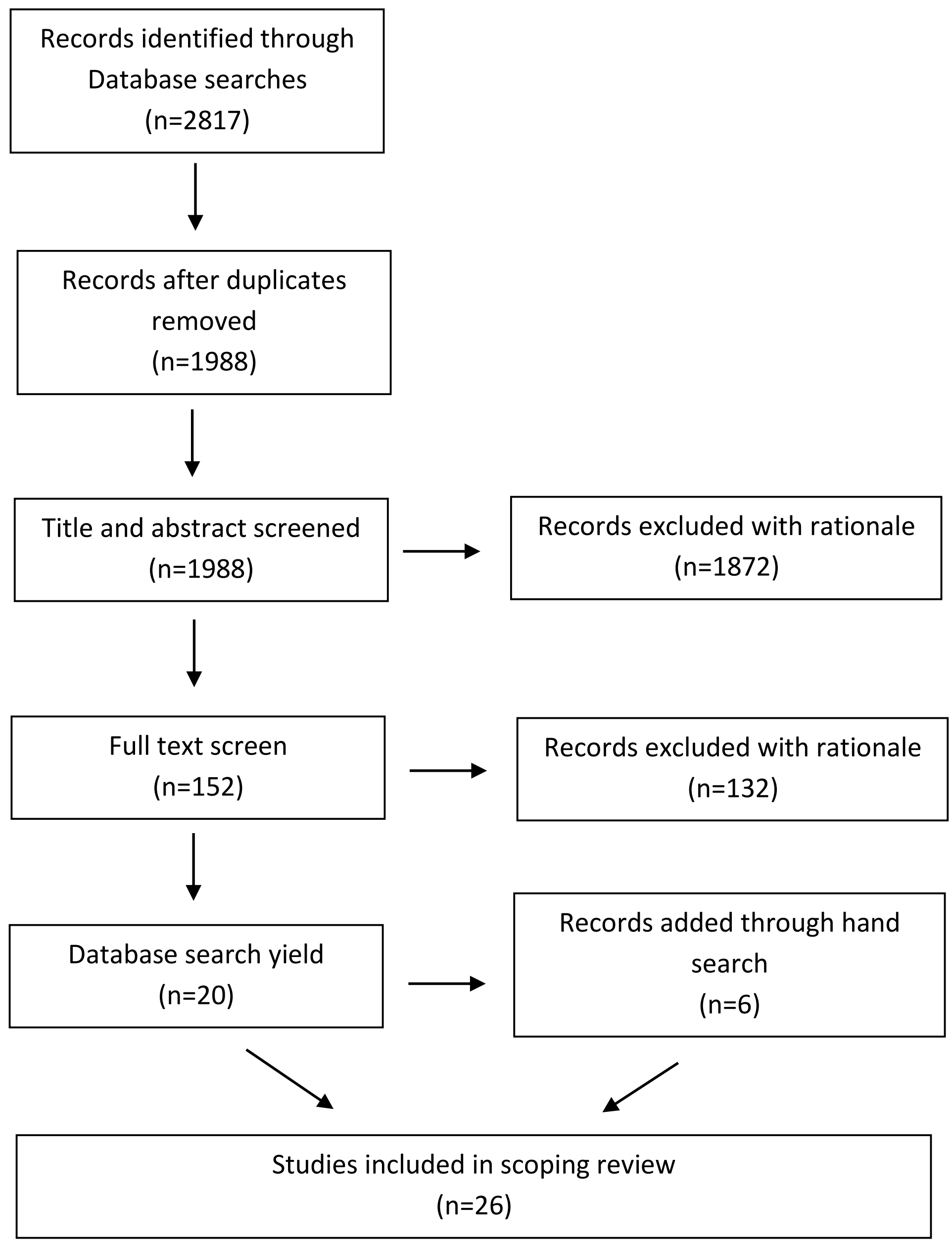
Stage 3: Study Selection

Title and abstract screening was performed independently by the first and second authors. The first and second authors independently reviewed articles for inclusion based on the following criteria; 1) full text, peer reviewed and written in English, 2) reported on original research, 3) a diagnosis of concussion or mTBI, 4) described the evaluation of a treatment or intervention, 5) the primary outcome was a concussion impairment, and 6) the mean or median age of participants in the study was under 19.

The database search identified 2817 potential articles for inclusion. After removing duplicates, 1988 articles remained. The title and abstract of each article was screened and 152 articles were identified for full text screening. Twenty articles met the inclusion criteria and an additional six articles were identified through hand searching. A PRISMA flow diagram[146] was prepared with details of articles included at each stage of the search process (figure 1).

The first author (DD) hand searched the articles selected from full text screening and identified an additional six studies. The second author (MM) verified the hand searched articles met inclusion criteria. Authors (DD and MM) met to discuss any discrepancies for study inclusion and came to consensus on included studies. A total of 26 studies were selected.

Figure 1: PRISMA flow diagram



Type of study designs used

Several study designs were considered for this scoping review except those reporting on single case studies. There is a dearth of evidence in the concussion literature regarding interventions.[135] Including only randomized control trials would result in too few studies to provide sufficient breadth and would not accurately summarize the extent of current research.[135] These criteria were utilized to provide adequate depth for the scoping review.

Stage 4: Charting the Data

A data extraction table was compiled. Study details for each article included; author and year of publication, study design, participant characteristics, inclusion/exclusion criteria, type of intervention, outcome measure(s), key findings, and the Down's and Black quality rating (table 2).

Table 2: Data extraction table

Author/ year	Study design	Participant Characteristics	Inclusion/Exclusion criteria	Type of Intervention	Outcome measure(s)	Key findings	Downs and Black Quality Rating
Ponsford et al., 2001	Four Groups, pre-test post-test design	mtBI Treatment group (*n*=61) Mean age ± SD: 11 ± 2.6 % Male: 71 mTBI control group (*n*=58) Mean age ± SD: 11.4 ± 3.2 % Male: 81 Orthopedic injured treatment group (*n*=45) Mean age ± SD: 10.9 ± 2.4 % Male: 67 Orthopedic injured control group (*n*=47) Mean age ± SD: 12.3 ± 2.1 % Male: 60	Inclusion: Diagnosed mTBI, LOC <30min, PTA<24 hrs., GCS 13-15 Exclusion: Focal neurologic signs	Goal: Evaluate impact of providing education (information booklet) on post-concussion symptoms, cognitive performance and psychological adjustment at 1 week and 3 months. Intervention: Information booklet provided 1-week post-injury. Control group: no treatment	Child Behaviour checklist, Rowe Behavioural Rating Inventory, Post-Concussion Syndrome Checklist, Peabody Picture Vocabulary Test, Wide Range Assessment of Memory and Learning, Wechsler Intelligence Scale for Children-III Digit Span and coding subtests, the 2.8-second pacing of the Children's Paced Auditory Serial Addition Task, Contingency Naming Task	Parents of mTBI intervention group reported significantly better post-concussion symptoms, and behaviour following intervention compared to mTBI controls at 3 months. *Did not address stated aim of study at 1 week (3 months only).	Fair
Gagnon et al., 2009	Retrospective cohort study. Single group, pre-test post-test design	Treatment group (*n*=16) Mean age ± SD: 14.5 ± 2.3 % Male: 68.75	Inclusion: Diagnosed concussion with persisting symptoms for 4 weeks Exclusion: none provided	Goal: Evaluate impact of active rehabilitation (Aerobic training, coordination, visualization & imagery, home program.) on children who are slow to recover.	Post-concussion symptom checklist, Bruininks-Oseretsky Test of Motor Proficiency (balance and coordination), neurological examination, physical examination	Symptoms (Mean ± SD : 30 ± 20.8) significantly improved post-treatment (Mean ± SD: 6.7 ± 5.7)	Poor
Moser et al., 2012	Retrospective cohort study , pre-test post-test design	Treatment group (*n*=49) Mean age ± SD: 15 ± 2.6 % Male: 67	Inclusion: Diagnosed concussion Exclusion: None provided	Goal: Retrospectively evaluate impact of cognitive and physical rest post-concussion symptoms and verbal memory, visual memory, processing speed and reaction time.	Concussion symptom scale, ImPACT (composite indices – verbal memory, visual memory, processing speed, reaction time)	Significant improvement in total symptoms and cognitive function.	Fair
Gibson et al., 2013	Retrospective chart review, single group cohort study	Treatment group (*n*=135) Mean age ± SD: 15 ± 3 % Male: 72	Inclusion: Diagnosed sport related concussion, symptom free at end of study period. Exclusion: Incomplete medical record, alternate diagnoses considered, not recovered by end of study period, more severe injury mechanism.	Goal: Retrospectively evaluate impact of cognitive rest on duration of symptoms. Intervention: Cognitive rest	Time to symptom resolution (Post-concussion symptom scale)	No significant relationship between prescribed cognitive rest and time to symptom resolution.	Fair

Pinchuk et al., 2013	Retrospective	Treatment group (*n*=44*) Mean age (SD): 13.6 (2.5) % Male: 86 *adolescent patients only	Inclusion: Chronic post-traumatic headache after a mild head injury Exclusion: None provided.	Goal: Provide a retrospective analysis of the results of the treatment of patients with HA by means of transcranial direct current stimulation (tCDS) with various localizations of stimulating electrodes on the scalp in patients with chronic post-traumatic headache after mild head injury.	Numerical Rating Scale (NRS), Number of days with headache per month, headache attack duration, headache intensity and duration, amount of analgesics used, depression, and anxiety scale parameters.	Significant improvement in pain rating, number of headaches per month, and attack duration after tDCS. tDCS had no effect in 20% of patients.	Fair
Schneider et al., 2014	Randomized Controlled trial	Treatment group (*n*=15) Median age (range): 15 (12-27) % Male: 73 Control group (*n*=16) Median age (range): 15 (13-30) % Male: 44	Diagnosed concussion, persistent symptoms >10 days of dizziness, neck pain and/or headaches, vestibular/cervical spine involvement Exclusion: Fracture, neurological conditions, musculoskeletal injury, medication affecting neural adaptation	Goal: Evaluate the influence of vestibular and cervical spine treatment on time to return to sport. Intervention: Cervical spine physiotherapy, vestibular rehabilitation. Control group: Non-provocative range of motion exercises, stretching, postural education (common to both groups).	Number of days from initiation of treatment until medical clearance to return to sport.	Significantly higher proportion of participants in intervention group (73.3%) returned to activity within 8 weeks compared to control (7.1%).	Good
Gagnon et al., 2015	Retrospective cohort study. Single group, pre-test post-test design	Treatment group (*n*=10) Mean age ± SD: 16.1 ± 1.2 % Male: 70	Inclusion: Diagnosed concussion with persisting symptoms for 4 weeks, not medically cleared to begin return to activity protocol Exclusion: Cervical, oculomotor, and/or vestibular impairment	Goal: Improvement of post-concussion symptoms and functioning. Intervention: Aerobic training, coordination, visualization & imagery, home program.	Post-Concussion Scale, Beck Depression Inventory, Pediatric Quality of Life Multidimensional Fatigue Scale, Body Coordination composite of the Bruininks-Oseretsky Test of Motor Proficiency, ImPACT	Significant improvement of post-concussion symptoms, depression, energy level and processing speed post-intervention.	Fair
Lynch et al., 2015	Case Study	Treatment group (*n*=2) Age range: 14-15 years % Male: 50	Inclusion: Post-concussion syndrome, visual complaints Exclusion: None provided	Goal: Report on a novel intervention using computer gaming glasses with 2 adolescents who had post-concussion syndrome.	ImPACT	Computer gaming glasses markedly lessened symptoms in both patients.	Poor
Maerlender et al., 2015	Randomized Pilot Study	Treatment group (*n*=13) % Male: 38 Control group (*n*=15) % Male: 20 Mean age: 19 years	Inclusion: Diagnosed concussion Exclusion: Injury severity could not prevent participation in protocol.	Goal: Determine the effect of moderate levels of physical activity on recovery from concussion.	Post-Concussion symptom return to baseline, ImPACT, neurocognitive test battery, Borg RPE.	No significant difference between groups on days until symptom recovery. Increased average daily vigorous activity associated with longer recovery time.	Fair
Moser et al., 2015	Cohort study. Single group, pre-test post-test design	Treatment group (*n*=13) Mean age ± SD: 15.1 ± 1.5 % Male: 57	Inclusion: Diagnosed concussion, ImPACT test within 1 month of injury, no comprehensive rest after	Goal: Improvement of neurocognitive performance and	Post-concussion symptom score total	Reported Significant improvement in post-concussion symptoms verbal memory, visual memory,	Fair

			injury, pre-intervention ImPACT completed, compliance with intervention, follow up ImPACT completed. Exclusion: none provided	concussion-related symptoms. Intervention: Comprehensive rest		reaction time, motor speed following 1 week of comprehensive rest.	
Thomas et al., 2015	Randomized controlled trial	Treatment group (*n*=45) Median age (IQR): 13.1(12.1-14.5) % Male: 64 Control group (*n*=43) Median age (IQR): 14.7(13-15.5) % Male: 67	Inclusion: Diagnosed concussion, presented to ED within 24 hours of injury. Exclusion: Non-English speaking, intellectual disability, mental defect/disease, intracranial injury, no legal guardian present, admitted to hospital.	Goal: To assess effect of rest on concussion symptoms, neurocognitive and balance performance Intervention: 5 days rest Control group: usual care (24 - 48hrs rest)	ImPACT, Balance error scoring system (BESS)	Intervention group reported higher total post-concussion symptoms and number of symptoms compared to usual care.	Good
Cordingley et al., 2016	Retrospective Chart Review	Treatment group (*n*=106) Mean age (range): 15.1 (11-19) % Male: 43.4	Inclusion: Diagnosis of sport related concussion or post-concussion syndrome, <19 years of age. Exclusion: Non-sport related concussion, Moderate to severe TBI, traumatic abnormalities detected on clinical neuroimaging.	Goal: Evaluate the safety, tolerability, and clinical use of graded aerobic treadmill testing in pediatric patients with sports-related concussion	PCSS, Tolerability (% needing to stop), Safety (% needing immediate medical attention)	97.9% tolerated treadmill test, no patients requiring immediate medical attention, 90% participants experienced clinically improved symptoms, 80% returned to sport.	Fair
Grabowski et al., 2016	Retrospective cohort study	Treatment group (*n*=25) Mean age (range): 15 (12-20) % Male: 44	Inclusion: Post-Concussion Syndrome diagnoses, > 12 years Exclusion: Symptoms less than 3 or over 36 weeks, less than 2 Physiotherapy visits	Goal: Assess whether an impairment-based treatment (subsymptom threshold exercise and comprehensive physiotherapy) plan could safely treat post-concussion symptoms.	Post-concussion symptom scale (PCSS), BESS, symptom-free exercise duration, and Symptom Free Heart Rate (HR) during exercise.	Significant improvement in symptoms from mean 18.2 at initial visit to 9.1 at final visit. Symptom free HR increased significantly. Significant improvement in BESS	Fair
Hugentobler et al., 2016	Retrospective Case series	Treatment group (*n*=6) Age range: 15-19 years % Male: 67	Inclusion: Consent to chart review, completed physiotherapy evaluation and 3 follow-up appointments, pre and post-treatment assessments. Exclusion: No plan to return to activity, non-compliant, abnormality on imaging, cardiovascular or neurological conditions	Goal: Describe multimodal interventions used to treat six pediatric patients with prolonged mTBI symptoms.	PCSS, return to pre-injury activity.	Four out of six patients returned to pre-injury activity.	Poor
Imhoff et al., 2016	Prospective Single group	Treatment group (*n*=15) Mean age (range) 15 (10-17) % Male: 40	Inclusion: Post-concussion symptoms lasting four weeks.	Goal: identify whether the addition of an individualized Active	Post-concussion symptom Inventory (PCSI), Rey Auditory	Significant improvement in symptoms, verbal episodic memory in total learning,	Fair

	Pre-post design		Exclusion: None provided.	Rehabilitation Intervention influences recovery of patients who are symptomatic at rest.	Verbal Learning Test, Delis-Kaplan executive function system, Digit Span from the Weschler Adult Intelligent Scale, Symbol Digit Modality Test, Continuous Performance Test II, State-Trait Anxiety Inventory, Modified Balance Error Scoring System (BESS), Modified Clinical Test of Sensory Interaction on Balance, Bruininks-Oseretsky Test of Motor Proficiency 2nd Edition (BOT2)	immediate recall, switching semantic verbal fluency, working memory, attention processes, single and tandem balance, BOT2 bilateral coordination, upper-limb coordination.	
Kurowski et al., 2016	Randomized Clinical Trial	Treatment group (*n*=15) cycling Mean age (SD): 15.22 (1.37) % Male: 33 Control group (*n*=15) stretching Mean age (SD): 15.5 (1.8) % Male: 53	Inclusion: Diagnosed mTBI, diagnosed post-concussion syndrome, symptoms exacerbated by physical activity. Exclusion: GCS <13, severe TBI, evidence of severe TBI on clinical imaging, neurologic impairment, psychological condition, cervicogenic neck pain, developmental delay, genetic disorders, metabolic disorders, hematologic disorders, ADHD requiring 2+ medications.	Goal: Describe the methodology and report primary outcomes of an exploratory RCT of aerobic training, compared to full body stretching, for management of prolonged symptoms after an mTBI in adolescents.	PCSI	Greater symptom improvement in cycling group compared to stretching	Good
Lin et al., 2016	Case Report	Treatment group (*n*=3) Mean range:8-18 years % Male: 33	Inclusion: Chronic post-concussive symptoms, no improvement with conventional treatment. Exclusion: None provided	Goal: Describe the integration of acupuncture for treating headaches and other symptoms following pediatric sport related concussion.	Numerical Rating Scale (NRS), Brief Pain Inventory (BPI), post-concussive symptoms questionnaire.	Satisfactory symptom improvement in all cases.	Poor
McNally et al., 2017	Retrospective Chart Review	Treatment group (*n*=31) Mean age (SD): 15.9 (2) % Male: 32	Inclusion: Diagnosed concussion, did not respond to first line services, intake visit between 3 weeks and 2 years post-concussion. Exclusion: None provided	Goal: Evaluate the efficacy of a brief cognitive behavioral intervention program (2-5 sessions) for children and adolescents experiencing persistent post-concussion symptoms.	PCSS, Pediatric Quality of Life Inventory, v4.0 (PedsQL), functional outcomes (school and physical activity)	Significant improvement of symptoms, PedsQL, over time, significant increase in proportion of patients returning to full school	Good
Chan et al., 2017	Randomized Controlled Trial	Treatment group (*n*=10) Mean age (SD): 15.9(1.66) % Male: 40	Inclusion: Sport-related concussion, 12-18 years old, >=4 weeks post-concussion, >= 2 persisting symptoms	Goal: Examine the safety and tolerability of an active rehabilitation (Aerobic training, coordination,	PCSS, Health related quality of life, Beck depression inventory for youth, Pediatric quality of	Greater reduction in symptoms in treatment group. In clinic symptom exacerbation occurred in	Good

		Control group (*n*=9) Mean age (SD): 15.1 (1.42) % Male: 11	Exclusion: history of developmental disorder, previous moderate-to-severe TBI, in active mental health treatment, concussion within previous 6 months of injury.	visualization & imagery, home program.) program for adolescents who are slow to recover from a sport-related concussion.	life multidimensional fatigue scale, BESS, ImPACT	30% of sample. Equal adverse events in both treatment groups.	
Chrisman et al., 2017	Retrospective cohort study	Treatment group (*n*=83) Mean age (SD) 14.9 (2.3) % Male: 43	Inclusion: Initial evaluation≥1 month & <300 days post-concussion, completed a Balke treadmill Test, seen by physical therapists in the SSTEP program at least twice. Exclusion: None provided	Goal: Explore the safety and potential benefits of a rehabilitative exercise intervention for treating youth with persistent concussion symptoms >1 month.	Change in symptoms (PCSS)	Symptoms demonstrated exponential decrease following initiation of intervention.	Fair
Dobney et al., 2017	Retrospective Case Series	Treatment group (*n*=677) Mean age (SD) 14.3 (2.3) % Male: 46	Inclusion: Symptomatic 2 weeks post-concussion, participated in Active Rehabilitation between April 2012 and March 2015. Exclusion: None provided	Goal: Estimate the time frame during which initiating an active rehabilitation intervention contributed to improvement in symptoms	Post-Concussion Scale-Revised	Significant improvements in post-concussion symptoms irrespective of start time.	Good
Dobney et al., 2017	Retrospective Case Series	Treatment group (*n*=277) Mean age (SD) 14.1 (2.3) % Male: 51	Inclusion: The patient started the Active Rehab program 3-4 weeks postinjury, follow-up appointment between 4-8 weeks post-injury. Exclusion: None provided	Goal: Estimate the extent to which post-concussion symptoms were influenced by participation in an Active Rehab	Post-Concussion Scale-Revised	Significant and clinically meaningful improvement in symptoms	Fair
Kurowski et al., 2016	Prospective open pilot	Treatment group (*n*=13) Mean age (SD) 14.3 (2) % Male: 69	Inclusion: ages 11-18 years, mTBI within 96 hours of ED presentation, English as primary language, Internet access at home, resided with a parent/legal guardian. Exclusion: history of 2 or more extra-cranial injuries, attention deficit hyperactivity disorder requiring more than 1 controlling medication, other pre-existing conditions that may impair baseline cognition, psychological, or developmental delays.	Goal: Evaluate the feasibility and potential benefits of an interactive, Web-based intervention for mTBI.	PCSS, patient reported activity (mental, physical, screen time), agreement with intervention	Significant improvement in symptoms, satisfaction with intervention was rated highly by parents and patients	Good
Mortenson et al., 2016	Randomized controlled pilot study	Treatment group (*n*=32) Mean age (Range): 11.9 (6-16)	Inclusion: Glasgow Coma Scale score of 13 or 14, observed loss of	Goal: Investigate the effectiveness and feasibility of early	PCSI, Family Burden of Injury Interview	No significant difference between the groups at 3	Good

		% Male: 75 Control group (*n*=34) Mean age (Range): 12.6 (5-16) % Male: 64	consciousness < 30 minutes, altered mental state at the time of injury; or posttraumatic amnesia < 24 hours. Exclusion: Injury required surgery or was associated with recreational drug use, prior concussion <2 years before enrollment, symptomatic from a prior concussion more than 2 years before enrollment, history of moderate or severe brain injury, significant premorbid neurological or psychiatric disorder by parental report	intervention telephone counseling with parents in limiting post-concussion symptoms and impacts on children and youth.		months postinjury in post-concussion symptoms	
Sufrinko et al., 2017	Randomized controlled trial (secondary analysis)	Treatment group (*n*=93) Mean age (SD): 13.87 (1.68) % Male: 64	Inclusion: 11-22 years, presented to the ED within 24 hours of a concussion. Exclusion: Non-English speaking, no legal guardian present, intracranial injury, admission to the hospital, unable to complete clinical assessments.	Goal: Evaluate if patients with signs of injury respond differently to prescribed rest after concussion compared with patients with symptoms only.	PCSS, BESS	Patients with predominantly symptoms were more likely to remain symptomatic after injury if prescribed rest, patients with signs of injury benefited from rest after a concussion.	Good
Worthen et al., 2017	Non-randomized, open label, controlled feasibility and efficacy	Treatment group (*n*=10) Mean age (SD): 17 (2) % Male: 30 Control group (*n*=9) Mean age (SD): 15 (2) % Male: 22	Inclusion: Pre-test symptom score of at least four points. Exclusion: Attention-deficit/hyperactivity disorder, additional injury, or illness between pre- and post-test, no self-reported barriers to compliance.	Goal: Evaluate whether a mobile health application that employs elements of social game design could compliment medical care for unresolved concussion symptoms.	PCSS, application use, satisfaction with intervention, barriers to compliance	Symptoms and optimism improved more for the experimental than for the active control cohort. High use and satisfaction with the application were reported.	Fair

Results

Stage 5: Collating, Summarizing, and Reporting the Results

Study Characteristics

Subjects in the included studies ranged in age from 5 – 19 years of age. Most studies were conducted in a hospital setting,[7,19,31,75,147-154] or concussion clinic.[30,77,118-120,155,156] Other settings included University sport medicine centres,[94,116,121,157] an outpatient research centre,[117] pediatric pain clinic,[158] and outpatient clinics.[159,160] The most common study designs included pre-test, post-test quasi-experimental designs. Most studies were retrospective in nature. There were seven randomized controlled trials.[19,75,94,117,120,121,153] Sample sizes ranged from two participants in a case study to 677 in one retrospective chart review.

Description of study outcomes

Assessment of post-concussion symptoms as an outcome measure was assessed in 25 out of 26 studies. Medical clearance to return to sport[94] and headache pain rating[159] were other outcomes. Seven studies used the ImPACT test as a main outcome.[31,75,77,120,121,155,157] Most studies used multiple outcomes including both patient report and objective performance measures. Except for post-concussion symptoms, outcome measures were consistently age appropriate. In one study a parent-proxy was used to report symptoms depending on the age of participants.[147] Measures were typically assessed pre-and post-intervention.

Interventions

Treatment or interventions evaluated in this scoping review were grouped into six categories; 1) Multimodal, 2) Rest, 3) Exercise, 4) Modalities, 5) Education and Behavioural Interventions, and 6) Manual Therapy.

Multimodal

Most studies in this scoping review were multimodal interventions.[7,31,116,118,120,151,154,160] Interventions consisted of multiple components, each including aerobic exercise. Five studies used what has been coined as 'Active Rehabilitation', first described by Gagnon et al.[7] This intervention consisted of aerobic exercise, coordination drills, visualization, and education.[7,31] Imhoff et al., modeled their intervention after Gagnon et al.,[7] using balance exercises in place of visualization and a gradual progression for aerobic exercise.[118] Two studies[116,160] used an impairment based approach in which patients received treatment based on their clinical examination. Treatment interventions included cardiovascular, musculoskeletal, postural control and vestibular/oculomotor,[116,160] sub-symptom threshold exercise, and cervical rehabilitation.[116] Outcomes among multimodal interventions included post-concussion symptoms,[7,31,116,118,120,151,154,160] balance,[7,31,116,118] and neuropsychological function.[118] Participants treated with active rehabilitation experienced significant improvements in post-concussion symptoms,[7,31,118,120,151,154] depression,[31] energy level, processing speed,[31] neuropsychological function, balance, and coordination.[118] Participants treated with an impairment-based, multimodal intervention displayed significant improvements in post-concussion symptoms, and balance.[116] Hugentobler et al., reported that four out of six participants returned to their pre-injury activities.[160]

Rest

Five studies[19,30,75,77,155] evaluated the influence of rest (cognitive and/or physical) for the treatment of post-concussion symptoms, balance, or neurocognitive performance as measured by the ImPACT test. Two studies were retrospective in nature,[30,77] one prospective single group design,[155] and 2 randomized controlled trials.[19,75] The most common length of time of rest was one week.[75,77,155] Two studies reported a positive result for the effect of rest,[77,155] two reported negative results,[30,75] and one was symptom dependent.[19]

Those studies indicating a positive influence of physical and cognitive rest were conducted by Moser et al.[77,155] Both studies examined the influence of being prescribed one week of rest on ImPACT scores (post-concussion symptoms, verbal and visual memory, processing speed and reaction time). Rest was defined as one week of abstaining from exercise, school attendance, homework, reading, computer usage, telephone, texting, videos, television, trips outside of the home and social visits in the home.[155] Participants included patients in both the acute and sub-acute phase of recovery. Participants demonstrated significant improvements in total symptoms,[77] cognitive function,[77] visual memory, reaction time, and motor speed[155] following rest.

Two studies[30,75] identified a negative influence of rest on post-concussion symptoms. Gibson et al., found that that there was no significant association between being prescribed cognitive rest and the duration of post-concussion symptoms.[30] In their study, cognitive rest was described as avoiding schoolwork, video game playing, online activities, and text messaging.[30] In a randomized controlled trial Thomas et al., compared 5 days of rest to 1-2 days of strict rest (usual care).[75] Strict rest was defined as no school, work, or physical activity.[75] Between group differences were observed for levels of cognitive activity, but not physical activity. Those participants who were assigned to 5 days of rest reported a significantly higher number and severity of symptoms in the follow-up period compared to usual care (1-2 days of rest).

The most recent study[19] evaluating patient's response to rest categorized patients according to their injury presentation. One group was characterized as having a predominantly symptom-based presentation (ex. Headache, nausea), while the other group demonstrated more signs of injury (ex. Loss of consciousness, amnesia). Those patients who benefitted most from rest were those with signs of injury, whereas patients with symptoms experienced a longer recovery following rest.

Exercise

Four studies examined the use of aerobic exercise for concussion management. Two pilot, randomized trials,[117,121] and two retrospective chart reviews[119,150] assessed the influence of aerobic exercise on post-concussion symptoms,[117,119,121,150] safety, tolerability,[119] and length of recovery.[121] Of the randomized trials, one study prescribed aerobic exercise in the acute phase (within 2 days of injury),[121] compared to patients in the sub-acute phase in the study by Kurowski et al.[117] Control groups consisted of patients with concussions undertaking full-body stretching[117] or rest.[121] Two studies used a subsymptom threshold approach to determining the exercise intensity and duration.[117,119] Those patients doing aerobic exercise in the acute phase performed 20 minutes of stationary cycling at a mild-moderate rating on a perceived exertion scale.[121] Patients engaging in aerobic exercise within 2 days of concussion did not differ on the number of days until recovery compared to controls. However, those patients with high vigorous activity had longer recovery times.[121] In the sub-acute phase, patients in the aerobic exercise group demonstrated greater symptom recovery compared to the full-body stretching group.[117] From the retrospective chart review, 97.9% of patients tolerated aerobic treadmill testing, 90% demonstrated clinical recovery, and 80% returned to sport.[119]

Modalities

Four studies,[156-159] used a modality as an intervention to treat post-concussion symptoms. These modalities included acupuncture,[158] computer gaming glasses,[157] transcranial direct stimulation (tCDS),[159] and a mobile phone app.[156] The acupuncture intervention involved the use of traditional Chinese medicine over a series of sessions that were deemed appropriate by the practitioner (the amount of treatments were not consistent between subjects).[158] The computer gaming glasses were used as a treatment tool for two subjects to reduce cortical stimulation from light and other visual stimulus. The intervention was not controlled and was used by the subject as they felt necessary.[157] The tCDS intervention involved 30-45 minutes of electrical stimulation over 5-9 sessions separated by 4-7 days.[159] The mobile phone application tracked symptoms, usage of the app, and provided a structured support network.[156]

Two studies[157,158] used a case study/report design, one study[159] used a retrospective study design, and one open label non-randomized controlled study.[156] The outcome measures used included the Numerical Rating Scale (NRS), Brief Pain Inventory (BPI), post-concussive symptoms questionnaire,[158] ImPact,[157] number of days with headache per month, headache attack duration, headache intensity and duration, amount of analgesics used, depression, and anxiety scale parameters.[159]

All four studies reported a positive effect of their intervention on post-concussion symptoms. Traditional Chinese Medicine was successful in reducing headaches in the participants, however no significance was reported.[158] The computer gaming glasses provided subjects with relief from their symptoms, and it was suggested that more research be conducted to evaluate specific parameters of their use.[157] The tCDS intervention provided significant improvement in pain rating, number of headaches per month, and attack duration,[159] it was also reported that tDCS had no effect in 20% of patients.[159] Post-concussion symptoms and optimism improved more for those patients randomized to using the mobile phone app compared to the control group.[156]

Education/Behavioural Interventions

Four studies[147,148,152,153] evaluated the influence of educational or behavioural interventions for the treatment of post-concussion symptoms. Interventions included an information booklet,[147] a cognitive behavioral program,[148] telephone counselling for parents,[153] and a Web-based Self-Management Activity-restriction and Relaxation Training program.[152]

The study designs included; four group pre-test, post-test,[147] a retrospective chart review,[148] a randomized controlled trial,[153] and a prospective open pilot.[152] The outcome measures for these interventions were the Child Behaviour checklist, Rowe Behavioural Rating Inventory, Post-Concussion Syndrome Checklist, Peabody Picture Vocabulary Test, Wide Range Assessment of Memory and Learning, Wechsler Intelligence Scale for Children-III Digit Span, and coding subtests, the 2.8-second pacing of the Children's Paced Auditory Serial Addition Task, Contingency Naming Task,[147] and Post-concussion symptom scale (PCSS),[152] Pediatric Quality of Life Inventory v4.0 (PedsQL), functional outcomes (school and physical activity).[148]

Three studies reported significant results as product of their intervention, and one found no difference between the treatment group and controls.[153] Significant improvements in post-concussion symptoms and behaviour were reported following the educational intervention.[147] Significant improvements in symptoms and PedsQL, and a significant increase in patients returning to full school were observed with a cognitive behavioural intervention.[148] Phone counselling produced no significant improvements in post-concussion symptoms compared to the control group.[153]

Manual Therapy

A single randomized controlled trial (*n*=31) by Schneider et al., evaluated the influence of an 8 week cervical and vestibular physiotherapy intervention on time to medical clearance.[94] Patients in this study were eligible if they had experienced dizziness, headache or neck pain for 10 days or more. The intervention group received cervical and vestibular physiotherapy based on their signs and symptoms. The control group received non-provocative range of motion exercises, stretching, and postural education. Patients were a mean 53 and 47 days post-concussion for the intervention and control groups respectively. The main outcome (time to medical clearance) was measured in days. A significantly higher proportion of participants were cleared to return to play in 8 weeks in the intervention group (73%) compared to the control group (7.1%). Participants in the intervention group were approximately ten times more likely to be returned to play in 8 weeks compared to controls.

Methodological Quality Assessment Results

The Downs and Black criteria assess five categories for methodological quality; 1) reporting, 2) external validity, 3) internal validity (bias), 4) internal validity (confounding/selection bias), and 5) power.[143] Based on the Downs and Black criteria, studies in this scoping review ranged from poor to good, with no study achieving an excellent rating.[144] Of the nine studies with a good quality rating, six were randomized controlled trials,[19,75,94,117,120,153] two retrospective chart reviews,[148,151] and one prospective open pilot.[152] The reporting section was generally well done in most studies. However, most studies failed to report on possible adverse events. Studies scored well on criteria related to external validity. Internal validity scores were low because, in the majority studies, participants could not be blinded to the intervention. In three studies, the assessor measuring the main outcome was blinded to the group assignment.[94,120,153] Criteria related to confounding/selection bias were low due to lack of randomization in most studies. Only two studies described power calculations demonstrating sufficient power to detect a clinically important effect.[94,117]

Discussion

Overall there are few published studies evaluating the effect of non-pharmacological interventions in children/youth following concussion. We identified 26 studies meeting our inclusion criteria. This scoping review revealed two important findings: 1) there is limited evidence regarding interventions that have been conducted in child/youth samples and 2) the quality of studies was fair in 12/26 manuscripts based on the Downs and Black criteria.

The low number of studies identified in this scoping review highlights a lack of literature on this topic. The study of concussion in children has been focused on assessment measures. Only within the last decade has the attention shifted to focus on interventions for concussion impairments. One of the major challenges of testing interventions for concussion is that there are currently no objective measures that accurately assess concussion impairments.[28,29,59,125] This issue makes it difficult to establish the effectiveness of a treatment. The inclusion criteria for this scoping review were intentionally broad to try to capture the extent of available research. Allowing various study designs was intended to broaden the scope of inquiry. Studies including an exercise component were most common in this review.

In general, the quality of manuscripts was low. There were methodological problems with most studies that led to uncertainty of findings or reported results. The measurement and timing of outcome measures was problematic in some studies. Most studies measured outcomes pre-and post-intervention. However, two studies,[7,118] measured the post-intervention at discharge, which was defined as being symptom free. A lack of control group was a common finding among articles. Each study acknowledged the inability to attribute changes in outcome to the intervention based on this design. There were two studies that included a control group in which attention to the control group and intervention was not matched.[94,147] Ponsford et al., examined the influence of providing early intervention and education to patients with a mTBI.[147] Similarly, in a randomized controlled trial examining the effectiveness of vestibular and cervical spine manual therapy[94] there did not appear to be a sham treatment for the control group to account for the influence of attention. There is evidence that personal attention, in the form of assessment or evaluation[161] and hands-on manual therapy have been known to have a treatment effect.[162] In studies examining the influence of a specific therapy or treatment, the control group needs to be matched based on time and technique, if possible, to accurately estimate the influence of the treatment. In several studies, the level of compliance to the intervention was not reported. In some cases, the retrospective design limited the ability to determine the patients level of adherence.[7,30,31,77,148,150,151,154,160] Thomas et al., used activity diaries to measure daily energy expenditure.[75] This study identified that the intervention and control groups did not actually differ in calculated energy expenditure for physical activity. However, there was a difference in mental activity. Measuring the level of adherence and compliance to a given intervention is necessary to establish effectiveness.

This scoping review has several limitations. The review was limited to peer reviewed publications in English which may have led to some articles being omitted. Regarding the methodological quality assessment, the Downs and Black criteria have equal weighting for each item.[144] This weighting may inadvertently result in a lower score, especially for non-randomized study designs.

Conclusions

The purpose of this scoping review was to summarize the extent, nature and quality of current evidence. There are some significant challenges in this field that hamper research. Concussion is a multi-faceted injury, which has uniquely individual presentations.[29] Despite positive results in most studies, low quality of these studies precludes generalizability. The uncertainty of the best approach to manage concussions is perhaps best captured by the fact that we identified interventions using opposing approaches. While some research examined the influence of rest following concussion, others examined physical exercise. A major shortcoming of treatment protocols is that they are developed as if concussive injuries are homogenous. It may not be realistic to identify a single intervention that will be an effective treatment for all children with concussion. Being able to link a given treatment to a set of clinical criteria and a method to identify which children would benefit from specific interventions would be helpful. This method was used in two multimodal, impairment-based interventions.[116,160] Further, establishing the timing of when to implement specific treatments would be a contribution to the literature. The timeframe upon which interventions were provided was highly variable between studies. We acknowledge a growing trend involving the use of exercise-based interventions for concussion management. Most studies we reviewed contained an aerobic exercise component with favourable outcomes. While variability existed with the timing, frequency, and intensity of exercise, it appears that exercise has potential benefits for promoting recovery from concussion. Currently, it is not clear which interventions offer benefit over usual care. This scoping review provided a clear picture of the extent and nature of non-pharmacological interventions in children and youth following concussion. Given that there are many challenges to conduct research in this population, the results of this review highlight the need for higher quality studies.

Chapter 6 – Integration of Manuscripts I and II

The first study (presented in manuscript I) was a scoping review of non-pharmacological interventions for children who have sustained a concussion. This review revealed a need for higher quality studies. Building a strong evidence base is important, as interventions for concussion management are relatively new. Interventions involving exercise-based strategies were most abundant and presented a promising avenue for further study. Significant limitations were identified in the reviewed literature, namely: lack of control groups, small sample sizes, and poor measurement of adherence to interventions. The lack of strong evidence creates uncertainty for clinicians providing therapeutic treatment for individuals following a concussion. We wanted to know if the lack of clarity from the literature was reflected in practitioners clinical practice habits.

In the second study (presented in manuscript II), our environmental scan explores clinical practice through the lens of practitioners. Given the changing nature of clinical guidelines and expert consensus, we wanted to identify the clinical practice habits of practitioners working with youth who present with impairments following concussion. The interest in this study stemmed from a gap in the literature. While there have been similar studies examining how physicians identify, diagnose, and manage concussions,[163-167] there was little exploring therapeutic rehabilitation. It was unclear how clinicians managed youth with persisting symptoms and what kind of strategies they used to manage these symptoms. Further, we wanted to clarify if clinicians felt comfortable providing care for youth with persisting symptoms, the type of practitioner they would refer to if needed, and ultimately if exercise-based strategies were part of their management strategies. In manuscript II we developed a survey with two clinical vignettes for Canadian Athletic, Occupational, and Physical Therapists to learn more about their practice habits. Because of our specific interest in exercise-based strategies post-concussion, we tailored our survey to explore this topic. The second manuscript is our attempt at understanding if there are gaps between practice and research to establish the need for future knowledge translation projects.

Chapter 7 – Manuscript II

Title: Concussion management practices of Canadian rehabilitation therapists

Danielle M. Dobney[1] CAT(C), MSc., Isabelle Gagnon pht, PhD[123]

1. School of Physical and Occupational Therapy, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.
2. Trauma Centre, The Montreal Children's Hospital, McGill University Health Center, Montreal, Quebec, Canada.
3. Department of Pediatric Emergency Medicine, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.

Abstract

Objective: To estimate the scope of concussion management practices used by Canadian Athletic, Occupational, and Physical Therapists. Additional exploratory objectives included estimating the type of treatment provided and the use of aerobic exercise.

Design: Cross sectional online survey

Setting and Participants: Members of three Canadian health care associations (Canadian Athletic Therapists Association - CATA, Canadian Association of Occupational Therapy - CAOT and Canadian Physiotherapy Association - CPA) were invited to participate.

Intervention: not applicable

Main outcome measure: An online survey was developed for the project. Two clinical vignettes were provided with a brief history including; details of an injury, the current symptom score of the patient, and information about school and physical activity. Respondents were asked questions related to the type of treatments they would provide each patient (e.g. manual therapy, education, aerobic exercise, return to learn/play protocol, goal setting etc.).

Results: The survey was completed by 555 clinicians. The completion rate was 57% (555/957). The top five treatment options included; education, sleep recommendations, energy management, goal setting, and manual therapy. Just over one-third of clinicians prescribed aerobic exercise. Having a high caseload of patients with concussions (75-100%) was a significant predictor of prescribing aerobic exercise. Most clinicians indicated they would refer patients based on the clinical vignette to another healthcare provider (e.g. psychologist, physician).

Conclusion: A wide variety of treatment options were selected, although most falling under the category of education (e.g. sleep recommendations, goal setting, energy management). Few clinicians use aerobic exercise as part of their concussion management strategy. Barriers exist that limit clinicians from using exercise-based strategies.

Keywords: brain injury, rehabilitation, therapeutics

Introduction

Over the last decade there has been a dramatic increase in attention to concussions. Thus, there is a greater supply of patients seeking care for concussion management, treatment, and rehabilitation. This supply of patients has been met by concussion clinics which are both public and privately funded. These clinics likely employ a variety of health care professionals including but not limited to; Physical, Athletic, and Occupational Therapists, who provide a breadth of services for their clientele.[168] It is likely that the services provided are highly variable[169] given the lack of evidence-based guidelines available for concussion management for those who do not recover quickly.[4] Clinical management of concussion is especially important for those individuals who experience persisting symptoms and impairments after injury. A recent study, using a Google search strategy to locate concussion clinics, found that healthcare providers in Canada offer diverse services, and in some cases these practices do not conform to current expert consensus guidelines.[168]

Multidisciplinary management for patients with concussion has been widely recommended.[28,59,170-173] This recommendation is emphasized for patients experiencing symptoms beyond ten days post-injury.[9] Although expert consensus advocates that the multidisciplinary team have experience with concussion, there is little knowledge about who may be acting in these roles or the types of services being provided. Given that challenges have been observed in multidisciplinary management of concussion,[169] further study is needed.

A useful strategy to better understand the role of the health care provider in concussion management is to examine their scope of practice, and the type of treatments they offer. This examination can be achieved using clinical vignettes. Vignettes have been used for measuring clinical practice habits in a variety of health care contexts.[174,175] They offer a cost-effective way to measure the process of care and clinical reasoning in various clinical settings,[176] which was ideally suited for our purposes.

Several studies have used surveys and clinical vignettes with primary care physicians to identify knowledge of concussion, diagnosis criteria, and management.[163-167] These studies focused on the acute management of concussion, generally conducted in a hospital setting. One study of American Physical Therapists explored practitioner’s attitudes, beliefs, and knowledge of concussion. This study contained a brief section (3 questions) about decision making based on clinical scenarios. Regarding clinical decision making, approximately half of the respondents identified a need for vestibular therapy, when it was indicated, while 43% opted to refer to a physician. When graded exertion was potentially indicated one third of respondents recommended discharging the patient.[177] Another study of chartered physiotherapists in Ireland identified a high level of knowledge of concussion from respondents. The management practice questions in their survey focused on acute management including removal from play and return to play decisions.[178] To our knowledge, no study to date has adequately assessed the clinical practice habits of rehabilitation therapists managing youth concussions in the sub-acute phase.

Objective

The purpose of this study was to estimate the scope of concussion management practices offered to patients by Canadian rehabilitation therapists. Specifically, we aimed to estimate the type of treatment services, the extent of multidisciplinary management, and the use of prescribed exercise used in the sub-acute phase for youth who are experiencing a prolonged recovery from concussion.

Methods

Reporting of this manuscript was conducted according to "Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES)".[179]

Design

A cross-sectional design was used. Purposive sampling[180] was conducted by electronic survey through three health care professional associations (Canadian Athletic Therapists Association - CATA, Canadian Association of Occupational Therapy - CAOT and Canadian Physiotherapy Association - CPA).

The study was approved by the Institutional Review Board. Informed consent was obtained from each participant. The first page of the survey contained information about the purpose of the research, the approximate length of time to complete the survey, how data would be used, and contact information for the study investigators. Participants consented to participate by clicking on the next button on the online page. Participants were informed that once the survey was started, consent could not be withdrawn.

Participants

Certified/registered health care providers registered with their professional association were eligible for participation. Student members were excluded from participation.

Survey Development

We developed two clinical vignettes and an electronic survey (Appendix 2) for this project using concepts from previously published work.[177] The survey development was a five-step process (Figure 1). We pre-screened the survey to evaluate question interpretation.[181,182] The survey was pre-screened by 6 experts; 3 Athletic Therapists (AT), 2 Occupational Therapists (OT), and 1 Physical Therapist (PT) in the field with a minimum 5 years of clinical experience in concussion management. Experts reviewed the survey for content, clarity, readability, comprehensiveness, and technical ease of use. Revisions recommended from pre-screening were made to improve readability and clarity. Following pre-screening, the survey was pilot tested by 9 clinicians with representation from each of the targeted professional associations (4 AT, 2 OT, 3 PT). Clinicians were provided with a Clinical Sensibility Testing Tool[181] to assess the comprehensiveness, clarity, and face validity of the survey. The Clinical Sensibility Testing Tool contained seven questions about question clarity, inappropriate or redundant items, and the likeliness of achieving the survey objective with the survey.[181] Technical functionality of the online survey occurred during pre-screening and pilot-testing. Both pre-screening, and pilot testing was conducted using the same online method of administration to improve results.[180] The survey was translated into French upon final revision. The French version was reviewed by the 2^{nd} author to ensure consistency. No revisions to the content were undertaken following pilot testing the French version.

Figure 1: Survey development process

Recruitment Process

An email invitation was distributed through each of the professional associations. The approximate membership at the time of recruitment of the CPA, CAOT, and CATA were 10,000, 9,000 and 1,000 respectively. The invitation to participate provided a short description of the study and encouraged clinicians to participate. A link to the survey was provided in the email invitation. Participation was voluntary, no incentives were offered.

Survey Administration

Surveys were completed anonymously via LimeSurvey, an online tool for surveys hosted on the McGill University (Montreal, QC) server and maintained by IT Service Centre Tools Implementation group. The survey was open for respondents from March 28th – September 11, 2017.

Question order was identical in all cases. No randomization of items or questions was used. Adaptive questioning was used for the question about type of treatment. Additional questions were generated if a respondent indicated using aerobic exercise, strength training, stretching, or education. The survey consisted of 12 demographic questions and 16 questions per clinical vignette for a total of 44 questions. The number of questions per clinical vignette varied based on adaptive questions. The survey consisted of three pages (1 demographic, 2 clinical vignettes). Respondents had the option to navigate backwards on the survey at any time.

Data Analysis

Analysis of data was conducted using R version 3.1.2 (2014-10-31). Survey responses were exported from LimeSurvey into an Excel spreadsheet. Descriptive statistics were used to summarize responses. Incomplete survey responses were included if the respondent completed the survey until the end of the first clinical vignette. We did not restrict entries based on IP address duplicates because we anticipated multiple clinicians using the same computer in a clinical setting. IP addresses were checked for duplicates. Entries with identical IP addresses and demographic data were compared for duplicates. To estimate which demographic characteristics (of the respondent) predicted prescribing aerobic exercise, we conducted a stepwise regression. McNemar's test was conducted to estimate if the treatment proportions differed between vignette 1 and vignette 2 for aerobic exercise. Open text sections were analyzed using qualitative content analysis. Open text responses were categorized using themes generated from the data.[183,184]

Results

Members of the CATA and CPA were contacted on two occasions by email. A reminder email was sent two weeks following the first invitation. The CATA and CPA have approximate memberships of 1,000 and 10,000 respectively. Members of the CAOT were notified of research opportunities in a national newsletter and via social media on two occasions. The CAOT has an approximate membership of 9,000. There were 957 visitors to the first page of the survey, 665 completing the first clinical vignette and 555 completing the entire survey. The completion rate was 57% (555/957), but variable across designations. Respondent demographic characteristics are outlined in table 1.

Table 1: Demographic Characteristics

	Vignette 1 n=665	Vignette 2 n=555
Age		
<24	10	7
25-34	275	226
35-44	162	133
45-54	136	119
55-64	68	59
65+	14	11
Sex distribution		
Female	478	399
Male	187	156
Designation		
Athletic Therapist	216	183
Occupational Therapist	11	9
Physical Therapist	413	343
Other	25	20
Years of experience		
<5	156	126
5-10	167	142
11-15	83	65
16-20	75	63
>21	184	159
Education Level		
Bachelor's	351	299
Master's	266	217
Doctorate	21	17
other	27	22
Work setting		
Private outpatient	410	344
Academic institution (post-secondary)	71	60
Health System/Hospital-based	41	34
School system	22	20
Concussion/mTBI clinic	23	17
Other:	98	80
Multidisciplinary setting		
Yes	476	399
No	189	156
Patients/year with concussion		
0	53	40
1-12	376	317
13-24	118	98

25+	118	99
Location of Practice		
Alberta	91	77
British Columbia	104	87
Manitoba	39	36
New Brunswick	15	15
Newfoundland and Labrador	4	3
Nova Scotia	25	22
Ontario	261	210
Prince Edward Island	4	3
Quebec	90	75
Saskatchewan	24	20
Yukon	2	2
Other	6	5

Treatment Prescribed

Regarding the type of treatment selected, the top four options (education, goal setting, sleep recommendations, and energy management) were identical for both clinical vignettes. All treatment options were endorsed, and, in both cases, some respondents indicated additional types of treatment by selecting ‘other’. The most frequently described ‘other’ treatments included; craniosacral therapy, osteopathic treatment, and additional assessments. While these ‘other’ treatments were most frequently described they were selected by less than 5% of the sample. When combining vignette one and two, rest was advised by five respondents.

Table 2: Type of treatment prescribed[a] n(%)

	Vignette 1 n=665	Vignette 2 n=555
Education	565 (85)	446 (80)
Sleep recommendations	430 (65)	322 (58)
Goal Setting	385 (58)	298 (54)
Energy Management	364 (55)	345 (62)
Manual Therapy	251 (38)	205 (37)

Aerobic exercise	237 (36)	195 (35)
Exertion	194 (29)	173 (31)
Return to Learn Protocol	192 (29)	227 (41)
Stretching	177 (27)	147 (26)
Return to Play Protocol	152 (23)	117 (21)
Visualization/imagery	131 (20)	76 (14)
Massage	114 (17)	88 (16)
Coordination Drills	108 (16)	87 (16)
Strength training	59 (9)	53 (10)
Acupuncture	54 (8)	41 (7)
Other	85 (13)	47 (8)

[a]Choices are not mutually exclusive

To evaluate consistency of prescribing aerobic exercise across clinical vignettes we conducted a McNemar's test. This analysis included only those participants who completed both clinical vignettes (n=555). There was a trend indicating clinicians were more likely to prescribe aerobic exercise for vignette two compared to vignette one, though not statistically significant (p=.054).

Table 3: Aerobic exercise by vignette matrix

	Vignette 2 Yes Aerobic Exercise	Vignette 2 No Aerobic Exercise
Vignette 1 Yes Aerobic Exercise	134	39
Vignette 1 No Aerobic Exercise	59	323

To estimate which demographic characteristics (of the respondent) predicted prescribing aerobic exercise, we conducted a stepwise regression. The dependent variable was selecting aerobic exercise. The following demographic characteristics were independent variables considered for the model; clinician designation, years of experience, age, work setting, location of practice, multidisciplinary setting, and percentage of caseload with concussions.

For clinical vignette one, using a backward stepwise regression, the final model included; clinician designation, multidisciplinary setting, and percentage of caseload with concussions as independent variables (table 4). The reference level in the model was Athletic Therapist, caseload <10% of patients with concussion, no multidisciplinary setting. For clinical vignette 1, those clinicians with the highest caseload of patients with a concussion were 2.7 times more likely to prescribe aerobic exercise (p=.024, 95% CI 0.13-1.91)

Table 4: Logistic Regression Results – vignette 1

Vignette 1			95% Confidence Interval		
	estimate	odds ratio	lower bound	upper bound	significance
intercept AT, <10%, no multidisc	-1.2862	0.2763188	-1.732176764	-0.8585084	7.47E-09
Physical Therapist	0.3502	1.4193514	-0.016571657	0.7245967	0.2458
Occupational Therapist	-0.9747	0.3773055	-2.932005468	0.5217082	0.435
Other	-0.3889	0.677802	-1.448396805	0.5365004	0.0636
11-25%	0.2622	1.2997865	-0.144045653	0.6638037	0.2025
26-50%	0.2429	1.2749411	-0.490330911	0.9420079	0.5028
51-75%	1.0555	2.8734115	-0.112052811	2.2961614	0.078
76-100%	**1.0125**	**2.7524736**	**0.13237355**	**1.910644**	**0.024[a]**
Multidisciplinary setting (yes)	0.3714	1.4497629	6.18262E-05	0.7528576	0.0528

[a]statistically significant

For clinical vignette two, using a backward stepwise regression, the final model included: clinician designation and percentage of caseload with concussions as independent variables (table 5). The reference level in the model was Athletic Therapist, caseload <10% of patients with concussion. For clinical vignette two, Physical Therapists, and clinicians with the two highest caseloads of patients with a concussion were significant predictors of prescribing aerobic exercise. Physical therapist were 1.7 times more likely to prescribe aerobic exercise compared to Athletic Therapists (*p*=.007, 95%CI .15-.97). Therapists with a majority of their caseload consisting of patients with a concussion were four (p=.02, 95%CI .23-3.1) and seven (p=.0004, 95%CI .92-3.13) times more likely to prescribe exercise compared to those therapists whose caseload consists of 10% or less concussion patients.

Table 5: Logistic Regression Results – vignette 2

Vignette 2			95% Confidence Interval		
	estimate	odds ratio	Lower bound	upper bound	significance
intercept (AT, <10% case load)	-1.13603	0.3210912	-1.5291272	-0.7614903	6.13E-09
Physical Therapist	**0.55883**	**1.7486254**	**0.1545221**	**0.9746775**	**0.007467**[a]
Occupational Therapist	-1.76453	0.1712673	-4.7928896	0.156387	0.126835
Other	0.07322	1.0759672	-1.033927	1.0656481	0.889501
11-25%	0.2373	1.2678214	-0.2088527	0.6779309	0.293232
26-50%	0.19356	1.2135622	-0.5843079	0.9309329	0.613391
51-75%	**1.54542**	**4.689941**	**0.2376358**	**3.1004179**	**0.02802**[a]
76-100%	**1.95476**	**7.0622239**	**0.9251095**	**3.1393899**	**0.000414**[a]

[a]statistically significant

Aerobic Exercise Characteristics

Vignette 1: Stationary cycling and treadmill were the most common modes of aerobic exercise. The most common methods of selecting the duration of aerobic exercise were based on a predefined number of minutes, the exacerbation of concussion symptoms, or until fatigue occurred.

The average length of time selected for the duration of exercise was 17 ± 6 minutes (table 6). The most common methods of selecting the intensity of exercise were based on a perceived exertion scale or, heart rate zone. For those clinicians using a perceived exertion scale, the most common exertion levels included: “easy”, “just feeling a strain”, and “starting to get hard”. On a 10-point scale these represent 3/10, 4/10, and 5/10. For those clinicians using a heart rate zone, 50-80% of the maximum heart rate was most common.

Vignette 2: Stationary cycling and treadmill were the most common modes of aerobic exercise. The most common methods of selecting the duration of aerobic exercise were based on a predefined number of minutes, the exacerbation of concussion symptoms, or until fatigue occurred. The average length of time selected for the duration of exercise was 17 ± 6 minutes (table 6). The most common methods of selecting the intensity of exercise were based on a perceived exertion scale or, heart rate zone. For those clinicians using a perceived exertion scale, the most common exertion levels included: “just feeling a strain”, “starting to get hard”, and “getting quite hard”. On a 10-point scale these represent 4/10, 5/10, and 6/10. For those clinicians using a heart rate zone, 50-80% of the maximum heart rate was most common.

Table 6: Aerobic Exercise Characteristics

	Vignette 1	Vignette 2
Prescribed (n)	237	195
Frequency (days/week)		
<=3	60	47
4-6	80	61
7	64	48
Symptom Dependent	13	14
Other	3	3
N/A	17	22

Education

In both clinical vignettes, education was the most highly endorsed treatment option. Seven educational themes were generated from the data including the following topics; 1) information about the injury, 2) recovery, 3) management, 4) nutrition/hydration/sleep, 5) reassurance, 6) goal setting, and 7) parent/guardian education. Goal setting was described by some clinicians as an educational strategy while others chose the 'goal setting' response in the treatment options. Information about recovery was focused on the risk of returning to activity too early, and possible referral options. Regarding managing the injury, information was provided about how to manage symptoms, school and activity modifications, handling emotional symptoms, and the use/restriction of electronics/screen time.

Refer

Most respondents indicated that they would refer patients from both vignettes. In vignette one, 64% of clinicians indicated they would refer to another practitioner compared to 50% for vignette two. For vignette one, the top two referrals were to a psychologist or physician. For vignette two, the top two referrals were to a physician and osteopath (table 7).

Table 7: Referral Frequencies[a]

Vignette 1 (n=423)	n (%)
Psychologist	207 (50)
Physician	168 (40)
Osteopath	73 (17)
Occupational Therapist	70 (17)
Massage Therapist	46 (11)
Physical Therapist	41 (10)
Neuropsychology/Neurology	40 (9)
Athletic Therapist	33 (8)
Kinesiologist	27 (6)

Vignette 2 (n=281)	n (%)
Physician	170 (60)
Osteopath	62 (22)
Occupational Therapist	49 (17)
Psychologist	36 (13)
Athletic Therapist	34 (12)
Physical Therapist	32 (11)
Massage Therapist	27 (10)
Neuropsychology/Neurology	22 (8)
Kinesiologist	20 (7)

Sport Medicine Physician	14 (3)
Concussion Clinic	11 (3)
More experienced therapist/Specialist (unspecified)	9 (2)
Eye specialist	9 (2)
Chiropractor	4 (1)
Acupuncture	5 (1)
Vestibular therapist	3 (1)
School counsellor	2 (<1)
Speech Language Pathologist	1 (<1)
Other	22 (5)

Concussion Clinic	9 (3)
Sport Medicine Physician	8 (3)
Eye specialist	7 (2)
More experienced therapist/Specialist (unspecified)	5 (2)
Chiropractor	3 (1)
Acupuncture	2 (1)
Vestibular therapist	1 (<1)
School counsellor	0 (0)
Speech Language Pathologist	2 (<1)
Other	19

[a]Choices are not mutually exclusive

Discussion

This study examined the concussion management practices of Canadian Athletic, Occupational, and Physical Therapists. To our knowledge, no study to date has explored the type of treatments clinicians prescribe following concussion in youth. While acute concussion management guidelines have become more consistent,[124] guidelines for the sub-acute phase are less clear, especially when patients remain symptomatic.[170] Patients who experience prolonged symptoms are more at risk of developing depression, and anxiety.[185] Further, persisting symptoms have a higher likelihood of interfering with school participation[186] and influencing academic performance.[187] The clinical management of patients experiencing a prolonged recovery from concussion can have long term implications.

We observed a high completion rate (57%) which is likely attributed to topic salience. We cannot say with certainty the total number of practitioners that received an invitation to participate in this research, and therefore cannot calculate a response rate. Concussions are widely discussed in the mainstream media and have garnered attention outside the clinical setting. The current climate and public attention has brought increased awareness to this topic and as a result some clinicians may have been more likely to participate in this research. Further, during recruitment, the Consensus statement on concussion in sport and other publications from the 5th International Conference on Concussion became available.[4] These publications are freely available, and widely distributed, which possibly added to the increased interest in our research.

The clinical vignettes used in the survey were non-specific as our interest was to observe if and how clinicians used aerobic exercise for concussion management. The results of this study suggest that a large variety of treatments were recommended for the clinical vignettes provided. Regarding the type of treatment prescribed, similar responses were observed for both clinical vignettes. Education, sleep recommendations, goal setting, and energy management were the most commonly selected treatments. A critical element of treatment and rehabilitation of any injury includes education. Education can cause changes in patients attitudes and behaviors, which can influence the recovery process.[188] Changes in both the quality and quantity of sleep post-mTBI have been observed in adolescents[189,190] and adults.[191] Sleep counseling and recommendations are critical since augmented sleep patterns can influence depressive symptoms,[189] return to school,[192] and cognitive function.[193] Evidence has shown that goal setting can enhance the effectiveness of clinical treatment.[194] Energy management, sometimes referred to as pacing, is a rehabilitative approach where patients decide how active they can be without aggravating their condition.[195] Giving patients the control to manage their symptoms and activity level is both necessary and empowering. While a variety of treatments were recommended for both clinical vignettes, the top interventions (goal setting, sleep recommendations, energy management) fall under the umbrella of educational strategies. A recent scoping review exploring rehabilitation interventions in youth following concussion, revealed that educational approaches, such as early intervention,[147] or phone counseling[153] had no significant effect on recovery.[196] Additional research is needed to explore if and how these educational approaches (energy management, goal setting, sleep recommendations) influence recovery from concussion.

Despite limited evidence-based research regarding treatment for concussive injuries, there is a trend moving toward classification-based approaches. For example, patients who present with balance deficits, and dizziness would be classified as having vestibular dysfunction and would be treated for those specific impairments.[137] We intentionally avoided specific classification types (ex. cognitive, cervical, vestibular) due to our interest in exercise as a therapeutic tool. Of the treatment options provided in the survey, only two have evidence-based research indicating a positive influence on recovery in youth; manual therapy[94] (when indicated) and aerobic exercise.[117]

A growing body of literature has shown that individualized, low-intensity, aerobic exercise is a viable treatment for youth experiencing persisting symptoms following a concussion, specifically in the sub-acute phase.[7,31,116-119,151,154,160,197] However, the use of exercise for concussion management is a dramatic paradigm shift from previous treatment recommendations which were heavily focused on physical rest. Expert consensus long advocated the necessity of physical rest following concussive injury.[29] Evidence to date has shown that complete physical rest until becoming asymptomatic may not be the best approach, especially when recovery takes longer than usual.[67,75,114] However, it is not clear if this evidence is currently used in practice. We find that just over one-third of respondents indicated that they would prescribe aerobic exercise in either clinical vignette. Interestingly, there was no significant difference in the percentage of clinicians prescribing aerobic exercise when comparing vignette one and two, though a trend was evident. Clinicians were not more likely to prescribe exercise even when a patient had been inactive for four weeks. Our results suggest that for patients experiencing persisting symptoms, there is likely a benefit from seeking treatment from a clinician who specializes in concussion care. Respondents who have a high caseload of patients with a concussion were more likely to prescribe exercise as a management strategy. Those clinicians specializing in the treatment of concussion are probably more likely to use evidence-based strategies. Research has shown that prolonged inactivity can contribute to persisting symptoms following a concussion.[75] However, there seem to be barriers that prevent clinicians from using exercise as a therapeutic tool for concussion management.

Limitations

The survey used in this study had been pilot tested but was not previously validated. We acknowledge that the questions are subject to interpretation and understanding which may vary amongst respondents. We only sampled clinicians from three national associations and acknowledge that other health care providers are involved in the management of concussive injuries, though we have not reached them in our sampling. Further, some rehabilitation therapists (PT & OT) are not required to register with their national association and as such our recruitment strategy may have excluded these potential participants. We acknowledge that our sample consists mostly of physical therapists working in a private, outpatient setting who reported seeing less than 12 concussion patients per year. As with any online survey, responder bias cannot be avoided.

Conclusions

Clinicians are prescribing a wide variety of treatments for youth with persisting symptoms following concussion. The most frequently observed responses indicated that educational strategies are commonly used. Limited evidence-based treatments were prescribed. Our results show that a large proportion of clinicians are prescribing treatment that is either ineffective or unnecessary. This finding aligns with evidence from knowledge translation indicating that approximately one-third of patients receive treatment that is ineffective.[198] Efforts are required to move evidence-based research into the hands of knowledge users.

Chapter 8 – Integration of Manuscripts II and III

In the second manuscript we showed that clinicians prescribed a variety of treatments when presented with vignettes of two youth patients with persisting concussion symptoms. The most frequently selected treatments fell under the category of education (sleep recommendations, goal setting, energy management). We found limited use of evidence-based treatments. Just over one-third of clinicians reported using exercise-based approaches. Although there was a trend for clinicians to prescribe exercise when the vignette patient had been inactive for a longer period, this result was not statistically significant. Those respondents with higher caseloads of patients with a concussion were more likely to prescribe exercise. Barriers exist that prevent clinicians from using exercise as a management strategy.

The first line of inquiry was an environmental scan of the current use of exercise-based interventions for concussion management. Our findings indicate that there are a wide variety of treatments in the literature for youth following concussion. Unfortunately, the quality rating of most studies was fair. Though we identified many studies in our scoping review using an exercise component, our clinician survey revealed that just over one-third of clinicians are using exercise in practice.

To contribute to our knowledge regarding the use of exercise-based interventions, our second line of inquiry was to estimate the effectiveness of exercise-based interventions in decreasing post-concussion symptoms. Therefore, the following three studies (reported in manuscripts III, IV and V) examine different aspects of effectiveness. Two studies (reported in manuscripts III and IV) examine an active rehabilitation program currently implemented at the Montreal Children's Hospital, McGill University Health Center. The mTBI Program/Concussion Clinic provides clinical services for hundreds of children and youth annually.

The active rehabilitation protocol and theoretical rationale (described in detail elsewhere),[7,31] consist of four components: 1) aerobic activity, 2) coordination/skill practice, 3) visualization and, 4) education and motivation. The active rehabilitation intervention is delivered by trained physiotherapists who work in the mTBI Concussion Clinic. Patients are seen initially by a clinical coordinator and physiotherapist for a complete history and physical assessment. Patients are referred to the Active Rehabilitation intervention if they continue to experience concussion signs or symptoms three weeks following injury. The intervention is initiated in-clinic with a physiotherapist. Patients are provided with a home program that is to be completed daily and includes the same components as those used during the physiotherapy session. Physiotherapists follow-up with patients (by phone or in-clinic) after one week of the intervention to modify or progress the home program.

To begin the active rehabilitation intervention aerobic exercise is started at 60% of age-predicted maximum heart rate on a stationary bicycle or treadmill for 15 minutes. Coordination and skill practice is completed for up to ten minutes and is individualized according to the participant's sport/activity preference. Activities could include stick handling, shooting, dribbling or other basic sport skills. Heart rate is monitored during aerobic training and coordination skill practice using a portable Polar heart rate monitor and chest strap (Polar Electro, Inc., Lake Success, NY, USA). Visualization involves five to ten minutes of sport/activity imagery based on participant preference. This visualization often mimicked the coordination and skill practice. If appropriate and able, participants were instructed to choose a specific skill and visualize it in a positive manner with realistic timing. Education is provided at each clinic visit by the coordinator or physiotherapist including information about recovery, coping with post-concussion symptoms and the process of returning to school and sport. Patients who experience worsening of symptoms during the aerobic or coordination phases stop the activity and make note of the amount of time completed if less than 15 minutes, this duration becoming the target duration to be used as a home program of exercise. Children continue the activities at home and fill out a log to report the daily levels of symptoms as well as level of involvement in the various activities. Children are instructed to contact the physiotherapist if they could not engage in activities without an increase in symptoms for 2 consecutive days. Clinicians are in contact with all patients to monitor compliance and tolerance, review the home program and adjust the exercise protocol as needed. Patients are symptom free for one week at rest are advised to start the stepwise, progressive return to play protocol.

To our knowledge it was the first of its kind to use an exercise-based intervention for youth with persisting symptoms from concussion.[7] Two studies have been published from their clinical population.[7,199] The initial study in 2009 reported on the intervention development, underlying principles, and preliminary data from a small cohort of patients. This study sampled all patients during the first 17 months of implementation.[7] In 2016, a case study reported the results of 10 patients who were consecutively referred to the program over a four-month period.[199] Results of both studies were positive and this foundational work inspired studies three and four. Our aim was to collaborate with the clinical team to build on previous research. The clinic maintains a database containing prospectively collected data obtained during clinical visits. Given the rich nature of this dataset, we wanted to explore important questions related to this unique intervention through the database. We conducted two retrospective studies of the participants included in the clinical database for manuscripts III and IV. The purpose of the third study was to identify if positive results from previous, small pilot studies, examining the effectiveness of the MCH intervention could be replicated in a larger, more diverse sample of patients.

Chapter 9 – Manuscript III

Title: Evaluation of an Active Rehabilitation Program for Concussion Management in Children and Adolescents

Danielle M. Dobney[1] CAT (C), MSc., Lisa Grilli[2] BSc, MSc pht., Helen Kocilowicz[2] BScN, Christine Beaulieu[2] BSc., PT, Meghan Straub[2] B.Sc., M.Sc., A. PhT, Debbie Friedman[234] BSc. pht. M. Mgmt. & Isabelle J. Gagnon[124] pht, PhD.

1. School of Physical and Occupational Therapy, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.
2. Trauma Center, The Montreal Children's Hospital, McGill University Health Center, Montreal, Quebec, Canada.
3. Canadian Hospitals Injury Reporting and Prevention Program,
4. Department of Pediatrics, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.

Published in Brain Injury 2017

Acknowledgements

We would like to thank the children and their families for participating in this study and The Montreal Children's Hospital Centre MTBI Program professionals for their support. As well, we wish to thank the Research Institute of the McGill University Health Centre for its support of this research.

Declaration of Interest:

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper. We acknowledge funding from Fonds de recherche du Québec – Santé (FRQS) and Canadian Institutes of Health Research (CIHR).

Abstract

Objective: To estimate the extent to which post-concussion symptoms were influenced by participation in an Active Rehabilitation (AR) program (aerobic exercise, coordination drills, visualization, and education) for children and adolescents who are slow to recover from concussion. A secondary exploratory objective included examining the influence of sex on symptom evolution.

Methods: Analysis of prospectively collected data was performed on 277 youth who initiated an AR program, between three and four weeks post-injury at a Concussion Clinic in a tertiary care pediatric teaching hospital.

Main Outcome Measure: Post-concussion symptom scale (PCSS) from Sport Concussion Assessment Tool-3 (SCAT 3).

Results: Children and adolescents participating in an active rehabilitation program displayed improved post-concussion symptom severity at follow-up (median=9.5) compared to pre-intervention (median=18) ($p<.05$). Patients demonstrated improved physical, cognitive, emotional, and sleep related post-concussion symptoms ($p<.05$). Female sex was associated with an increased post-concussion symptom severity at follow-up.

Conclusions: Youth experiencing persisting symptoms three to four weeks post-concussion demonstrated improved post-concussion symptoms scores (physical, cognitive, emotional, and sleep related) with participation in an active rehabilitation program.

Introduction

Although the majority of youth recover from concussion within two weeks, approximately one third of them experience persisting symptoms for up to four weeks.[2,200] Persisting symptoms have been shown to interfere with day to day activities in children and adolescents.[16] Evidence has also shown that there appear to be sex related differences in how males and females report post-concussion symptoms.[201,202] Further, sex has been found to influence the length of recovery after concussive injury.[2,202,203] At present, there is little evidence available to guide decisions on how to best help children and adolescents who experience persisting post-concussion symptoms.[114]

Expert consensus has long advocated for the necessity of physical rest following concussion[29] until becoming asymptomatic.[9,28,58,59,204] Evidence supporting physical rest have been largely based on the animal model, where a period of neurometabolic crisis occurs following concussion, and exercise in this acute phase would further exacerbate the demand for brain metabolites, which are in low supply during this period. Further, animals who are permitted to exercise very early after an induced concussion demonstrate poorer cognitive function.[205] Evidence from the animal model therefore appears to justify supporting rest, at least in the acute period following the injury.

However, when applied to humans and to the subacute period post-injury, evidence obtained from the animal model must be carefully examined for its suitability as the traditional approach of physical rest until symptoms resolve,[206] could in fact be detrimental to this unique group of kids. Indeed, prolonged rest from physical activity, following injury in humans, has been found to have some negative consequences on recovery.[67] Possible harmful effects of prolonged inactivity following injury include: 1) anxiety about the recovery process, 2) psychological complications, and 3) physical deconditioning.[205] These effects have been shown to induce concussion like symptoms which further complicates recovery. Indefinite, prolonged physical rest in youth with persisting symptoms may not be the best approach to concussion management.

In 2009, Gagnon et al, introduced an exercise-based intervention for children and adolescents with persisting symptoms port-concussion, which they called "Active Rehabilitation" (AR). In this initial paper, they described the principles for the development of the approach, as well as presented data from a case series from the Rehabilitation After Concussion program at the Montreal Children's Hospital.[7] This program, which was to be added to the usual rest-based recommendations, activity restrictions and school accommodations, has been described extensively.[7,31,207] It consists of four main components: aerobic exercise, coordination drills, visualization and education/motivation and each of these will be detailed in the methods section of this paper. This program, initiated at a clinical visit with a physiotherapist, is continued as a home program and progressed until complete recovery is achieved. The novelty of the AR program was that it was the first to use an intervention that was exercise-based, co-constructed with the participant, empowering and engaging for youth experiencing persisting symptoms. The decision to use exercise to treat concussion symptoms lies in lines of evidence demonstrating the positive effect of exercise on general physical well-being and conditioning, but also on mood, sleep and cognition, all commonly reported as problematic following concussion. Although the benefits of physical activity are widely acknowledged for a variety of conditions, its use to manage concussions was somewhat controversial at the time.

Taken as a whole, studies proposing physical activity to manage persistent concussion symptoms in the last 10 years have generally been positive. Studies to date have demonstrated that individualized, physical activity strategies appear safe, feasible[31] and may promote recovery[7,117,160] by improving symptoms which are physical, sleep-related, cognitive and emotional in nature.[113] However, these studies have been limited by small sample sizes, methodological concerns, and no data on adherence or adverse events. Understanding if findings from our two previous case series on AR can be replicated in a larger, more diverse clinical sample was the rationale for the present study. Since 2007, The Montreal Children's Hospital Trauma Centre has offered AR after concussion through the Mild Traumatic Brain Injury Program/Concussion Clinic. This program sees over 400 children and adolescents annually who are slow to recover and maintains a comprehensive prospective clinical database. This clinical population presents an opportunity to evaluate the influence of participating in AR in a significantly larger sample of patients. The primary objective of this study was therefore to estimate the extent to which post-concussion symptoms were influenced by participating in the Active Rehabilitation program in children and adolescents who were symptomatic at least four weeks after concussion and thus considered to have persisting symptoms or being "slow to recover". A secondary, exploratory objective was to estimate the extent to which sex influenced post-concussion symptom evolution in the group of children receiving AR.

Methods

Participants and Procedures

Participants had been referred to the MTBI program/Concussion Clinic of The Montreal Children's Hospital, McGill University Health Centre (MCH-MUHC), a tertiary care paediatric trauma centre and teaching hospital affiliated with McGill University in Montreal, Canada, from various sources (emergency department, community physicians, regional centres, adult trauma centres). All participants had a confirmed diagnosis of MTBI or concussion from the referring physician based on the WHO case definition.[208] Ethical approval was obtained from the Pediatric Research Ethics Board of the McGill University Health Centre.

All patients first had an intake visit with a Trauma Coordinator (registered Physiotherapist or registered Nurse) within 48-72 hours of referral. During the intake visit, the coordinator conducted a clinical interview assessing for history of present and previous concussions, as well as for medically diagnosed anxiety, depression, and learning disabilities as reported by participants and their parent/guardian. Additionally, the clinic coordinator obtained information about the use of any current medications. During the intake visit patients were educated about energy conservation, activity restrictions, and school accommodations. Following the intake visit, participants were instructed to inform the Coordinator if symptoms persisted beyond three weeks post-injury. At this time, patients were considered eligible to begin the AR program. Based on the presence of previously diagnosed psychological conditions or on the existence of current school difficulties, some patients were additionally referred for neuropsychological or psychological services as determined by the clinical care team.

Participants who were referred for AR between April 2012 and March 2015 (n=677) were screened for eligibility for inclusion in the present study. Eligible participants were identified from the clinical database and included if they met the following criteria; 1) the patient started the Active Rehabilitation program between three and four weeks post-injury, and 2) had a follow up appointment between four and eight weeks post-injury. These criteria were established to improve the methodological quality of the study and use timelines that are consistent with typical intervention lengths.

Outcome Measure

The primary outcome was post-concussion symptoms, measured by the Post-Concussion Symptom Scale (PCSS) included in the Sport-Concussion Assessment Tool-2 and 3[9,28]). This measure is a 22-item patient-report questionnaire that measures the presence and severity of a variety of common post-concussion symptoms.[55] The PCSS addresses a number of symptom clusters including physical, cognitive, emotional, and sleep related items based on factor analysis presented by Lau[209] and Pardini.[20] The physical symptoms include; headache, pressure in the head, neck pain, nausea, dizziness, blurred vision, balance problems, sensitivity to light, and sensitivity to noise. The cognitive symptoms include; feeling slowed down, feeling like in a fog, don't feel right, difficulty concentrating, difficulty remembering, and confusion. The emotional symptoms include; feeling more emotional, irritability, sadness, and nervous or anxious. The sleep symptoms include; fatigue, drowsiness, and trouble falling asleep.

Individual symptoms are rated on a 7-point Likert scale with anchors to qualify the numbered scale (none = 0, mild = 1-2, moderate = 3-4, severe = 5-6). The range of possible scores for symptom severity is 0-132, with a higher score indicating increased presence and severity of symptoms. [17,55] The internal consistency, using Cronbach's Alpha, in a sample of concussed high school and college athletes, was 0.94.[55] Significant differences in post-concussion symptom scores have been found between concussed individuals and healthy controls.[17] To this day, post-concussion symptoms are the most commonly used marker to diagnose concussion and track recovery.[55]

Intervention

The Active Rehabilitation protocol has been described previously by Gagnon et al.[7,31,207] It consists of four components: 1) aerobic activity, 2) coordination/skill practice, 3) visualization and, 4) education.

1. Aerobic activity:

Upon completion of the clinical assessment the physiotherapist equips the patient with a Polar heart rate monitor and chest strap (Polar Electro, Inc., Lake Success, NY, USA). The target heart rate zone (50-60%) is calculated based on age-appropriate formulae.[210] The physiotherapist advises the patient of the target heart rate zone. The patient is provided with the Pictorial Children's Effort Rating Table (PCERT) as a visual guide for the intensity of aerobic exercise to be used for the home program.[211] The patient identifies the level of intensity on the PCERT that corresponds to the target heart rate zone. Once the desired mode of exercise is chosen (stationary bike or treadmill) the physiotherapist advises the patient to begin exercise. The symptom status is reviewed prior to starting aerobic exercise and re-checked every five minutes. The physiotherapist adjusts the speed of treadmill or resistance on the stationary bike until the target heart rate is achieved. The physiotherapist instructs the patient to notify them if any symptoms increase more than two points (on the 7-point Likert scale) during activity. The patient continues aerobic activity until they achieve fifteen minutes in the target heart rate zone or until symptoms worsen requiring stopping. If symptom exacerbation results in stopping aerobic activity, the duration of the tolerated period is noted.

2. Coordination/Skill Practice:

The coordination/skill practice is individualized based on the patient's preference and performed for a maximum of ten minutes. Coordination/skill practice are individual exercises without risk of further injury. Examples of exercise include; stick handling, dribbling, shooting, or agility drills. Symptom status is monitored throughout, and exertion intensity cannot be greater than that used for the aerobic component.

3. Visualization:

Imagery techniques are introduced to promote positive experiences related to physical activity participation. The patient is asked to select a motor task. This task often corresponds to the patient's coordination exercise. The physiotherapist instructs the patient to perform positive visualization of the motor task.

4. Education:

The patient and family review education regarding recovery, managing symptoms, return to play and return to school recommendations, energy conservation, sleep hygiene, nutrition, hydration, and self-management tools. Clinicians also discuss the process of activity resumption as well as the gradual return to play protocol.

Finally, the patient is provided with a home program to continue AR. The home program is identical to the tasks completed at the in-clinic visit and lasts for twenty to thirty minutes. The physiotherapist provides the patient with a home program log and advises the patient to complete it daily. For safety, patients are advised to stop the current activity session if any symptom increases by more than one point. If symptoms remain elevated the next day, they are instructed to call the clinic for follow-up. Once patients begin the AR, regular follow-up visits, completed by telephone or in-person, are scheduled. When patients become asymptomatic for one week (based on patient report), have a normal clinical exam, return to complete cognitive/school activities, and successfully complete an exertion test, they are instructed to begin a stepwise, progressive return to play protocol as per current guidelines.

Statistical Analysis

Analysis of data were conducted using R version 3.1.2 (2014-10-31). Statistical significance was set at $P<.05$. Data were checked for normality using the Shapiro-Wilk test. To estimate the extent to which PCSS total score and individual clusters scores were influenced by participation in AR, changes from pre-intervention to follow-up were analyzed. Total symptom severity score was obtained by summing the score of each individual symptom, while cluster scores were obtained by summing the physical, cognitive, emotional, and sleep related items respectively. Non-parametric testing using the Wilcoxon rank sum was conducted for variables that did not demonstrate a normal distribution. To address our secondary objective and explore the influence of sex on post-concussion symptoms we conducted a linear regression.

Results

Descriptive Statistics

Of the 677 eligible patients, 277 participants met the inclusion criteria. The pre-intervention appointment was a mean 28 ± 3.3 days following injury. The follow-up in-person visit was conducted on average 40 ± 7.4 days post-concussion. The average age was 14.1 ± 2.3 years old at the time of injury. Table 1 outlines the participant characteristics. The sample was comprised of 135 (48.7%) female and 142 (51.3) male participants. The most common cause of injury reported by 217 (78%) participants was sport-related.

Table 1: Participants Characteristics (n=277)

Variable		N (%) if not stated
Age (mean ± SD)		14.1 ± 2.3
Gender	Female	135
	Male	142
History of Concussion		104 (37.5)
History of Anxiety		99 (35.7)
History of Depression		14 (5)
Learning Disability		8 (2.9)
History of Sleep Disorder		57 (20.6)
Initial symptoms (at time of injury)	Headache	97 (35)
	Dizziness	52 (18)
	Nausea	37 (13)
	Vomiting	5 (1)
	Confusion	6 (2)
	Difficulty Concentrating	10 (3)
	Fatigue	15 (5)

Post-Concussion Symptoms

To estimate the influence of participating in the AR program, the pre-intervention and follow-up visit PCSS scores were compared. The distribution of symptom severity scores demonstrated a right skew. Testing assumptions of univariate normality using the Shapiro-Wilk test revealed that symptom scores at pre-intervention and follow up were not normally distributed ($p<.05$). Based on the non-normal distribution of symptom scores, a non-parametric Wilcoxon Rank Sum test was conducted. The total symptom severity score at follow-up (median=9.5) was improved compared to pre-intervention (median=18), z = -7.35, p<.05 (table 2). Each of the symptom clusters (physical, cognitive, emotional, and sleep) was improved at follow-up compared to pre-intervention (p<.05) (table 2). Total post-concussion symptoms and cluster scores at both time points were higher in female participants compared to males (figures 1 and 2). A multiple linear regression established that sex, and pre-intervention symptoms could statistically predict post-concussion symptoms at follow-up. A significant regression equation was found (F(2, 273) =189.8, p<.001), with an adjusted R^2 of 0.57. Female sex was associated with an increased post-concussion symptom severity at follow-up.

Table 2: Post-Concussion Symptom Severity Scores at Pre-intervention and Follow-up

		Pre-initiation of AR Median (IQR)	**Follow-up visit** Median (IQR)	**Significance**
Total PCSS Score		18 (9-34)	9.5 (3.75-24.25)	<.001
PCSS clusters	Cognitive Symptoms	4 (2-9)	2 (0-5)	<.001
	Emotional Symptoms	2 (0-6)	1 (0-4)	<.001
	Sleep Symptoms	3 (1-6)	1 (0-4)	<.001
	Physical Symptoms	8 (4-14)	5 (1-11)	<.001

Figure 1: Post-Concussion Symptom Severity Total Score by Sex

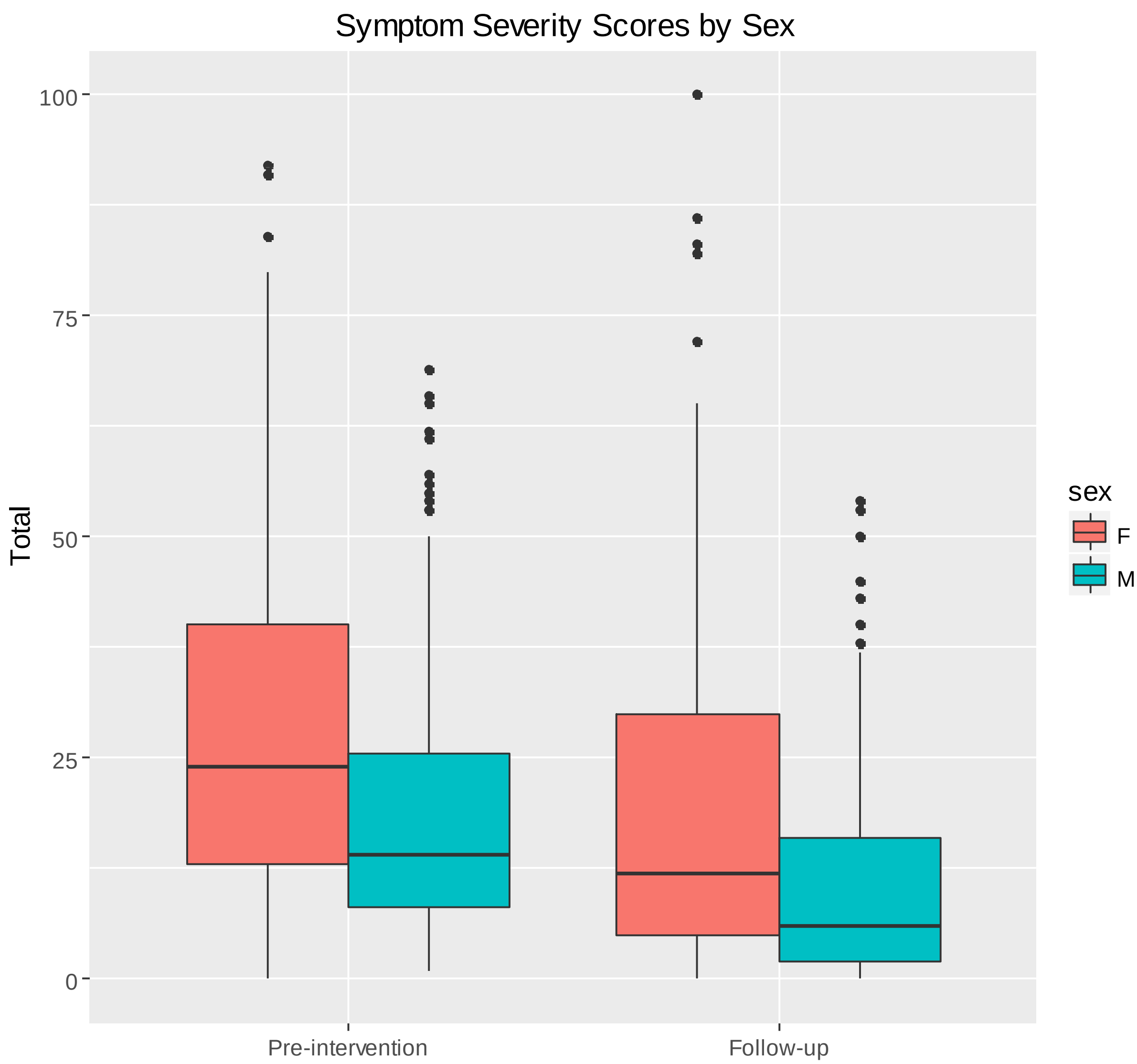
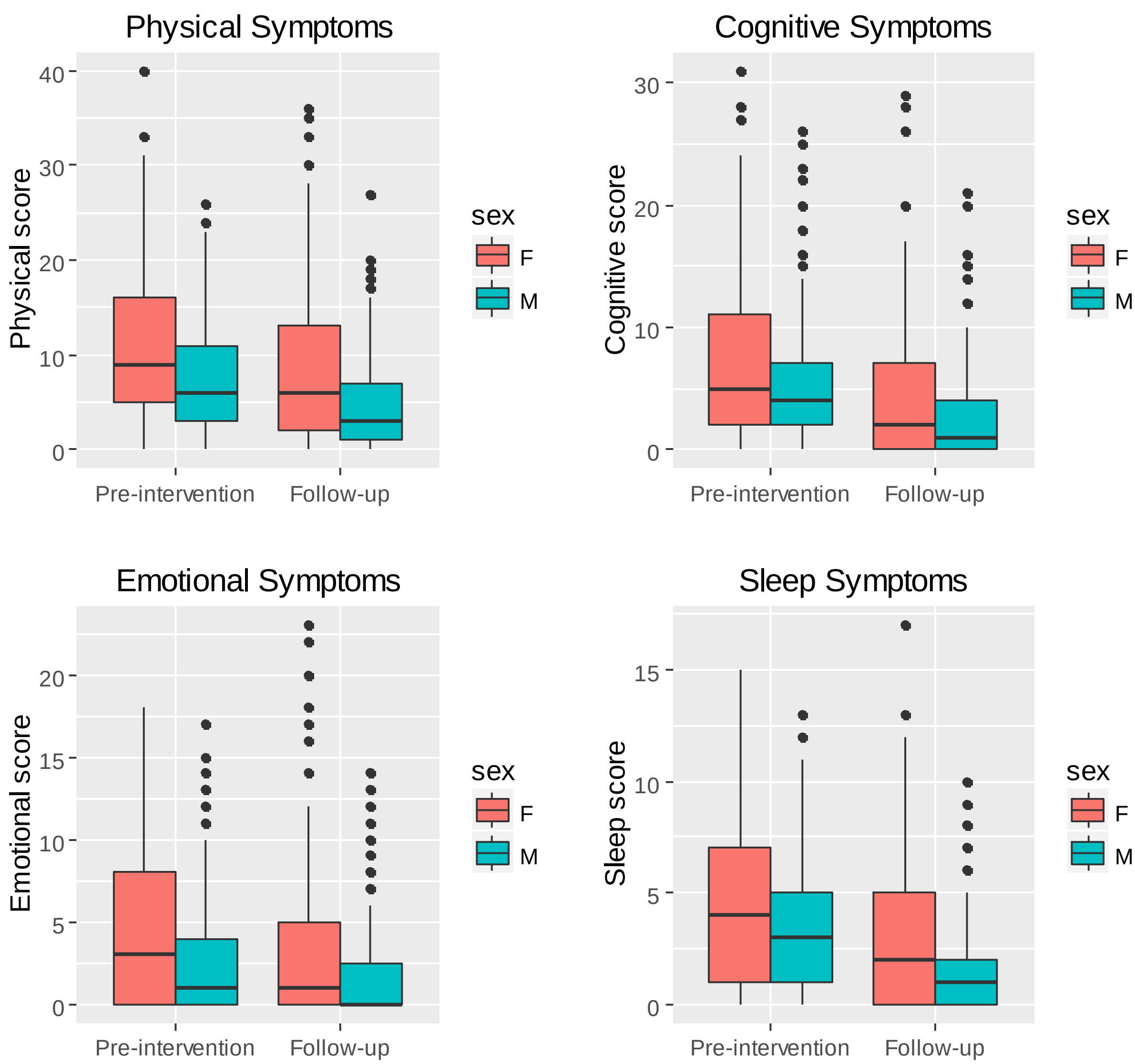


Figure 2: Post-Concussion Symptom Cluster Scores by Sex



Discussion

This study was a retrospective analysis of prospectively collected information evaluating the influence of participating in an AR program on post-concussion symptoms in children and adolescents who were slow to recover from concussion. The clinical database from the MTBI program/Concussion Clinic at the Montreal Children's Hospital Trauma Centre of the McGill University Health Centre was the source of information. Overall, our results showed that participation in an active rehabilitation program was associated with decreased post-concussion symptom severity compared to pre-intervention. We also found that each symptom cluster, namely physical, cognitive, emotional and sleep related, was significantly lower at follow-up.

Our sex-based results showed that female participants in this sample reported higher post-concussion symptoms compared to males at pre-intervention and follow-up. Both the total symptom severity and the cluster scores were higher in females compared to males. This trend has been observed in other studies both at baseline,[212] and post-concussion.[202] Our regression analysis revealed that female sex was a significant predictor of increased total post-concussion symptoms at follow-up. Despite observed sex differences we find that both males and females experience improved symptoms while participating in active rehabilitation post-concussion.

Findings from this study are consistent with three previous studies using active rehabilitation strategies in youth.[7,31,117] Two studies by Gagnon et al., a case series (n=16),[7] and pilot study (n=10)[31] observed statistically significant improvements in post-concussion symptoms while participating in active rehabilitation. A randomized trial by Kurowski et al., found subsymptom exacerbation aerobic training to induce greater improvement in post-concussion symptoms compared to a full body stretching group.[117] The mean age of participants was similar in all studies. Patients were symptomatic for at least 3 weeks in all studies. The length of the interventions and the timing of outcomes differed between studies. Nonetheless, each study demonstrated that patients experiencing persisting symptoms experienced improvement of symptoms while engaging in individualized physical activity. The strength of the current study lies in its sample size and real-life effectiveness. To our knowledge, this study reports on the largest sample of participants engaging in active rehabilitation for concussion management.

Our study focused on a unique group of children and adolescents who experienced persistent post-concussion symptoms three to four weeks following injury and sometimes referred to as being “slow to recover”. Approximately one third of youth will have prolonged symptoms,[2] yet there are currently few options or evidence as to how these patients should be managed.[114] The AR program uses an exercise-based approach to promote recovery. This is in contrast to typical management practices which advocate rest. There is growing evidence that traditional approaches do not work well in this unique sample of children and adolescents.

Our sample had a high proportion of youth with a self-reported, or medically documented, history of concussion. We found that 37.5% of participants reported a previous concussive injury. Other studies in similar age groups have reported a history of concussion of 22% [2], 26.7% [213], and 31%.[214] Further, subsequent concussions have been shown to result in longer recovery times compared to first time concussive injuries.[215]

Participants in the present study demonstrated an improvement in PCSS of approximately eight points while engaging in AR. Two studies have examined post-concussion symptom change scores in similar samples. One study identified that a ten-point change in post-concussion symptoms indicated reliable change.[216] This study used a different version of the post-concussion scale which contained only 21-items compared to the 22-item scale used in our study. Another study of slightly older athletes, reported a change score of 6.8 points to be clinically meaningful.[55] In light of change scores observed in similar samples, we propose that the statistically significant change (from pre-intervention to follow up) in this study may reflect a clinically meaningful change.

Limitations

Obtaining data from a clinical setting presents several challenges. Firstly, in order to examine a relatively homogenous group of participants we adopted specific inclusion criteria. These criteria were necessary because the characteristics of the clinical sample were highly variable. By establishing specific inclusion criteria, we were able to more accurately estimate the influence of the active rehabilitation program. Secondly, there was no control group for comparison. As such, it is not possible to identify if the achieved outcomes are directly related to the active rehabilitation program. Since active rehabilitation is a clinical program we had limited ability to estimate the frequency of symptom exacerbation during the home program. Lastly, although clinicians were in contact with patients there was no specific monitoring of the duration or frequency of activities during the home program.

Conclusion

There is little evidence supporting the use of any intervention for children following concussion, let alone those who have persisting symptoms.[123] Evidence from this study continues to highlight the potential use of an active rehabilitation program. Future research would be strengthened by three methodological inclusions; 1) including a control group for comparison, 2) monitoring exercise duration and frequency, and 3) monitoring the safety of this type of management strategy. These study details would allow the effectiveness of the active rehabilitation program to be evaluated. Continued work in this area has real-world implications. Clinicians are currently providing care in the absence of a solid foundation of evidence. Overall, we find continued support for active rehabilitation for children and adolescents experiencing prolonged symptoms.

Chapter 10 – Integration of Manuscripts III and IV

In the third manuscript we identified that positive results from previous small pilot studies (examining Active Rehabilitation post-concussion) could be replicated in a larger, more diverse clinical sample. Our results revealed statistically significant, and clinically meaningful, improvements in post-concussion symptom severity, and symptom clusters (physical, cognitive, emotional, and sleep) while participating in an active rehabilitation program. Further, we found that female sex was associated with increased post-concussion symptom severity at follow-up compared to male participants.

As outlined in the literature review (chapter 2), few studies have examined the exercise characteristics (frequency, duration, intensity, timing of initiation post-injury) of exercise-based interventions. Understanding the best approach to using exercise for concussion management requires a stronger knowledge of the timing component. The initial interest in the timing component stems from the animal model.[73] Griesbach et al., demonstrated the concept of an optimal timeframe in which exercise promoted recovery. While no such study has been conducted in humans, it is plausible that an optimal timing window exists. There is evidence indicating immediate return to sport or physical activity following a concussion prolongs recovery.[217,218] In essence, exercise too soon impedes recovery. Conversely, patients who experience persisting concussion symptoms and long periods of inactivity have negative consequences.[75] A large, multi-centre, prospective study found that children and adolescents who reported physical activity within 7 days of concussion had a lower risk of persisting symptoms 1 month later compared with those youth who reported no physical activity.[219] While some factors are unknown regarding the reported activity (frequency, duration, intensity, timing, type) the study presents the possible benefit of early physical activity on concussion recovery. However, the intensity of activity may also play an important role. In a study of youth hockey players, moderate to vigorous activity within the first few days of initial assessment was associated with longer time until being medically cleared.[220] It is evident that further study is needed to elucidate the influence of time to initiation of exercise following concussion. In the fourth study, we aimed to address the timing component. We studied children and adolescents who had received the MCH Active Rehabilitation intervention at different times in their recovery process to identify if an ideal timeframe existed.

Chapter 11 – Manuscript IV

Title: Is there an optimal time to initiate an active rehabilitation protocol for concussion management in children? A case series.

Danielle M. Dobney[1] CAT (C), MSc., Lisa Grilli[2] BSc, MSc pht., Helen Kocilowicz[2] BScN, Christine Beaulieu[2] BSc., PT, Meghan Straub[2] B.Sc., M.Sc., A. PhT, Debbie Friedman[234] BSc. pht. M. Mgmt. & Isabelle J. Gagnon[124] pht, PhD.

1. School of Physical and Occupational Therapy, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.

2. Trauma Center, The Montreal Children's Hospital, McGill University Health Center, Montreal, Quebec, Canada.

3. Canadian Hospitals Injury Reporting and Prevention Program,

4. Department of Pediatrics, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.

Published in the Journal of Head Trauma and Rehabilitation 2017

Conflicts of interest: The authors report no conflict of interest.

Disclosure of funding: Fonds de recherche du Québec – Santé (FRQS) and Canadian Institutes of Health Research (CIHR).

Acknowledgments: We would like to thank the children and their families for participating in this study and The Montreal Children's Hospital Trauma Program professionals for their support. As well, we wish to thank the Research Institute of the McGill University Health Center for its support of this research.

Abstract

Objective: To estimate the time frame during which initiating an active rehabilitation intervention (aerobic exercise, balance, and sport specific skills) after concussion contributed to improvement in symptoms at follow-up in children and adolescents who are slow to recover (symptoms persisting beyond 2 weeks) from concussion.

Setting: Concussion clinic at a tertiary care paediatric teaching hospital.

Participants: 677 children and adolescents with concussion aged 7-18 years.

Design: Case series of participants starting active rehabilitation <2, 2, 3, 4, 5, or 6+ weeks post-concussion.

Main Measure: Symptom severity measured by the 22-item Post-Concussion Scale (PCS)-revised.

Results: All patients experienced significant improvement of symptoms while participating in active rehabilitation, irrespective of the start time post-onset. Patients initiating active rehabilitation at 2 ($p<0.001$), or 3 ($p=0.039$) weeks post-injury demonstrated less severe PCS at follow-up than those starting at 6 weeks or later. Patients starting at 2 weeks had lower symptom severity than patients starting less than 2 weeks ($p=0.02$), 4 weeks ($p=0.20$) or 5 weeks post-injury ($p=0.04$). Lastly, patients starting less than 2 weeks and 6 weeks, or more post-injury yielded equivalent outcomes.

Conclusions: The findings support the use of active rehabilitation in children and adolescents who are slow to recover from concussion. Participants starting active rehabilitation less than two weeks and up to six or more weeks post-concussion demonstrated significant symptom improvements, but improvement was observed in all groups, regardless of the time to start active rehabilitation.

Key words: *mild traumatic brain injury, brain concussion, exercise therapy, Post-concussion syndrome*

Introduction

Expert consensus concerning management of concussion favors a gradual return to physical activity once asymptomatic.[29] The current management practice is appropriate for the majority of patients who recover within two weeks.[16,200] However, for patients who experience prolonged symptoms, expert consensus provides limited evidence-based recommendations.[29] In many cases these patients remain inactive for prolonged periods. Patients with prolonged symptoms (lasting upwards of one month)[28,31,221] are more likely to experience secondary consequences of being inactive.[67] The issue of mitigating secondary symptoms is critical to developing treatment protocols for patients exhibiting prolonged symptoms.

Physical activity immediately following concussion has been reported to be detrimental to recovery[29,48,72] and may lead to longer term impairments.[127,222-226] Animal studies have shown that exercise too soon can lead to neurometabolic energy imbalances within the brain,[34] yet, there is also evidence to suggest that prolonged inactivity in humans may exacerbate symptoms.[67,221] Indeed, in a randomized controlled trial, five days of strict rest prescribed immediately after concussion did not provide benefit beyond that in those who rested for one to two days.[75] Determining the ideal time frame during which to initiate exercise is thus an important factor in concussion management, since evidence has shown that exercise either too early or too late can have negative implications.

Few studies have evaluated the effectiveness of exercise interventions in individuals with persistent symptoms following concussion.[123] Three published studies have examined the impact of active rehabilitation, including exercise, in children[7,31] and adults[113] who are slow to recover (symptoms persisting beyond 2 weeks) from concussion. Although these studies differed in exercise characteristics (e.g. mode, duration, frequency, intensity), they demonstrated that individualized, closely monitored exercise can be both safe and effective in the management of persistent post-concussion symptoms. The next logical step is to determine the ideal time frame following concussion to begin an exercise-based intervention. This paper offers initial evidence in support of that aim.

Objective

The primary objective of this study was to estimate the time frame during which initiating an active rehabilitation protocol post-concussion contributed to a significant decrease in symptoms at the follow-up visit. We hypothesized that; similar to findings from the animal model, exercise too early or too late may delay recovery and have a negative impact on the presence and severity of post-concussion symptoms.

Setting

The Montreal Children's Hospital Trauma Center (MCH) of the McGill University Health Center (MUHC) is a tertiary care paediatric teaching hospital affiliated with McGill University in Montreal, Canada. Patients were assessed at the mTBI Program/Concussion Clinic that is part of the MCH Trauma Center. Ethics approval was obtained from the Research Institute of McGill University Health Centre.

Participants

A total of 677 patients participated in the active rehabilitation protocol between April 2012 and March 2015. Concussion was diagnosed by a physician prior to entry into the Concussion clinic based on the WHO case definition,[208] and referral for active rehabilitation was triggered in the presence of post-concussion symptoms persisting for more than 2 weeks. The sample was 54% female. The active rehabilitation intervention is an ongoing program at the mTBI Program/Concussion Clinic.

Procedures

Post-concussion symptoms were assessed at three-time points; 1) intake visit to the mTBI Program/Concussion Clinic, 2) initial physiotherapy visit at which time intervention was begun, and 3) follow-up physiotherapy visit, when outcome was re-assessed. Because in some cases the intake visit and initial physiotherapy visit occurred on the same day, the initial physiotherapy visit was considered the "pre-intervention" visit for the purpose of this study. For both the pre-intervention and follow-up visits, symptoms were assessed before the exercise-based treatment during the physiotherapy assessment portion of the clinical visit.

Methods

Data were obtained from a database collected prospectively from the mTBI Program/Concussion Clinic of the MCH between April 2012 and March 2015. After initial concussion management, participants were instructed to inform the clinic coordinator if symptoms were present 2 weeks following injury for referral to the active rehabilitation intervention, which was then scheduled to start between 3 to 4 weeks post-injury (see *Gagnon et al, 2009* for details). Clinical judgment and scheduling issues (vacation, school, parent availability etc.) resulted in some participants beginning the active rehabilitation protocol prior to 2 weeks.

Outcome Measures

The primary outcome measure was post-concussion symptom severity measured with the Post-Concussion Scale-Revised (PCS) as seen in the Sport Concussion Assessment Tool 3. This 22-item self-report questionnaire measures the presence and severity of post-concussion symptoms.[29] Symptoms are rated on a 7-point Likert scale with anchors to describe the numerical scale values (none = 0, mild = 1-2, moderate = 3-4, severe = 5-6). The total symptom score, also referred to as the symptom severity score, is calculated by summing the individual symptom ratings, yielding a range from 0-132, with higher scores indicating greater presence and severity of symptoms. Evaluating post-concussion symptoms is routinely done in the clinical assessment and management of concussion. Resolution of post-concussion symptoms is a common marker of recovery from concussion.[29] During the intake visit, the clinic coordinator conducted an interview assessing for history of concussion as well as medically-diagnosed anxiety, depression, and learning disabilities as reported by participants and their parent/guardian. In addition, the clinic coordinator obtained information about current medications.

Intervention

The active rehabilitation protocol and theoretical rationale (described in detail elsewhere),[7,31] consisted of four components: 1) aerobic activity, 2) coordination/skill practice, 3) visualization and, 4) education and motivation. The active rehabilitation intervention was delivered by a trained physiotherapist. Participants were provided with a home program that was to be completed daily and which included the same components as those used during the physiotherapy session.

Aerobic training was started at 60% of age-predicted maximum heart rate on a stationary bicycle or treadmill for 15 minutes. Coordination and skill practice was completed for up to ten minutes and was individualized according to the participant's sport/activity preference. Activities could include stick handling, shooting, dribbling or other basic sport skills. Heart rate was monitored during aerobic training and coordination skill practice using a portable Polar heart rate monitor and chest strap (Polar Electro, Inc., Lake Success, NY, USA). Visualization involved five to ten minutes of sport/activity imagery based on participant preference. This visualization often mimicked the coordination and skill practice. If appropriate and able, participants were instructed to choose a specific skill and visualize it in a positive manner with realistic timing. Education was provided at each clinic visit by the coordinator or physiotherapist including information about recovery, coping with post-concussion symptoms and the process of returning to school and sport. Patients who experienced worsening of symptoms during the aerobic or coordination phases would stop the activity and make note of the amount of time completed if less than 15 minutes, this duration becoming the target duration to be used as a home program of exercise. Children were to continue the activities at home and fill out a log to report the daily levels of symptoms as well as level of involvement in the various activities. Children were instructed to contact their rehabilitation professional if they could not engage in activities without an increase in symptoms for 2 consecutive days. Clinicians were in contact with all patients to monitor compliance and tolerance, review the home program and adjust the exercise protocol as needed. Patients who became symptom free for one week at rest were advised to start the stepwise, progressive return to play protocol.

Statistical Analysis

Data were imported to SPSS version 23 (IBM) for analysis. Continuous variables were reported with the mean and standard deviation. Dichotomous pre-injury participant characteristics were analyzed at the intake visit to examine the numbers in each group using chi-square tests. Participant characteristics included sex and presence of learning disability, history of concussion, anxiety, and depression. In order to estimate the influence of time to initiate active rehabilitation, treated as a categorical variable with less than two weeks, two, three, four, five, and, six weeks or later post-injury (between-subjects factor), on the evolution of post-concussion symptoms between the initial physiotherapy visit and the first follow-up physiotherapy visit (within-subjects factor), a Mixed-design ANOVA was conducted. The time interval between initial visit and follow-up, history of previous concussion, and other pre-injury characteristics were considered as covariates, but none had effects on the outcome of the analysis and were therefore not used in the final analysis.

Results

Descriptive Statistics

The patient characteristics are presented in table 1. Participants were a mean 14.3 ± 2.3 years old at the time of injury. There were no significant differences at the intake visit in the number of patients with learning disabilities, anxiety or depression. The most frequently reported current medications were Advil and/or Tylenol used by 137 participants. Medications were also reported for ADD/ADHD (12), asthma (7), migraines (4), depression (3), oral contraception (3), infection (3), allergies (2), and acne (1). The distribution of sex was equal among groups. There were no significant differences in the number of participants with a history of a previous concussion. As post-concussion symptom scores were right-skewed at both time points, we opted to compute log transformation to achieve normality in order to meet assumptions for the mixed-design ANOVA. However, note that in the tables, we used absolute values in order to facilitate interpretation.

Table 1 – Patient characteristics

	Total	<2 weeks	2 weeks	3 weeks	4 weeks	5 weeks	6 + weeks
Sample size (% Male)	677 (46)	26 (35)	33 (52)	175 (56)	183 (44)	62 (40)	198 (41)
Age (Mean, SD)	14.3 (2.3)	14.1 (2.3)	14.5 (1.9)	13.8 (2.5)	14.3 (2.2)	14.6 (2.5)	14.5 (2.1)
History of Concussion n(%)	262 (38.7)	4 (15.4)	13 (39.4)	66 (37.7)	74 (40.4)	24 (38.7)	81 (40.9)
History of Anxiety n(%)	261 (38.5)	9 (34.6)	12 (36.4)	68 (38.9)	70 (38.3)	22 (35.5)	80 (40.4)
History of Depression n(%)	36 (5.3)	2 (7.7)	0 (0)	9 (5.1)	9 (4.9)	5 (8.1)	11 (5.6)
Learning Disability n(%)	40 (5.9)	1 (3.8)	2 (6.1)	8 (4.6)	7 (3.8)	10 (16.1)	12 (6.1)
Time interval between pre-intervention and follow-up (days)	13.5 (9.9)	10.8 (5.2)	10.6 (4.3)	13.4 (9.8)	14.1 (10.3)	12.9 (8.3)	13.8 (10.7)

The mean time to begin active rehabilitation intervention (initial physiotherapy visit) in this sample was 45 days post-concussion. Participants in the <2 weeks group started active rehabilitation a mean 8.5 days post-concussion. The group of participants in the 6+ weeks or later group initiated active rehabilitation a mean 87 days post-concussion (range 43-370 days). The follow up physiotherapy appointment was a mean of 13.5 ± 9.9 days later as per clinical standards (follow-up visit scheduled 2 weeks after initial visit), and there were no differences between groups for this time interval. Symptom severity scores at both time points for each group displayed in table 2 show that all groups demonstrated decreasing symptom severity scores from the start of active rehabilitation to the follow-up appointment.

Table 2: Symptom severity scores[a] by group

	Initial Physiotherapy visit		**Follow-up Physiotherapy visit**	
	Mean (SD)	Range	Mean (SD)	Range
<2 weeks	25.2 (15.2)[b]	0-51	16.7 (11.8)	0-42
2 weeks	20.3 (15.9)	3-63	8.4 (10.5)[cd]	0-37
3 weeks	22.7 (19.2)	1-104	15.2 (17.1) [c]	0-86
4 weeks	25.6 (19.8)	0-92	16.0 (17.5)	0-100
5 weeks	26.4 (18.3)	5-77	19.9 (17.3)	0-80
6+ weeks	35.2 (23.1)[b]	3-106	22.2 (19.7)	0-93

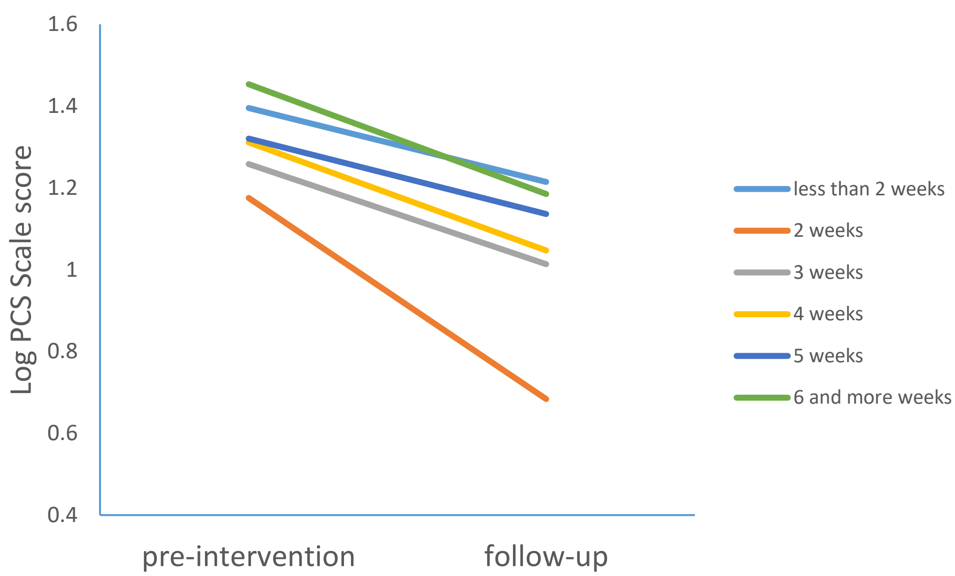
[a]Symptom scores are absolute values
[b]Significant difference (p<.05) compared to 2,3,4, and 5 weeks
[c]Significant difference (p<.05) compared 6+ weeks
[d]Significant difference (p<.05) compared to <2, 4, and 5 weeks

Differences between time to initiate active rehabilitation and evolution of symptoms over time

The transformed data met the normality assumption as assessed by Q-Q plots. There was homogeneity of variances ($p>0.01$) and covariances ($p>0.01$) as assessed by Levene's test of homogeneity of variances and Box's M test, respectively. There was a statistically significant interaction between “delay to rehabilitation” and time, on severity of PCS ($F=2.385$; $p=0.037$; partial $\eta^2=0.02$). Because of this significant interaction, we examined simple main effects for between- and within-group factors. Simple main effect for time was examined using repeated measures ANOVAs for each group separately and revealed significant decreases of PCS over time for all groups with eta-squared effect sizes ranging from 0.279 for the 3-week group to 0.569 for the 2-week group.

Simple main effects for “rehab delay” (between-group factor) were examined using separate one-way ANOVAs for each of the two-time points. At the pre-intervention assessment, PCS symptoms were significantly more severe in two of the groups (6+ and <2 weeks) compared to all other groups. Post-intervention pairwise comparisons using the Bonferroni correction revealed that those patients initiating active rehabilitation at 2 ($p<0.001$) or 3 ($p=0.039$) weeks post-injury demonstrated less severe PCS at follow-up than those patients starting at 6 weeks or later. Patients starting at 2 weeks had lower symptom severity than patients starting fewer than 2 weeks ($p=0.02$), 4 weeks ($p=0.20$) or 5 weeks post-injury ($p=0.04$). Lastly, patients starting within 2 weeks and 6 weeks or more post-injury achieved equivalent outcomes. The evolution of post-concussion symptoms is presented in figure one.

Figure 1: Evolution of post-concussion symptoms for rehabilitation groups



Discussion

The primary objective of this study was to identify a time frame during which initiating an active rehabilitation protocol contributed to a significant decrease in post-concussion symptom severity. Our data indicate that significant improvements in post-concussion symptom severity occur in youth participating in an active rehabilitation program and that this improvement occurs for all youth, irrespective of when they begin active rehabilitation.

Participants experienced symptom severity improvements ranging from 6.5 to 13 points over the 2-week follow-up period; this is of interest since improvements of 6.8 points on the Post-Concussion Symptom Scale are considered clinically meaningful.[227] Previous smaller case series by Gagnon et al.[7,31] reported similar improvements in this population, so it is promising to see consistency of findings from this larger, more diverse clinical sample. Similar improvements were observed across symptom clusters (emotional, cognitive, physical, and sleep), which provides support for the global effects of exercise on all these spheres of functioning.[74,228,229]

Our study adds to the increasing body of literature on exercised-based interventions after concussion in youth. Other recent reports have also demonstrated positive results.[113,117] A retrospective chart review in over one hundred patients identified that youth with persisting post-concussion symptoms tolerate aerobic exercise well and that 90% of the sample was clinically improved at follow-up.[119] A recent exploratory, randomized clinical trial by Kurowski et al. found that a six-week aerobic training intervention was associated with a greater rate of symptom improvement compared to a full body stretching group.[117] These authors (whose sample was similar to the age range of our participants) cited the need to identify the timing of rehabilitation initiation as an important next step.

Of the previous studies that have used exercise-based interventions following concussion, none had examined whether the time frame of initiation influenced post-concussion symptom resolution. In studies using an animal model to study recovery from concussion, initiating exercise within the first week after experimental injury has led to delayed recovery.[73] Thus, the time variable is an important factor that has not been well studied in humans, as exercise too soon is generally thought to have negative implications for patients.[113,224,230,231] As in animal studies, negative consequences have been reported in humans when they were not immediately removed from play following a sport-related concussion. College students who continued to play following a concussive injury were more than twice as likely to experience a longer recovery period compared to those who were immediately removed.[217] There are two specific concerns with uncontrolled exercise, such as that experienced in an athletic context. First, there is a high risk of repeated head trauma, which has been shown to delay recovery.[232] Second, following concussion the brain experiences neurophysiological changes that appear to be negatively influenced by vigorous exercise.[74,111] Re-introduction of safe, graduated, physical activity at the right time is a critical component in managing concussions. Previous studies in children using post-concussion exercise have initiated exercise after three[116] or four[7,31,118,119] weeks of persisting symptoms. Our study demonstrated that starting exercise earlier (fewer than two weeks post-concussion) was also associated with significant improvements in post-concussion symptoms. Given that prolonged inactivity can influence the presence and severity of post-concussion symptoms, the timing of initiating exercise is an important factor.

Our study has important implications for clinicians working with patients who have been experiencing persisting symptoms. Introducing physical activity, even as late as six or more weeks post-concussion, was associated with improvement of symptoms, even if these children present with more symptoms at the start of treatment. There has been a tendency to prescribe continued rest for patients who continue to experience prolonged symptoms.[78] Our data suggest that individualized exercise is a positive alternative that is associated with meaningful improvements in post-concussion symptoms.

Of interest is that our sample reported a high incidence of self- and parent- identified pre-injury anxiety. It is not clear if this finding was influenced by the current concussive injury. Although anxiety levels were similar across groups, a closer look at the influence of pre-injury anxiety on symptom reporting may provide a greater understanding of recovery. Some studies have identified pre-existing anxiety conditions as a possible contributing factor to increased symptoms[23] and prolonged recovery[24] following concussion. Aerobic exercise is associated with reductions in state anxiety.[106] Few high quality studies have evaluated the influence of exercise as a treatment for anxiety disorders in children. However, exercise has been shown to decrease anxiety symptoms in healthy children and adolescents compared to no exercise.[233] Active rehabilitation strategies that include aerobic exercise may be an efficient intervention for those children with pre-existing anxiety conditions.

Limitations

As this study was an analysis of data from an existing clinical program, there are several limitations that warrant discussion. There is no control group for this study; therefore, it cannot be determined if the observed improvement in symptoms was a result of the active rehabilitation protocol, nor can we rule out natural recovery. Compliance with the active rehabilitation program was not directly measured. Although clinicians discussed compliance with participants at follow-up visits, no specific outcome measure was obtained. As such, we acknowledge that the participants in this study may have varying levels of adherence to the prescribed active rehabilitation program. Compliance is a critical component when assessing the effectiveness of an exercise-based intervention and will be included in future studies. We acknowledge that there are multiple components of the active rehabilitation intervention and it is not clear which components may offer benefit over other. Our decision to categorize the exposure (time to initiate active rehabilitation) was based on clinical feasibility; however, analyses in a continuous manner may also provide relevant information. We considered symptom clusters in our analysis, but this investigation did not reveal any telling information regarding the timeline for commencing an active rehabilitation intervention.

Conclusion

The results from this study continue to support active rehabilitation in youth who are slow to recover from concussion. Initiating active rehabilitation within a wide time frame (<2 to 6+ weeks) post-concussion was associated with significant improvements in symptoms, irrespective of the start time. Although the results of this study alone are not sufficient to promote the use of exercise-based interventions as early as 10-14 days post-injury, they provide support for the idea of introducing more active management strategies earlier than usually promoted in current guidelines.

Chapter 12 – Integration of Manuscripts IV and V

In the fourth manuscript we studied participants from the MCH clinical database to explore the timing component of active rehabilitation. We identified that regardless of the time to initiate active rehabilitation, all groups demonstrated improved symptoms at follow-up. This finding further supports the use of an exercise-based approach. Overall, we found that initiating active rehabilitation two or three weeks post-concussion was associated with the greatest symptom improvement at the follow-up appointment. Like studies using animal models we found that those patients who started active rehabilitation very early (less than 2 weeks post-concussion) or very late (6 weeks or later post-concussion) demonstrated less improvement compared to starting 2 or 3-weeks post-injury. Through the clinical database from the mTBI Program/Concussion Clinic we addressed three limitations identified from previous studies, namely improved methodology (manuscript I), the need for larger studies (manuscript III), and the need to address the timing of initiation (manuscript IV).

In our fifth and final study we use evidence gained from both the literature and our previous studies to estimate the feasibility and safety of initiating the exercise-based intervention 2 weeks after injury, compared to the current timing of 3-4 weeks post-injury. To achieve this objective, we designed a randomized feasibility trial. The need for a feasibility study was indicated because no existing studies had initiated an exercise-based intervention 2-weeks post-concussion in youth. In previous studies, exercise was initiated 3-4 weeks post-injury.[7,116-118,120,199] Concussion research is being produced at a rapid rate. During the course of this thesis, there have been dramatic changes in clinical recommendations about when and how exercise should be introduced when concussion symptoms persist.[4,9] In 2013 it was recommended that individuals become asymptomatic before engaging in physical activity.[9] The most recent International Consensus on Concussion in Sport guidelines in 2017 recommend individualized, symptom-limited aerobic exercise for patients with persistent concussion symptoms.[4] The reason for this recommendation is two-fold. First, evidence showed that prolonged rest appeared to aggravate rather than alleviate symptoms.[75] Second, studies using exercise interventions were demonstrating therapeutic benefit.[113,234] Empirical evidence was needed to support these recommendations specifically for children and youth.

The purpose of the feasibility study was to estimate the ability to recruit participants, assess the safety and acceptability, measure adherence to the intervention, and the potential efficacy. For ethical reasons, we were not able to have a control group not receiving any intervention for comparison because active rehabilitation is considered standard of care at the Montreal Children's Hospital. As such, we provided the same intervention to both groups but varied the timing of initiation.

Chapter 13 – Manuscript V

Title: Feasibility of early active rehabilitation for concussion recovery in youth: a randomized trial

Danielle M. Dobney[1] CAT(C), MSc., Lisa Grilli[2] PT MSc., BScN, Christine Beaulieu[2] PT., Meghan Straub[2] PT M.Sc., A., Carlo Galli[2] PT, Mitchell Saklas[1] BSc, Debbie Friedman[23567] BSc pht MMgmt., Alexander Sasha Dubrovsky MDCM MSc[4] & Isabelle J. Gagnon[124] PT, PhD.

1. School of Physical and Occupational Therapy, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.
2. Trauma Centre, The Montreal Children's Hospital, McGill University Health Center, Montreal, Quebec, Canada.
3. Canadian Hospitals Injury Reporting and Prevention Program
4. Department of Pediatric Emergency Medicine, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.
5. Department of Pediatric Surgery, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.
6. Assistant Dean of Student Affairs, Schools (Physical and Occupational Therapy, Communication Sciences and Disorders, Nursing), Faculty of Medicine McGill University, Montreal, Quebec, Canada.
7. Department of Pediatrics, Faculty of Medicine, McGill University, Montreal, Quebec, Canada.

Under review: Clinical Journal of Sports Medicine

Acknowledgements

We would like to thank the children and families for participating in this research study. Thank you to Fatemeh Bahrpeyma for assistance recruiting participants. Thank you to Dr. Jérôme Gauvin-Lepage for translating study documents into French.

Funding Source: This work was supported by a grant from the Canadian Institutes of Health Research and the Fonds de la recherche du Québec-santé

Financial Disclosure: The authors have no financial relationships relevant to this article to disclose.

Conflict of Interest: The authors have no conflicts of interest relevant to this article to disclose.

Clinical Trial Registration: Safety and Feasibility of Early Active Rehabilitation in Children After Concussion: US National Institutes of Health NCT03103529

Contributors' Statement:

Danielle Dobney conceptualized and designed the study, carried out the analyses, drafted the manuscript, reviewed/revised and approved the final manuscript as submitted.

Lisa Grilli assisted with study design, recruited participants, data acquisition, reviewed and approved the final manuscript as submitted.

Christine Beaulieu, Meghan Straub, and Carlo Galli assisted with study design, data acquisition, reviewed and approved the final manuscript as submitted.

Mitchell Saklas recruited participants, coordinated and supervised data acquisition, reviewed and approved the final manuscript as submitted.

Debbie Friedman assisted with study design, reviewed and approved the final manuscript as submitted.

Dr. Alexander Sasha Dubrovsky conceptualized the study, reviewed/revised and approved the final manuscript as submitted.

Dr. Isabelle Gagnon conceptualized and designed the study, reviewed/revised and approved the final manuscript as submitted.

Abstract

Objective: The primary objective is to evaluate the feasibility (safety & acceptability) of implementing early Active Rehabilitation (AR) for concussion management in youth with symptoms persisting 2-weeks post-injury. A secondary and exploratory objective was to estimate the potential efficacy of early AR compared to standard AR. We hypothesize AR at 2-weeks post-concussion will be safe and acceptable to patients.

Methods: Single centre, parallel randomized clinical trial examining early AR (initiated 2-weeks post-injury) compared to standard AR (initiated 4-weeks post-injury). Twenty youth (9-17 years old) with post-concussion symptoms for at least 2-weeks were randomized to early AR (n=10) or to standard AR (n=10). Active Rehabilitation (aerobic exercise, coordination drills, visualization, education/reassurance) was administered by physiotherapists in-person, and then continued as a home program.

Results: Post-Concussion Symptoms decreased over time for both groups. Two adverse events (one in each group) were identified through an online survey more than one-month post-concussion.

Conclusions: The results from this pilot study indicate that a full clinical trial estimating the efficacy of early Active Rehabilitation (starting 2-weeks post-injury) is feasible. Further study is needed to determine the superiority of this strategy over current treatment approaches.

Key words: *concussion, rehabilitation*

Background

Concussion management and return to activity decision-making is a complicated process. Evidence to support management practices are scarce. Expert consensus guidelines have been developed to assist with this process.[4,9,58-60] Most return to play guidelines are initiated with physical activity limitations until asymptomatic. Once asymptomatic, patients begin a gradual return to activity protocol.[29,60] Because 70% of patients will become asymptomatic within four weeks,[55] they respond well to activity limitations and gradual return to activity.

However, research has shown that approximately 30% of children will experience concussion symptoms beyond four weeks.[2] In following the standard guidelines for returning to activity, these children would be limited in their physical activities during this time.[235] Patients who are inactive for prolonged periods can experience secondary complications which delay recovery.[236] A small randomized control trial on physical and cognitive rest indicated that 1-2 days of strict rest (no school, work, or physical activity) was superior to 5 days of rest for recovery.[75] The ideal length of activity limitation after concussion is unknown.[75] Removal from meaningful activities has been found to increase feelings of depression and stress, both of which are symptoms of concussion.[237] Prolonged activity limitations increases concussion-like symptoms which often results in the recommendation of further activity limitations.

Recently, there has been a shift in concussion management that follows a more active approach, specifically for those who experience persisting symptoms. This approach encourages low level, individualized activity which is thought to assist with recovery.[7,31,113,117,160] Exercise-based strategies have been used in children and adults with promising preliminary results.

Exercise immediately after concussion has been shown to prolong recovery in animals,[73] and humans.[217] Vigorous activity within 2 days of concussion led to longer recovery compared to those exercising at lower intensities.[121] Conversely, after a period of rest in the acute phase, exercise is associated with improvement in concussion symptoms. However, most studies that have used exercise as a post-concussion intervention have started exercise at least 1-month post-injury.[7,120,150,154,199] Early exercise may promote recovery, assuming it is safe to do so. The purpose of this study was therefore to investigate the feasibility, safety, and potential efficacy of an exercise-based intervention (Active Rehabilitation) 2-weeks post-concussion.

Objectives

To estimate the feasibility of implementing early active rehabilitation (AR) for children and adolescents with persisting symptoms from a concussion. Specifically, we wished to estimate the safety and acceptability of initiating early active rehabilitation at 2 weeks post-injury compared to usual care (4 weeks) at the Montreal Children's Hospital Concussion clinic.

The specific aims of this project were to estimate; 1) the rates of recruitment and consent; 2) acceptability to patients/families and clinicians; 3) the utility of data collection using an online symptom and activity survey; 4) the safety of early AR; 5) the extent of patient adherence to prescribed exercise; and 6) the potential efficacy of early AR on post-concussion symptoms.

Methods

Setting

The study was conducted at The Montreal Children's Hospital of the McGill University Health Center (MCH-MUHC), a tertiary care paediatric teaching hospital affiliated with McGill University in Montreal, Canada. In this setting, AR is offered to children and adolescents 4-weeks post-injury through the Mild Traumatic Brain Injury (mTBI) Program/Concussion clinic. Data were collected prospectively through the mTBI Program/Concussion clinic.

Participants

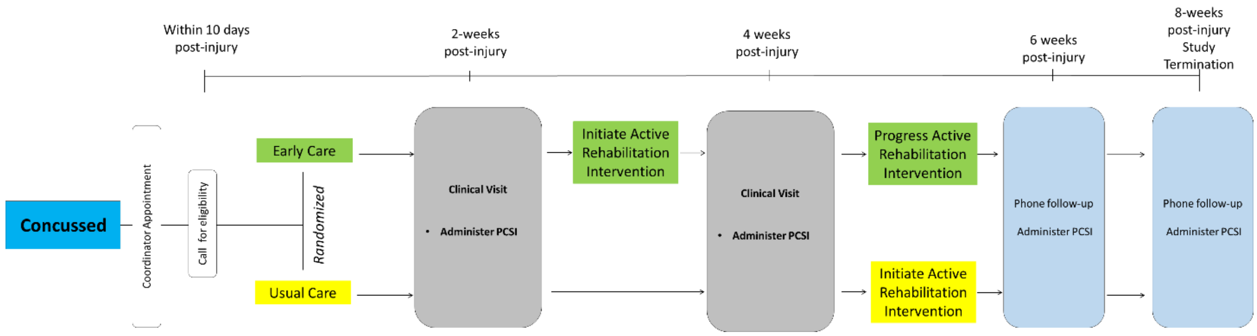
Patients were referred to the mTBI program/Concussion clinic from various sources (emergency department, family physician). The administrative staff and clinic coordinators introduced patient/families to the study and asked their interest in being called about participating in a study. Patients were eligible if they met the following criteria; 1) physician diagnosed concussion, 2) presence of symptoms 2-weeks post-concussion, defined as; a) three individual symptoms rated above the retrospective baseline (self-report), or b) any symptom interfering with daily activities (self or parent report), or c) a symptom severity score greater than seven points (parent proxy or PCSI-SR13 adolescent form), or d) a parent proxy score of one or greater on the following question "In general, to what degree is your child acting differently than before the injury (not acting like himself or herself)? 3) aged 6 to 17, and 4) spoke English or French. Patients were excluded if they had a previous concussion within 6 months of the current injury, a co-existing injury preventing participation in the intervention, or if the patient engaged in moderate to vigorous physical activity/exercise/sport prior to enrolment.

Intervention

Randomization was conducted using a sequence generated by www.randomization.com on May 26th, 2016 by a research assistant (MS). Randomization was concealed from patients and clinicians until patients started the intervention. Participants were randomized to receiving early AR (2 weeks post-injury) or to receiving usual care AR (4 weeks post-injury). Participants in the usual care group did not receive clinical care between the 2 and 4-week appointments. Participants, families, clinicians, and those measuring outcomes were not blinded to group allocation. A research assistant (MS) and the primary author (DD) enrolled and assigned participants to groups.

The intervention provided to both groups (early and usual care) was identical. Only the time of starting the intervention differed. The AR intervention has been published previously by Gagnon et al.[7,31] The intervention included four components: 1) aerobic activity, 2) coordination/skill practice, 3) visualization and, 4) education. Active rehabilitation was delivered in-clinic by physiotherapists who work in this clinical setting. The 2 and 4-week appointments were conducted at the Concussion Clinic. The physiotherapy appointment included a clinical assessment (standard neurological, physical examination, balance, and coordination) (Figure 1). The AR program was initiated in clinic and continued as a home program. The safety and adherence monitoring for this study focusses solely on the aerobic activity component of the intervention.

Figure 1: Study timeline



Outcomes

Measures

An online questionnaire was used in this study. The online survey contained 7 post-concussion symptoms as seen in the Post-Concussion Symptom Inventory (PCSI)[99] (headache, nausea, balance problems, dizziness, fatigue, sadness, nervous/anxious). This patient-reported measure was used to track and monitor post-concussion symptoms and the aerobic exercise portion of the AR home program. Participants were asked to provide information about their home program, specifically the mode, intensity, and duration of aerobic exercise. Participants rated post-concussion symptoms pre- and post-exercise when applicable (appendix 3). Online surveys were emailed to all participants everyday starting after the 2-week physiotherapy appointment until one of the following criteria were met; 1) the end of the study period (8 weeks), 2) the patient reported five consecutive days of being symptom free, or 3) the patient was discharged by physical therapy.

To estimate the potential efficacy of the intervention, the total post-injury symptom severity score was obtained using the PCSI.[99] The PCSI is a self-report questionnaire documenting the presence and severity of post-concussion symptoms. Two versions of the PCSI were used, the adolescent self-report form for ages 13-18 (PCSI-SR13) and the older child self-report form for ages 8-12 (PCSI-SR8).The highest total symptom scores for the PCSI-SR13 and PCSI-SR8 are 156 and 50 respectively.[99] A higher score indicates greater severity of post-concussion symptoms. PCSI was evaluated at four times; 2, 4, 6, and 8-weeks post-concussion. Evaluation at 2 and 4 weeks was conducted by a physiotherapist during the clinical visit. The 6 and 8-week evaluations were performed over the phone by a trained research assistant (MS) or the primary author (DD).

Definitions

Safety was defined as the ability to perform AR with minimal symptom exacerbation. We measured safety with an adverse event definition. An adverse event was defined as an increase in the 7-symptom online scale reported during or following aerobic exercise in which there was; 1) an individual symptom greater than one point (6-12 years, or two points (13-18 years), 2) a total severity score increase of two points (6-12 years), or three points (13-18 years). A stopping rule was implemented if an adverse event occurred on three subsequent aerobic exercise sessions.

Acceptability was defined as; 1) a willingness of clinicians to prescribe comparable home programs to both groups, and 2) a willingness of patients to follow clinician recommendations. Acceptability was evaluated by comparing the online activity survey responses and patient charts.

Adherence was defined as the extent to which participants reported exercise characteristics that were consistent with those prescribed by clinicians.

Feasibility was composed of safety and acceptability. Feasibility was also inferred based on recruitment, utility of data collection, and the potential efficacy of the intervention.

Sample Size

A sample size of twenty participants was determined sufficient for the objectives of this pilot study.[238,239]

The trial was registered with the US National Institutes of Health NCT03103529 (www.clinicaltrials.gov). Reporting results of this trial was guided by the CONSORT guidelines for randomised pilot and feasibility trials.[240] Ethics approval was obtained from the Research Ethics Board of the Montreal Children's Hospital, McGill University Health Centre.

Statistical Analysis

Analysis of data were conducted using R version 3.1.2 (2014-10-31). Descriptive statistics were compiled for feasibility objectives. To estimate patient adherence, descriptive statistics were obtained for exercise frequency, intensity, and duration. The total post-concussion scores were calculated by summing the scores of each individual symptom. Symptom scores on the PCSI-SR8 were transformed to a 7-point scale by multiplying each individual item by 3. This transformation was conducted so that all participants symptoms could be reported on the same scale. Variables not meeting normality assumptions are presented as the median and range.

Results

Recruitment and Consent (objective 1)

Fifty patients were contacted for participation in the study. Participants were between the ages of 9-17 years old. At the initial screening, 44 patients met the eligibility criteria and approximately 57% (25/44) enrolled in the study. The most common reason for not participating was scheduling. Of the 25 patients who consented to participate study, five became symptom free before the 2-week appointment making them ineligible. After allocation, no participants dropped out of the study.

Recruitment occurred between May 21 and November 17, 2016. The final follow-up was completed December 29, 2017. Figure 2 shows the flow of participants in the trial. The most common cause of injury was sport-related (80%). Groups were similar with respect to gender, age, and history of; concussion, migraines, anxiety, learning disabilities, or sleep disorders. Most participants (17/20) reported academic accommodations such as; reduced school days, breaks during the day, limited workload, or exam exemptions over the study period. The 2 and 4-week visits occurred an average 16 ± 2.4 and 30 ± 4.6 days post-concussion respectively.

Figure 2: CONSORT Diagram

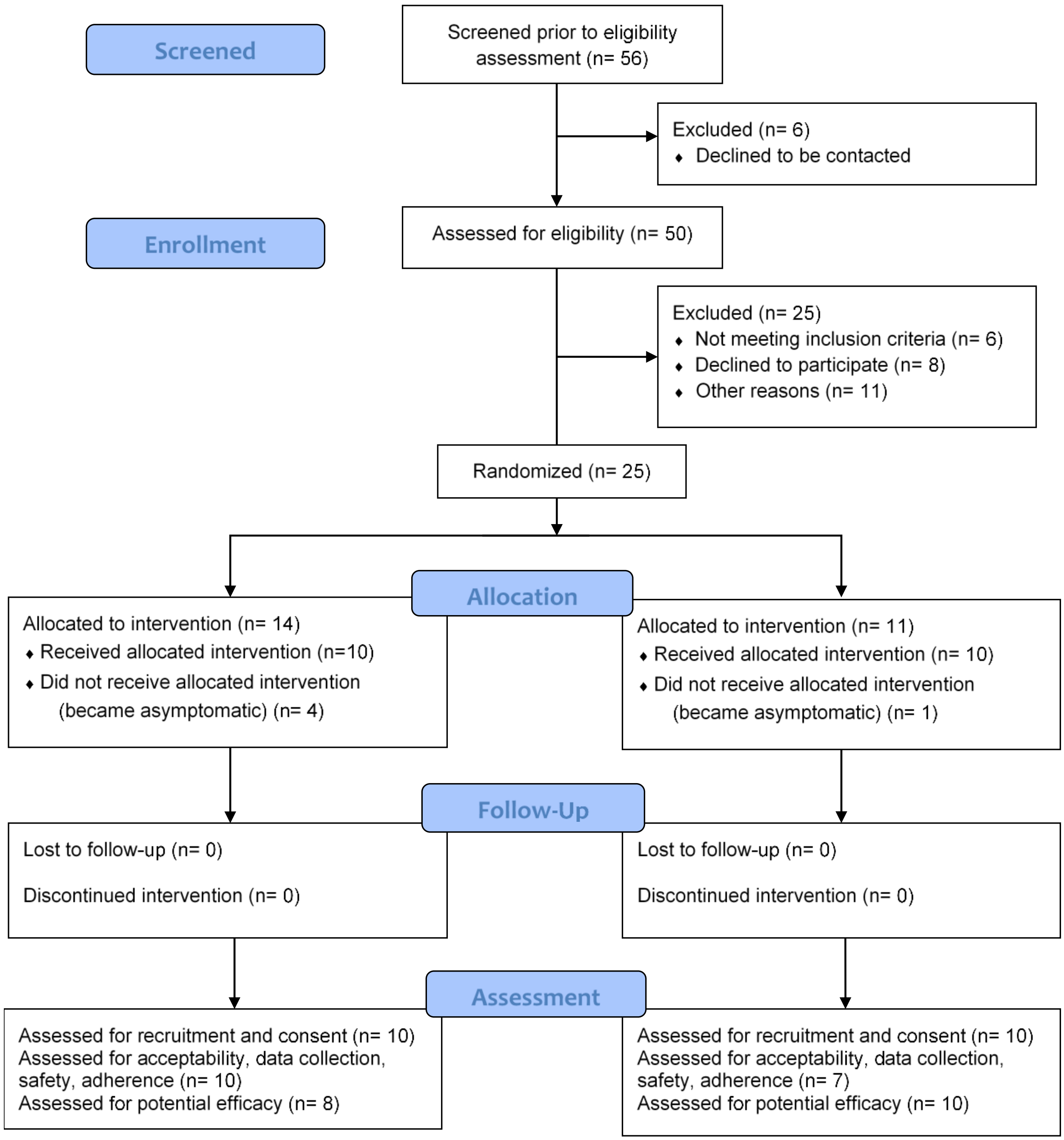


Table 1: Enrolled Participant Characteristics

Variable		Early AR (n=10)	Usual Care (n=10)
Age (mean, SD)		15.6 (1.8)	14.3 (2.7)
Sex (n)	Female	4	4
	Male	6	6
History of Concussion (n)		5	3
History of Anxiety (n)		3	5
History of Migraines (n)		2	3
Learning Disability (n)		2	2
History of Sleep Disorder (n)		4	3
Initial symptoms (n)	Headache	4	6
(at time of injury)	Dizziness	1	2
	Nausea	2	2

Acceptability (objective 2)

Clinicians demonstrated a willingness to prescribe AR to patients at 2-weeks post-concussion. Exercise characteristics prescribed to patients were similar in both groups indicating acceptability of clinicians (table 2).

Utility of Data Collection (objective 3)

During the study period the online questionnaire was emailed to participants 478 times. We received 326 completed surveys for a response rate of 68%. We were able to measure PCSI at all four-time points. One participant was unreachable for the 8-week phone call and we carried forward their PCSI value from the 6-week visit. The 6-week and 8-week follow-up phone calls were conducted an average 6.1 ± 0.69 and 7.8 ± 1.06 weeks post-concussion respectively.

Safety (objective 4)

Two adverse events occurred during the study. Events occurred in one female participant (early AR group) and one male participant (usual care group) at 31 and 37 days post-concussion respectively. Participants reported increased symptom severity on the online survey following aerobic exercise. In both cases, symptoms resolved within one hour of terminating exercise. Both participants continued with the intervention.

Patient Adherence (objective 5)

Exercise characteristics obtained from the online survey for frequency, intensity, and duration of aerobic exercise are displayed in table 2. Patients reported being adherent to the recommendations prescribed by clinicians, for exercise intensity and duration. Patients reported being less compliant with prescribed frequency. The most common modes of exercise were; walking/jogging and stationary cycling.

Table 2: Aerobic Exercise Characteristics

Variable	**Early AR (n=10)**		**Usual care (n=7[a])**	
	Prescribed	Reported	Prescribed	Reported
Frequency (mean days/week)	7	3.7	7	4.2
Intensity (mean (SD) P-CERT)	2.7 (0.5)	2.5 (0.9)	3.1 (0.6)	3.2 (1.2)
Duration (mean (SD) minutes)	16.1 (5.2)	18.5 (11.4)	16.7 (4.4)	21.2 (21.2)

[a]Three participants were discharged prior to starting AR

Potential Efficacy (objective 6)

Post-concussion symptoms improved over time for both groups (table 3). Two participants in the early AR group were excluded from symptom analysis. One participant admitted to falsifying symptom reports at 4-weeks. The other participant was enrolled based on parent-reported symptoms and self-reported no symptoms on the PCSI. We excluded the latter participant as their data artificially influenced the descriptive statistics. We found that participants in the early AR group reaches a symptom severity score that is within a normal limit range[212] by 4-weeks post-injury compared to 6-weeks in the usual care group.

Table 3: Median (Range) Post-Concussion Symptom Severity Scores

	Early Rehab (n=8[a])	**Usual Care (n=10)**	
	Youth n=8 (PCSI-SR13)	Youth n=8 (PCSI-SR13)	Child[b] n=2 (PCSI-SR8)
2-weeks	21 (4-59)	25 (6-35)	29 (12-45)
4-weeks	3 (0-49)	11 (0-35)	22 (8-33)
6-weeks	2 (0-21)	8 (0-27)	18 (0-36)
8-weeks	3 (0-9)	2.25 (0-24)	15 (0-30)

[a]Two patients excluded from symptom analysis
[b]Child scores on PCSI-SR8 have been transformed to a 7-point scale (all scores multiplied by 3)

Discussion

The primary objective of this study was to determine the feasibility of a future clinical trial implementing early AR. Due to the feasibility nature of this study we did not conduct inferential statistics. Literature regarding feasibility trials indicates that analysis should be descriptive in nature rather than hypothesis driven.[241,242]

The recruitment rate was above 50% which is considered high. Recruitment is a common problem in clinical trials with rates as low as 3-20%.[243] Our study had only one additional clinical appointment compared to usual care provided at the concussion clinic. Our recruitment strategy allowed patients and families to get information about the study before being asked to participate.

Our data collection strategy to monitor safety and adherence was a strength of the study. Monitoring and adherence are two methodological components that have not been well controlled in previous studies. Although previous studies reported the use of log books to measure adherence, none have presented data on these variables.[116,117,119] Exacerbation of symptoms during recovery from concussion is one of the most commonly cited reasons for the need for activity limitations.[9,78,244] Given this concern, monitoring what patients are doing and how it influences their symptoms is critical to a management strategy involving physical activity. Half of our families elected to have the online survey delivered to both the participant and parent/guardian email addresses. In other cases, the email was sent only to the parent/guardian email address (n=6) or the participants email address (n=4). The rate of response was highest for delivery to the parent's email address (78%) compared to both parent/participant (67%), or the participant only (53%). To our knowledge this method of monitoring has not been used previously during recovery from concussion. Importantly, we demonstrated it was a feasible method to identify adverse events. Similar to a recent randomized trial,[117] we found serial repetition of the PCSI to be feasible in our study.

Regarding the prescribed exercise, the usual care group reported higher frequency, intensity, and durations of aerobic exercise compared to the early AR group. Patients in both groups displayed a high level of adherence to the prescribed intensity and duration, but not frequency. Neither group was able to complete their home program at the frequency recommended by the physiotherapist. Further study is required to investigate factors related to exercise adherence in post-concussion populations. Patient adherence to prescribed interventions varies considerably.[245] If future studies aim to estimate the efficacy of this concussion management approach, exercise characteristics and adherence must be measured.

At the study conclusion most patients (15/20) demonstrated symptom scores that were at or below the level of their pre-injury, retrospective baseline. Although expert consensus advocates patients be asymptomatic before return to full activity[9] there is growing evidence that youth experience concussion like symptoms in the absence of concussive injury.[246] Healthy teen athletes (no concussion) aged 13 to 17 displayed symptom severity scores ranging from 4.06-9.17 on the same symptom scale we used in the present study (PCSI).[212] Both groups achieved comparable levels of post-concussion symptoms at the end of the study period. Of note, patients in the early group reached a level of symptom severity that could be considered "normal" (equal to baseline in healthy youth) at 4-weeks post-concussion, compared to 6-weeks in the usual care group. Starting exercise 2-weeks post-concussion did not delay recovery.

Limitations

Considering our findings, we acknowledge a few limitations. We do not have a true control group for comparison and the evaluation of outcomes was not blinded. The study sample consisted mostly of older adolescents with only three of our participants under the age of twelve. The low number of participants under the age of twelve may be a result of differing rates of recovery in these age groups. Research has shown that patients 13 years and older are more likely to experience prolonged symptoms compared to younger patients.[2] We cannot say with certainty that our findings can be generalized to a younger sample of patients. It is also unclear if our data collection methods (online surveys) would be suitable for younger children. We acknowledge that the online activity surveys were patient reported and coupling this with an objective measure would provide better accuracy. Physical activity reporting in children has low to moderate correlation with direct measures such as accelerometers. Further, children have been found to both over and under estimate their level of physical activity when compared to direct measures.[247] We acknowledge that our sample had a high proportion of participants with pre-existing co-morbidities (ex. History of anxiety, migraine, learning, disabilities, sleep disorders). Forty percent of the participants in our sample reported a previous concussive injury. Prior studies have reported rates ranging from 22%[50] to 31%[214] in similar age groups. These co-morbidities have been associated with prolonged recovery from concussive injuries in youth.[228] This sample may not be representative of the youth population in general. Lastly, related to the intervention, we did not measure all components of the home program (coordination drills & visualization). While we did not exclude patients, who were receiving additional care outside of the study protocol, 3 patients (early care n=1, usual care n=2) reported receiving treatment (osteopathy, physiotherapy) for concurrent neck injuries during the study period.

Conclusion

The results from this study indicate that a clinical trial estimating the efficacy of active rehabilitation 2-weeks post-concussion is feasible. Little evidence exists to determine when patients with prolonged symptoms should resume physical activity. The introduction of physical activity (at 2-weeks post-injury) that we implemented is important given that extended physical inactivity is associated with prolonged recovery. This study provides a foundation upon which a future efficacy study could be conducted. Future work building on the current study would have a large impact on concussion rehabilitation and the use of exercise-based approaches. Further study is needed to determine the superiority of this strategy over current treatment approaches.

Chapter 14 – Discussion

The overall aim of this thesis was to contribute evidence towards an exercise-based concussion management approach for youth with persisting symptoms. To achieve this objective, two broad lines of inquiry were pursued. First, an environmental scan of current practice in the use of exercise-based interventions (manuscripts I and II). Second, estimating the effectiveness of an exercise-based intervention in decreasing post-concussion symptoms (manuscripts III, IV, and V).

In our first line of inquiry (environmental scan) we identified a need for more high-quality studies. While the role of exercise-based interventions was emerging in the literature, just over one-third of clinicians indicating its use as a concussion management strategy.

Our second line of inquiry (effectiveness of exercise-based interventions) revealed that participating in an exercise-based intervention was associated with improved post-concussion symptoms and that these improvements were observed within a large timeframe (<2 to 6 or more weeks post-injury). Further, our feasibility study did not reveal any barriers to implementation.

Strengths and limitations of the thesis

This thesis has several strengths and a few limitations. One of the main strengths of each manuscript was that we took deliberate steps to improve the quality of our studies from a methods perspective. In the scoping review (manuscript I), we added a quality assessment using a validated tool. In our clinician survey (manuscript II), we pre-screened and pilot-tested our questionnaire. In the retrospective database studies (manuscripts III and IV) we selected specific inclusion criteria (start and follow-up times) to achieve a more homogenous sample to study. While limitations of our retrospective studies existed, we aimed to address those in the fifth manuscript. In our feasibility study (manuscript V), we used a strong study design and modified the study in such a way that we were able to create a "quasi-control group". Further, we developed and tested a method to measure adherence and safety of the home exercise program.

Implications for future research

The work presented here fits into a larger context of concussion research. From a broad perspective, the single-most important need for research in this field is to improve the overall quality of studies. This recommendation can be achieved through several avenues. One approach could be designing studies using a validated quality assessment tool (ex. Downs and Black criteria). Although these tools are generally used to determine the quality when a study has been completed, the tool can be very informative during the design phase. In this way, researchers could make modifications to the design before the study is underway to ensure good quality is achieved. A second design consideration is to include a control group. For ethical reasons, we were not able to have a control group that received no treatment. As such, we opted to modify our fifth study to alter the timing of the intervention because we could not withhold treatment altogether. This limitation is significant in estimating the effectiveness of any intervention. Further work would benefit from including a control group.

Our feasibility study (manuscript V) acts as a springboard for future research. While exercise-based interventions have shown promise, there has yet to be an effectiveness study conducted. A full clinical trial that estimates the influence of individualized exercise on concussion symptoms and recovery would be a significant contribution to the field. Future studies would benefit from using objective measures (ex. Heart rate monitoring, actigraphy etc.) to accurately quantify exercise characteristics (ex. Intensity, duration, frequency). A continuation of this research could be to explore those exercise characteristics further. Understanding how the frequency, intensity, duration, and type of exercise influences recovery from concussion would provide much needed parameters for clinicians.

To look more broadly at concussion management, one must consider the heterogeneity of injury. This heterogeneity may be one of the most challenging aspects of designing research studies. While it is straightforward to evaluate the effectiveness of a single treatment, (ex. Cervical therapy, vestibular therapy, academic accommodations) the reality is that individuals may require several different treatments to achieve full recovery. Studies that provide a multi-factorial intervention tailored to each patient would likely be more accurate from a clinical perspective.

Implications for clinical practice

The collection of work presented here have implications for clinical practice. Our findings from the scoping review indicate that clinicians should be judicious in their application of findings from the literature. While results are often presented positively, the quality of most studies was too low to validate use in clinical practice. Based on our quality assessment, those studies of good quality used cervical spine manual therapy, cognitive behavioural therapy, active rehabilitation, web-based self-management, and individualized exercise. Our clinician survey shows that limited evidence-based treatment is being used for youth with persisting symptoms. There is a strong need for knowledge translation. Understanding the barriers that prevent clinicians from using exercise-based strategies will aid in determining a targeted approach for knowledge translation.

We provide additional support for active rehabilitation strategies specifically for youth with persisting symptoms following a concussion. This thesis provides a unique perspective in that we replicated findings from small, pilot samples in a large, diverse clinical sample. Clinicians should find benefit in the specific safety monitoring we conducted and our initial exploration of exercise frequency, duration, and intensity (manuscript V). Considering the limited evidence available to clinicians for youth with persisting symptoms, we encourage the use of individualized, sub-symptom threshold exercise as a rehabilitative strategy. As with any health condition, matching the clinical needs of each patient to a therapeutic technique is paramount. However, returning to physical activity following a period of inactivity will likely be a common need for most youth recovering from concussion.

The exercise-based intervention we explored through the Montreal Children's Hospital Concussion Clinic was largely a home program. While the initial visit was conducted in the clinical setting, patients performed much of the intervention at home. Interventions like the one explored in this thesis are heavily dependent on self-management. This self-management may also require support, encouragement, and supervision from family members. Patients adherence to clinical recommendations varies considerably.[248] In the concussion context, patients may be experiencing symptoms that make them feel unwell, which could be a barrier to performing home exercise. We found that although our clinicians prescribed exercise 7-days per week, our participants only reported exercising 3-4 days per week (manuscript V). This result provides some insight into what clinicians can expect regarding adherence to post-concussion exercise prescription. For clinicians to be able to guide patients, we need a better understanding of the barriers that patients and families face in carrying out a concussion management home program.

Chapter 15 – Conclusion

Throughout the course of study, we focused our attention on addressing limitations from previous work, and in doing so we were able to make several novel contributions. The thesis represents a multi-dimensional approach to exploring exercise-based interventions for concussion management in youth. The environmental scan revealed that while most interventional studies from our scoping review contained an exercise-based component, few clinicians are incorporating exercise as a concussion management strategy. In estimating the effectiveness of an exercise-based intervention, we identified that youth engaging in an exercise-based intervention demonstrated improved symptoms. Further, these improved symptoms were evident irrespective of the time to initiate the exercise (<2 to 6 or more weeks post-concussion). Lastly, no barriers to implementation were identified in our feasibility study.

Our investigation of clinical practice, existing data, and prospective work highlights the breadth of this thesis. The doctoral work provides much needed, empirical support for current consensus guidelines regarding the use of exercise-based interventions. This thesis constitutes a substantial contribution to the literature given the limited evidence-based research that exists.

Complete references

1. Halstead ME, Walter KD, Council on Sports M, Fitness. American Academy of Pediatrics. Clinical report--sport-related concussion in children and adolescents. *Pediatrics.* 2010;126(3):597-615.
2. Zemek R, Barrowman N, Freedman SB, et al. Clinical Risk Score for Persistent Postconcussion Symptoms Among Children With Acute Concussion in the ED. *JAMA.* 2016;315(10):1014-1025.
3. Bressan S, Babl FE. Diagnosis and management of paediatric concussion. *Journal of Paediatrics and Child Health.* 2016;52(2):151-157.
4. McCrory P, Meeuwisse W, Dvorak J, et al. Consensus statement on concussion in sport—the 5th international conference on concussion in sport held in Berlin, October 2016. *British Journal of Sports Medicine.* 2017.
5. Davis GA, Purcell LK. The evaluation and management of acute concussion differs in young children. 2014.
6. Leddy JJ, Baker JG, Willer B. Active Rehabilitation of Concussion and Post-concussion Syndrome. *Physical medicine and rehabilitation clinics of North America.* 2016;27(2):437-454.
7. Gagnon I, Galli C, Friedman D, Grilli L, Iverson GL. Active rehabilitation for children who are slow to recover following sport-related concussion. *Brain Injury.* 2009;23(12):956-964.
8. Rose SC, Weber KD, Collen JB, Heyer GL. The Diagnosis and Management of Concussion in Children and Adolescents. *Pediatric Neurology.* 2015;53(2):108-118.
9. McCrory P, Meeuwisse W, Aubry M, et al. Consensus statement on Concussion in Sport - The 4th International Conference on Concussion in Sport held in Zurich, November 2012. *Physical Therapy in Sport.* 2013;14(2):e1-e13.
10. Giza CC, Hovda DA. The new neurometabolic cascade of concussion. *Neurosurgery.* 2014;75:24-33.
11. Canada PHAo. Leading causes of hospitalizations, Canada, 2005/06, males and females combined: counts (crude rate per 100,000). 2008.
12. Gordon KE, Dooley JM, Wood EP. Descriptive Epidemiology of Concussion. *Pediatric Neurology.* 2006;34(5):376-378.
13. Cassidy JD, Carroll L, Peloso P, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *Journal of rehabilitation medicine.* 2004;36(0):28-60.
14. Williamson I, Goodman D. Converging evidence for the under-reporting of concussions in youth ice hockey. *British journal of sports medicine.* 2006;40(2):128-132.
15. Barlow M, Schlabach D, Peiffer J, Cook C. Differences in change scores and the predictive validity of three commonly used measures following concussion in the middle school and high school aged population. *International journal of sports physical therapy.* 2011;6(3):150-157.
16. Babcock L, Byczkowski T, Wade SL, Ho M, Mookerjee S, Bazarian JJ. Predicting postconcussion syndrome after mild traumatic brain injury in children and adolescents who present to the emergency department. *JAMA pediatrics.* 2013;167(2):156-161.
17. Gioia G, Schneider J, Vaughan C, Isquith P. Which symptom assessments and approaches are uniquely appropriate for paediatric concussion? *British Journal of Sports Medicine.* 2009;43(Suppl 1):i13-i22.
18. Alla S, Sullivan SJ, Hale L, McCrory P. Self-report scales/checklists for the measurement of concussion symptoms: a systematic review. *British Journal of Sports Medicine.* 2009;43(Suppl 1):i3-i12.
19. Sufrinko AM, Kontos AP, Apps JN, et al. The Effectiveness of Prescribed Rest Depends on Initial Presentation After Concussion. *Journal of Pediatrics.* 2017;185:167-172.

20. Pardini D, Stump J, Lovell M, Collins M, Moritz K, Fu F. The post-concussion symptom scale (PCSS): a factor analysis. *Br J Sports Med.* 2004;38(5):661.
21. Eisenberg MA, Meehan Iii WP, Mannix R. Duration and Course of Post-Concussive Symptoms. *Pediatrics.* 2014;133(6):999-1006.
22. Sim A, Terryberry-Spohr L, Wilson KR. Prolonged recovery of memory functioning after mild traumatic brain injury in adolescent athletes. 2008.
23. Baillargeon A, Lassonde M, Leclerc S, Ellemberg D. Neuropsychological and neurophysiological assessment of sport concussion in children, adolescents and adults. *Brain injury.* 2012;26(3):211-220.
24. Brosseau-Lachaine O, Gagnon I, Forget R, Faubert J. Mild traumatic brain injury induces prolonged visual processing deficits in children. *Brain Injury.* 2008;22(9):657-668.
25. Gagnon I, Swaine B, Friedman D, Forget R. Children show decreased dynamic balance after mild traumatic brain injury. *Archives of physical medicine and rehabilitation.* 2004;85(3):444-452.
26. Gagnon I, Swaine B, Friedman D, Forget R. Visuomotor response time in children with a mild traumatic brain injury. *The Journal of head trauma rehabilitation.* 2004;19(5):391-404.
27. Reed N, Taha T, Keightley ML. Concussion and strength performance in youth ice hockey players. *British Journal of Sports Medicine.* 2013;47(5):e1-e1.
28. McCrory P, Meeuwisse W, Johnston K, et al. Consensus statement on Concussion in Sport–the 3rd International Conference on Concussion in Sport held in Zurich, November 2008. *South African Journal of Sports Medicine.* 2009;21(2).
29. McCrory P, Meeuwisse WH, Aubry M, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. *British Journal of Sports Medicine.* 2013;47(5):250-258.
30. Gibson S, Nigrovic LE, O'Brien M, Meehan WP. The effect of recommending cognitive rest on recovery from sport-related concussion. *Brain Injury.* 2013;27(7/8):839-842.
31. Gagnon I, Grilli L, Friedman D, Iverson G. A pilot study of active rehabilitation for adolescents who are slow to recover from sport-related concussion. *Scandinavian journal of medicine & science in sports.* 2015.
32. Signoretti S, Lazzarino G, Tavazzi B, Vagnozzi R. The pathophysiology of concussion. *PM&R.* 2011;3(10):S359-S368.
33. Guskiewicz Kevin MK. Biomechanics of sport concussion: quest for the elusive injury threshold. *Exercise and Sport Sciences Reviews.* 2011;39(1):4-11.
34. Giza CC, Hovda DA. The neurometabolic cascade of concussion. *Journal of athletic training.* 2001;36(3):228.
35. Crooks DA. The pathological concept of diffuse axonal injury; its pathogenesis and the assessment of severity. *Journal of Pathology, The.* 1991;165(1):5.
36. Barkhoudarian G, Hovda DA, Giza CC. The molecular pathophysiology of concussive brain injury. *Clinics in sports medicine.* 2011;30(1):33-48.
37. Henry LC, Tremblay S, Boulanger Y, Ellemberg D, Lassonde M. Neurometabolic changes in the acute phase after sports concussions correlate with symptom severity. *Journal of neurotrauma.* 2010;27(1):65-76.
38. Shenton M, Hamoda H, Schneiderman J, et al. A review of magnetic resonance imaging and diffusion tensor imaging findings in mild traumatic brain injury. *Brain imaging and behavior.* 2012;6(2):137-192.
39. Vagnozzi R, Signoretti S, Tavazzi B, et al. Temporal window of metabolic brain vulnerability to concussion: A pilot 1H-magnetic resonance spectroscopic study in concussed atheltes - part III. *Neurosurgery.* 2008;62(6):1286-1296.

40. Bonne O, Gilboa A, Louzoun Y, et al. Cerebral blood flow in chronic symptomatic mild traumatic brain injury. *Psychiatry Research - Neuroimaging.* 2003;124(3):141-152.
41. Wang Y, Nelson LD, LaRoche AA, et al. Cerebral blood flow alterations in acute sport-related concussion. *Journal of neurotrauma.* 2016;33(13):1227-1236.
42. Maugans TA, Farley C, Altaye M, Leach J, Cecil KM. Pediatric sports-related concussion produces cerebral blood flow alterations. *Pediatrics.* 2012;129(1):28-37.
43. Len T, Neary J. Cerebrovascular pathophysiology following mild traumatic brain injury. *Clinical physiology and functional imaging.* 2011;31(2):85-93.
44. Len TK, Neary JP, Asmundson G, Goodman DG, Bjornson B, Bhambhani YN. Cerebrovascular reactivity impairment after sport-induced concussion. *Med Sci Sports Exerc.* 2011;43(12):2241-2248.
45. Gall B, Parkhouse W, Goodman D. Heart rate variability of recently concussed athletes at rest and exercise. *Medicine and science in sports and exercise.* 2004;36:1269-1274.
46. Goodman B, Vargas B, Dodick D. Autonomic Nervous System Dysfunction in Concussion (P01. 265). *Neurology.* 2013;80(Meeting Abstracts 1):P01. 265.
47. Camm A, Malik M, Bigger J, et al. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation.* 1996;93(5):1043-1065.
48. Gall B, Parkhouse W, Goodman D. Exercise following a sport induced concussion. *British journal of sports medicine.* 2004;38(6):773-777.
49. Abaji JP, Curnier D, Moore RD, Ellemberg D. Persisting effects of concussion on heart rate variability during physical exertion. *Journal of neurotrauma.* 2016;33(9):811-817.
50. Zemek RL, Farion KJ, Sampson M, McGahern C. Prognosticators of persistent symptoms following pediatric concussion: a systematic review. *JAMA pediatrics.* 2013;167(3):259-265.
51. Meehan WP, Mannix RC, Stracciolini A, Elbin RJ, Collins MW. Symptom Severity Predicts Prolonged Recovery after Sport-Related Concussion, but Age and Amnesia Do Not. *The Journal of Pediatrics.* 2013;163(3):721-725.
52. Lau B, Lovell MR, Collins MW, Pardini J. Neurocognitive and symptom predictors of recovery in high school athletes. *Clinical Journal of Sport Medicine.* 2009;19(3):216-221.
53. Swaine BR, Tremblay C, Platt RW, Grimard G, Zhang X, Pless IB. Previous head injury is a risk factor for subsequent head injury in children: a longitudinal cohort study. *Pediatrics.* 2007;119(4):749-758.
54. Corwin DJ, Zonfrillo MR, Master CL, et al. Characteristics of prolonged concussion recovery in a pediatric subspecialty referral population. *The Journal of pediatrics.* 2014;165(6):1207-1215.
55. Lovell MR, Iverson GL, Collins MW, et al. Measurement of symptoms following sports-related concussion: reliability and normative data for the post-concussion scale. *Applied neuropsychology.* 2006;13(3):166-174.
56. Meehan WP, Taylor AM, Proctor M. The pediatric athlete: younger athletes with sport-related concussion. *Clinics in sports medicine.* 2011;30(1):133-144.
57. DeMatteo C, Stazyk K, Singh SK, et al. Development of a conservative protocol to return children and youth to activity following concussive injury. *Clinical Pediatrics.* 2015;54(2):152-163.
58. Aubry M, Cantu R, Dvorak J, et al. Summary and agreement statement of the 1st International Symposium on Concussion in Sport, Vienna 2001. *Clinical journal of sport medicine : official journal of the Canadian Academy of Sport Medicine.* 2002;12(1):6-11.

59. McCrory P, Johnston K, Meeuwisse W, et al. Summary and agreement statement of the 2nd International Conference on Concussion in Sport, Prague 2004. *British journal of sports medicine.* 2005;39(4):196-204.
60. McCrory P, Meeuwisse W, Johnston K, et al. Consensus statement on concussion in sport: the 3rd International Conference on Concussion in Sport held in Zurich, November 2008. *British journal of sports medicine.* 2009;43(Suppl 1):i76-i84.
61. Meehan WP, Bachur RG. The recommendation for rest following acute concussion. *Pediatrics.* 2015;135(2):362-363.
62. McCrea MA, Nelson LD, Guskiewicz K. Diagnosis and management of acute concussion. *Physical Medicine and Rehabilitation Clinics.* 2017;28(2):271-286.
63. Grady MF, Master CL, Gioia GA. Concussion pathophysiology: rationale for physical and cognitive rest. *Pediatric Annals.* 2012;41(9):377-382.
64. Keightley ML, Cote P, Rumney P, et al. Psychosocial consequences of mild traumatic brain injury in children: Results of a systematic review by the international collaboration on mild traumatic brain injury prognosis. *Archives of Physical Medicine and Rehabilitation.* 2014;95(3 SUPPL):S192-S200.
65. Iverson GL. Misdiagnosis of the persistent postconcussion syndrome in patients with depression. *Archives of Clinical Neuropsychology.* 2006;21(4):303-310.
66. Iverson GL. Outcome from mild traumatic brain injury. *Current opinion in psychiatry.* 2005;18(3):301-317.
67. Silverberg ND, Iverson GL. Is rest after concussion" the best medicine?": recommendations for activity resumption following concussion in athletes, civilians, and military service members. *The Journal of head trauma rehabilitation.* 2013;28(4):250-259.
68. Fortney SM, Schneider VS, Greenleaf JE. The physiology of bed rest. *Comprehensive Physiology.* 1996.
69. Dillard C, Ditchman N, Nersessova K, et al. Post-concussion symptoms in mild traumatic brain injury: findings from a paediatric outpatient clinic. *Disability & Rehabilitation.* 2017;39(6):544-550.
70. Saunders RL, Harbaugh RE. The second impact in catastrophic contact-sports head trauma. *Jama.* 1984;252(4):538-539.
71. Cantu RC. Second-impact syndrome. *Clinics in Sports Medicine.* 1998;17(1):37-44.
72. McCrory PR, Berkovic SF. Second impact syndrome. *Neurology.* 1998;50(3):677-683.
73. Griesbach GS, Hovda D, Molteni R, Wu A, Gomez-Pinilla F. Voluntary exercise following traumatic brain injury: brain-derived neurotrophic factor upregulation and recovery of function. *Neuroscience.* 2004;125(1):129-139.
74. Griesbach GS, Gómez-Pinilla F, Hovda DA. Time window for voluntary exercise-induced increases in hippocampal neuroplasticity molecules after traumatic brain injury is severity dependent. *Journal of neurotrauma.* 2007;24(7):1161-1171.
75. Thomas DG, Apps JN, Hoffmann RG, McCrea M, Hammeke T. Benefits of Strict Rest After Acute Concussion: A Randomized Controlled Trial. *Pediatrics.* 2015;135(2):213-223.
76. Buckley TA, Munkasy BA, Clouse BP. Acute Cognitive and Physical Rest May Not Improve Concussion Recovery Time. *Journal of Head Trauma Rehabilitation.* 2016;31(4):233-241.
77. Moser RS, Glatts C, Schatz P. Efficacy of immediate and delayed cognitive and physical rest for treatment of sports-related concussion. *The Journal of pediatrics.* 2012;161(5):922-926.
78. Moser RS, Schatz P. A case for mental and physical rest in youth sports concussion: It's never too late. *Frontiers in Neurology.* 2012;3 DEC (no pagination)(Article 171).
79. Vina J, Sanchis-Gomar F, Martinez-Bello V, Gomez-Cabrera M. Exercise acts as a drug; the pharmacological benefits of exercise. *British journal of pharmacology.* 2012;167(1):1-12.

80. Archer T, Svensson K, Alricsson M. Physical exercise ameliorates deficits induced by traumatic brain injury. *Acta Neurologica Scandinavica.* 2012;125(5):293-302.
81. Widmaier EP, Raff H, Strang KT. *Vander's human physiology: the mechanisms of body function.* McGraw-Hill Higher Education; 2011.
82. Neufer PD, Bamman Marcas M, Muoio Deborah M, et al. Understanding the Cellular and Molecular Mechanisms of Physical Activity-Induced Health Benefits. *Cell Metabolism.* 2015;22(1):4-11.
83. Marques-Aleixo I, Oliveira PJ, Moreira PI, Magalhães J, Ascensão A. Physical exercise as a possible strategy for brain protection: evidence from mitochondrial-mediated mechanisms. *Progress in neurobiology.* 2012;99(2):149-162.
84. Meeusen R, De Meirleir K. Exercise and brain neurotransmission. *Sports Medicine.* 1995;20(3):160-188.
85. Goldsmith RL. Exercise and autonomic function. *Coronary Artery Disease.* 2000;11(2):129.
86. Carter JB, Banister EW, Blaber AP. Effect of endurance exercise on autonomic control of heart rate. *Sports medicine.* 2003;33(1):33-46.
87. Perini R. The influence of exercise intensity on the power spectrum of heart rate variability. *European Journal of Applied Physiology and Occupational Physiology.* 1990;61(1-2):143.
88. Rosenwinkel ET. Exercise and autonomic function in health and cardiovascular disease. *Cardiology Clinics.* 2001;19(3):369.
89. Ogoh S, Ainslie PN. Regulatory mechanisms of cerebral blood flow during exercise: new concepts. *Exercise and sport sciences reviews.* 2009;37(3):123-129.
90. Hellström G, Fischer-Colbrie W, Wahlgren NG, Jogestrand T. Carotid artery blood flow and middle cerebral artery blood flow velocity during physical exercise. *Journal of applied physiology (Bethesda, Md : 1985).* 1996;81(1):413-418.
91. Linkis PP. Dynamic exercise enhances regional cerebral artery mean flow velocity. *Journal of Applied Physiology.* 1995;78(1):12-16.
92. Janssen I, LeBlanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. *International journal of behavioral nutrition and physical activity.* 2010;7(1):40.
93. Hoffer ME, Gottshall K, Viirre ES. Vestibular consequences of mTBI. *Traumatic brain injury: A clinician's guide to diagnosis, management, and rehabilitation*. New York, NY: Springer Science + Business Media; US; 2012:139-147.
94. Schneider KJ, Meeuwisse WH, Nettel-Aguirre A, et al. Cervicovestibular rehabilitation in sport-related concussion: a randomised controlled trial. *British Journal of Sports Medicine.* 2014;48(17):1294-1298.
95. Leddy J, Baker JG, Haider MN, Hinds A, Willer B. A Physiological Approach to Prolonged Recovery From Sport-Related Concussion. *Journal of Athletic Training.* 2017;52(3):299-308.
96. Darabaneanu S, Overath C, Rubin D, et al. Aerobic exercise as a therapy option for migraine: a pilot study. *International journal of sports medicine.* 2011;32(06):455-460.
97. Fitterling JM, Martin JE, Gramling S, Cole P, Milan MA. Behavioral management of exercise training in vascular headache patients: an investigation of exercise adherence and headache activity. *Journal of Applied Behavior Analysis.* 1988;21(1):9.
98. Varkey E, Cider Å, Carlsson J, Linde M. A study to evaluate the feasibility of an aerobic exercise program in patients with migraine. *Headache: The Journal of Head and Face Pain.* 2009;49(4):563-570.
99. Sady MD, Vaughan CG, Gioia GA. Psychometric characteristics of the postconcussion symptom inventory in children and adolescents. *Archives of clinical neuropsychology.* 2014:acu014.

100. Lees C, Hopkins J. Peer reviewed: effect of aerobic exercise on cognition, academic achievement, and psychosocial function in children: a systematic review of randomized control trials. *Preventing chronic disease.* 2013;10.
101. Verburgh L, Königs M, Scherder EJ, Oosterlaan J. Physical exercise and executive functions in preadolescent children, adolescents and young adults: a meta-analysis. *British journal of sports medicine.* 2013:bjsports-2012-091441.
102. Ferris LT, Williams JS, Shen C-L. The effect of acute exercise on serum brain-derived neurotrophic factor levels and cognitive function. *Medicine & Science in Sports & Exercise.* 2007;39(4):728-734.
103. Neeper SA, Gomezpinilla F, Choi J, Cotman C. Exercise and brain neurotrophins. *Nature.* 1995;373(6510):109-109.
104. Tomporowski PD, Ganio MS. Short-term effects of aerobic exercise on executive processing, memory, and emotional reactivity. *International Journal of Sport and Exercise Psychology.* 2006;4(1):57-72.
105. Chen J-K, Johnston KM, Petrides M, Ptito A. Neural substrates of symptoms of depression following concussion in male athletes with persisting postconcussion symptoms. *Archives of General Psychiatry.* 2008;65(1):81-89.
106. Petruzzello SJ, Landers DM, Hatfield BD, Kubitz KA, Salazar W. A meta-analysis on the anxiety-reducing effects of acute and chronic exercise. *Sports medicine.* 1991;11(3):143-182.
107. Steptoe A, Cox S. Acute effects of aerobic exercise on mood. *Health Psychology.* 1988;7(4):329.
108. Brand S, Gerber M, Beck J, Hatzinger M, Pühse U, Holsboer-Trachsler E. High exercise levels are related to favorable sleep patterns and psychological functioning in adolescents: a comparison of athletes and controls. *Journal of Adolescent Health.* 2010;46(2):133-141.
109. Chennaoui M, Arnal PJ, Sauvet F, Léger D. Sleep and exercise: a reciprocal issue? *Sleep medicine reviews.* 2015;20:59-72.
110. Flausino NH, Da Silva Prado JM, Queiroz SS, Tufik S, Mello MT. Physical exercise performed before bedtime improves the sleep pattern of healthy young good sleepers. *Psychophysiology.* 2012;49(2):186-192.
111. Griesbach GS. Exercise after traumatic brain injury: is it a double-edged sword? *PM&R.* 2011;3(6):S64-S72.
112. Giza CC, DiFiori JP. Pathophysiology of sports-related concussion an update on basic science and translational research. *Sports Health: A Multidisciplinary Approach.* 2011;3(1):46-51.
113. Leddy JJ, Kozlowski K, Donnelly JP, Pendergast DR, Epstein LH, Willer B. A preliminary study of subsymptom threshold exercise training for refractory post-concussion syndrome. *Clinical Journal of Sport Medicine.* 2010;20(1):21-27.
114. Schneider KJ, Iverson GL, Emery CA, McCrory P, Herring SA, Meeuwisse WH. The effects of rest and treatment following sport-related concussion: a systematic review of the literature. *British Journal of Sports Medicine.* 2013;47(5):1-5.
115. Schneider KJ, Leddy JJ, Guskiewicz KM, et al. Rest and treatment/rehabilitation following sport-related concussion: a systematic review. *Br J Sports Med.* 2017:bjsports-2016-097475.
116. Grabowski P, Wilson J, Walker A, Enz D, Wang S. Multimodal impairment-based physical therapy for the treatment of patients with post-concussion syndrome: A retrospective analysis on safety and feasibility. *Physical Therapy in Sport.* 2016.
117. Kurowski BG, Hugentobler J, Quatman-Yates C, et al. Aerobic Exercise for Adolescents With Prolonged Symptoms After Mild Traumatic Brain Injury: An Exploratory Randomized Clinical Trial. *The Journal of Head Trauma Rehabilitation.* 2016.

118. Imhoff S, Fait P, Carrier-Toutant F, Boulard G. Efficiency of an Active Rehabilitation Intervention in a Slow-to-Recover Paediatric Population following Mild Traumatic Brain Injury: A Pilot Study. *Journal of Sports Medicine Journal of Sports Medicine.* 2016;2016(2):1-11.
119. Cordingley D, Girardin R, Reimer K, et al. Graded aerobic treadmill testing in pediatric sports-related concussion: safety, clinical use, and patient outcomes. *Journal of Neurosurgery: Pediatrics.* 2016:1-10.
120. Chan C, Iverson GL, Purtzki J, et al. Safety of active rehabilitation for persistent symptoms after pediatric sport-related concussion: A randomized controlled trial. *Archives of Physical Medicine & Rehabilitation.* 2017;05:05.
121. Maerlender A, Rieman W, Lichtenstein J, Condiracci C. Programmed Physical Exertion in Recovery From Sports-Related Concussion: A Randomized Pilot Study. *Developmental neuropsychology.* 2015;40(5):273-278.
122. Comper P, Bisschop S, Carnide N, Tricco A. A systematic review of treatments for mild traumatic brain injury. *Brain Injury.* 2005;19(11):863-880.
123. Winkler R, Taylor NF. Do Children and Adolescents With Mild Traumatic Brain Injury and Persistent Symptoms Benefit From Treatment? A Systematic Review. *The Journal of head trauma rehabilitation.* 2015.
124. Davis GA, Anderson V, Babl FE, et al. What is the difference in concussion management in children as compared with adults? A systematic review. *British journal of sports medicine.* 2017;51(12):949-957.
125. Aubry M, Cantu R, Dvorak J, et al. Summary and agreement statement of the first International Conference on Concussion in Sport, Vienna 2001. *British journal of sports medicine.* 2002;36(1):6-7.
126. Dillard C, Ditchman N, Nersessova K, et al. Post-concussion symptoms in mild traumatic brain injury: findings from a paediatric outpatient clinic. *Disability and rehabilitation.* 2016:1-7.
127. Guskiewicz KM, McCrea M, Marshall SW, et al. Cumulative effects associated with recurrent concussion in collegiate football players: the NCAA Concussion Study. *Jama.* 2003;290(19):2549-2555.
128. Røe C, Sveen U, Alvsåker K, Bautz-Holter E. Post-concussion symptoms after mild traumatic brain injury: influence of demographic factors and injury severity in a 1-year cohort study. *Disability and rehabilitation.* 2009;31(15):1235-1243.
129. Kleffelgaard I, Roe C, Soberg HL, Bergland A. Associations among self-reported balance problems, post-concussion symptoms and performance-based tests: a longitudinal follow-up study. *Disability and rehabilitation.* 2012;34(9):788-794.
130. Kirkwood MW, Yeates KO, Wilson PE. Pediatric sport-related concussion: a review of the clinical management of an oft-neglected population. *Pediatrics.* 2006;117(4):1359-1371.
131. McCrory P, Collie A, Anderson V, Davis G. Can we manage sport related concussion in children the same as in adults? *British journal of sports medicine.* 2004;38(5):516-519.
132. Giedd JN. The teen brain: insights from neuroimaging. *Journal of Adolescent Health.* 2008;42(4):335-343.
133. Guskiewicz KM, McLeod TCV. Pediatric sports-related concussion. *PM&R.* 2011;3(4):353-364.
134. Halstead ME, Walter KD. Sport-related concussion in children and adolescents. *Pediatrics.* 2010;126(3):597-615.
135. Burke MJ, Fralick M, Nejatbakhsh N, Tartaglia MC, Tator CH. In search of evidence-based treatment for concussion: characteristics of current clinical trials. *Brain Injury.* 2015;29(3):300-305.
136. Leddy JJ, Sandhu H, Sodhi V, Baker JG, Willer B. Rehabilitation of concussion and post-concussion syndrome. *Sports Health: A Multidisciplinary Approach.* 2012;4(2):147-154.

137. Ellis MJ, Leddy JJ, Willer B. Physiological, vestibulo-ocular and cervicogenic post-concussion disorders: An evidence-based classification system with directions for treatment. *Brain injury.* 2014;29(2):238-248.
138. Boake C, McCauley SR, Levin HS, et al. Diagnostic criteria for postconcussional syndrome after mild to moderate traumatic brain injury. 2014.
139. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *International journal of social research methodology.* 2005;8(1):19-32.
140. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci.* 2010;5(1):1-9.
141. Colquhoun HL, Levac D, O'Brien KK, et al. Scoping reviews: time for clarity in definition, methods, and reporting. *Journal of Clinical Epidemiology.* 2014;67(12):1291-1294.
142. Daudt HM, Van Mossel C, Scott SJ. Enhancing the scoping study methodology: a large, inter-professional team's experience with Arksey and O'Malley's framework. *BMC medical research methodology.* 2013;13(1):48.
143. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *Journal of epidemiology and community health.* 1998;52(6):377-384.
144. O'Connor SnR, Tully MA, Ryan B, Bradley JM, Baxter GD, McDonough SM. Failure of a numerical quality assessment scale to identify potential risk of bias in a systematic review: a comparison study. *BMC Res Notes BMC Research Notes.* 2015;8(1).
145. World Health Organization. Adolescent Health. 2015; http://www.who.int/topics/adolescent_health/en/. Accessed September 14, 2105.
146. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of internal medicine.* 2009;151(4):264-269.
147. Ponsford J, Willmott C, Rothwell A, et al. Impact of early intervention on outcome after mild traumatic brain injury in children. *Pediatrics.* 2001;108(6):1297-1303.
148. McNally KA, Patrick KE, LaFleur JE, Dykstra JB, Monahan K, Hoskinson KR. Brief cognitive behavioral intervention for children and adolescents with persistent post-concussive symptoms: A pilot study. *Child Neuropsychology.* 2017:1-17.
149. DeMatteo C, Volterman KA, Breithaupt PG, Claridge EA, Adamich J, Timmons BW. Exertion Testing in Youth with Mild Traumatic Brain Injury/Concussion. *Medicine and science in sports and exercise.* 2015;47(11):2283-2290.
150. Chrisman SPD, Whitlock KB, Somers E, et al. Pilot study of the Sub-Symptom Threshold Exercise Program (SSTEP) for persistent concussion symptoms in youth. *Neurorehabilitation.* 2017;40(4):493-499.
151. Dobney DM, Grilli L, Kocilowicz H, et al. Is There an Optimal Time to Initiate an Active Rehabilitation Protocol for Concussion Management in Children? A Case Series. *Journal of Head Trauma Rehabilitation.* 2017;18:18.
152. Kurowski BG, Wade SL, Dexheimer JW, Dyas J, Zhang N, Babcock L. Feasibility and potential benefits of a web-based intervention delivered acutely after mild traumatic brain injury in adolescents: A pilot study. *Journal of Head Trauma Rehabilitation.* 2016;31(6):369-378.
153. Mortenson P, Singhal A, Hengel AR, Purtzki J. Impact of Early Follow-Up Intervention on Parent-Reported Postconcussion Pediatric Symptoms: A Feasibility Study. *Journal of Head Trauma Rehabilitation.* 2016;31(6):E23-E32.
154. Dobney DM, Grilli L, Kocilowicz H, et al. Evaluation of an active rehabilitation program for concussion management in children and adolescents. *Brain Injury.* 2017:1-7.
155. Moser RS, Schatz P, Glenn M, Kollias KE, Iverson GL. Examining prescribed rest as treatment for adolescents who are slow to recover from concussion. *Brain Injury.* 2015;29(1):58-63.

156. Worthen-Chaudhari L, McGonigal J, Logan K, Bockbrader MA, Yeates KO, Mysiw WJ. Reducing concussion symptoms among teenage youth: Evaluation of a mobile health app. *Brain Injury*. 2017:1-8.
157. Lynch JM, Anderson M, Benton B, Green SS. The Gaming of Concussions: A Unique Intervention in Postconcussion Syndrome. *Journal of Athletic Training Journal of Athletic Training.* 2015;50(3):270-276.
158. Lin K, Tung C. Acupuncture for Recovery from Pediatric Sport-Related Concussion. *Medical Acupuncture.* 2016;28(4):217-222.
159. Pinchuk D, Pinchuk O, Sirbiladze K, Shugar O. Clinical Effectiveness of Primary and Secondary Headache Treatment by Transcranial Direct Current Stimulation. *Front Neurol Frontiers in Neurology.* 2013;4.
160. Hugentobler JA, Vegh M, Janiszewski B, Quatman-Yates C. Physical therapy intervention strategies for patients with prolonged mild traumatic brain injury symptoms: A case series. *International journal of sports physical therapy.* 2015;10(5):676.
161. Turner JA, Deyo RA, Loeser JD, Von Korff M, Fordyce WE. The importance of placebo effects in pain treatment and research. *Jama.* 1994;271(20):1609-1614.
162. Bialosky JE, Bishop MD, George SZ, Robinson ME. Placebo response to manual therapy: something out of nothing? *The Journal of Manual & Manipulative Therapy.* 2011;19(1):11-19.
163. Zonfrillo MR, Master CL, Grady MF, Winston FK, Callahan JM, Arbogast KB. Pediatric providers' self-reported knowledge, practices, and attitudes about concussion. *Pediatrics.* 2012;130(6):1120-1125.
164. Carl RL, Kinsella SB. Pediatricians' Knowledge of Current Sports Concussion Legislation and Guidelines and Comfort With Sports Concussion Management: A Cross-Sectional Study. *Clinical Pediatrics.* 2014;53(7):689-697.
165. Kinnaman KA, Mannix RC, Comstock RD, Meehan 3rd WP. Management of pediatric patients with concussion by emergency medicine physicians. *Pediatric Emergency Care.* 2014;30(7):458-461.
166. Zemek R, Eady K, Moreau K, et al. Knowledge of paediatric concussion among front-line primary care providers. *Paediatrics & child health.* 2014;19(9):475-480.
167. Zemek R, Eady K, Moreau K, et al. Canadian pediatric emergency physician knowledge of concussion diagnosis and initial management. *CJEM.* 2015;17(02):115-122.
168. Ellis MJ, Ritchie L, Selci E, Chu S, McDonald P, Russell K. Googling Concussion Care: A Critical Appraisal of Online Concussion Healthcare Providers and Practices in Canada. *Clinical Journal of Sport Medicine.* 2016;10.
169. Wilkins SA, Shannon CN, Brown ST, et al. Establishment of a multidisciplinary concussion program: impact of standardization on patient care and resource utilization. *Journal of Neurosurgery Pediatrics.* 2014;13(1):82-89.
170. Makdissi M, Cantu RC, Johnston KM, McCrory P, Meeuwisse WH. The difficult concussion patient: what is the best approach to investigation and management of persistent (> 10 days) postconcussive symptoms? *British journal of sports medicine.* 2013;47(5):308-313.
171. Giza CC, Kutcher JS, Ashwal S, et al. Summary of evidence-based guideline update: Evaluation and management of concussion in sports Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology.* 2013;80(24):2250-2257.
172. Harmon KG, Drezner JA, Gammons M, et al. American Medical Society for Sports Medicine position statement: concussion in sport. *British Journal of Sports Medicine.* 2013;47(1):15-26.
173. West TA, Marion DW. Current recommendations for the diagnosis and treatment of concussion in sport: a comparison of three new guidelines. *Journal of neurotrauma.* 2014;31(2):159-168.

174. Hughes R, Huby M. The application of vignettes in social and nursing research. *Journal of advanced nursing.* 2002;37(4):382-386.
175. Peabody JW, Luck J, Glassman P, Dresselhaus TR, Lee M. Comparison of vignettes, standardized patients, and chart abstraction: a prospective validation study of 3 methods for measuring quality. *Jama.* 2000;283(13):1715-1722.
176. Aguinis H, Bradley KJ. Best practice recommendations for designing and implementing experimental vignette methodology studies. *Organizational Research Methods.* 2014;17(4):351-371.
177. Yorke AM, Littleton S, Alsalaheen BA. Concussion Attitudes and Beliefs, Knowledge, and Clinical Practice: Survey of Physical Therapists. *Physical therapy.* 2016.
178. McGrann P, Keating L. A survey of chartered physiotherapists' knowledge and current clinical practice regarding concussion in sport. 2012.
179. Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *J Med Internet Res.* 2004;6(3):e34.
180. Kelley K, Clark B, Brown V, Sitzia J. Good practice in the conduct and reporting of survey research. *International Journal for Quality in Health Care.* 2003;15(3):261-266.
181. Burns KE, Duffett M, Kho ME, et al. A guide for the design and conduct of self-administered surveys of clinicians. *Canadian Medical Association Journal.* 2008;179(3):245-252.
182. Collins D. Pretesting survey instruments: an overview of cognitive methods. *Quality of life research.* 2003;12(3):229-238.
183. Forman J, Damschroder L. Qualitative content analysis. *Empirical methods for bioethics: A primer*: Emerald Group Publishing Limited; 2007:39-62.
184. Malterud K. Systematic text condensation: a strategy for qualitative analysis. *Scandinavian Journal of Social Medicine.* 2012;40(8):795-805.
185. Broshek DK, De Marco AP, Freeman JR. A review of post-concussion syndrome and psychological factors associated with concussion. *Brain injury.* 2015;29(2):228-237.
186. Carson JD, Lawrence DW, Kraft SA, et al. Premature return to play and return to learn after a sport-related concussion: physician's chart review. *Canadian Family Physician.* 2014;60(6):e310, e312-315.
187. Ransom DM, Vaughan CG, Pratson L, Sady MD, McGill CA, Gioia GA. Academic effects of concussion in children and adolescents. *Pediatrics.* 2015:peds. 2014-3434.
188. Gahimer JE, Domholdt E. Amount of patient education in physical therapy practice and perceived effects. *Physical therapy.* 1996;76(10):1089-1096.
189. Tham SW, Fales J, Palermo TM. Subjective and objective assessment of sleep in adolescents with mild traumatic brain injury. *Journal of neurotrauma.* 2015;32(11):847-852.
190. Tham SW, Palermo T, Vavilala M, Rivara F. Assessment of sleep disturbances in adolescents with mild traumatic brain injury. *Journal of Neurotrauma.* 2012;29 (10):A17.
191. Mollayeva T. Sleep stage distribution in persons with mild traumatic brain injury: a polysomnographic study according to American Academy of Sleep Medicine standards. *Sleep Medicine.* 2017;34:179.
192. Sady MD, Vaughan CG, Gioia GA. School and the concussed youth: recommendations for concussion education and management. *Physical medicine and rehabilitation clinics of North America.* 2011;22(4):701-719.
193. O'Brien LM. The neurocognitive effects of sleep disruption in children and adolescents. *Child and adolescent psychiatric clinics of North America.* 2009;18(4):813-823.
194. Baker SM, Marshak HH, Rice GT, Zimmerman GJ. Patient participation in physical therapy goal setting. *Physical Therapy.* 2001;81(5):1118-1126.

195. Goudsmit EM, Nijs J, Jason LA, Wallman KE. Pacing as a strategy to improve energy management in myalgic encephalomyelitis/chronic fatigue syndrome: a consensus document. *Disability and rehabilitation.* 2012;34(13):1140-1147.
196. Dobney DM, Miller MB, Tufts E. Non-pharmacological rehabilitation interventions for concussion in children: a scoping review. *Disability and rehabilitation.* 2017:1-13.
197. Swanson E, Kurowski B, Hugentobler JA, Quatman-Yates C. Feasibility and potential benefits of active rehabilitation for post-concussion syndrome in adolescents *American Journal of Physical Medicine & Rehabilitation.* 2014:a94-a94.
198. Menon A. Knowledge Translation; The "in" thing in Rehab Research. Powerpoint slides ed2014.
199. Gagnon I, Grilli L, Friedman D, Iverson GL. A pilot study of active rehabilitation for adolescents who are slow to recover from sport-related concussion. *Scandinavian Journal of Medicine & Science in Sports.* 2016;26(3):299-306.
200. Barlow KM, Crawford S, Stevenson A, Sandhu SS, Belanger F, Dewey D. Epidemiology of postconcussion syndrome in pediatric mild traumatic brain injury. *Pediatrics.* 2010;126(2):e374-e381.
201. Brown DA, Elsass JA, Miller AJ, Reed LE, Reneker JC. Differences in Symptom Reporting Between Males and Females at Baseline and After a Sports-Related Concussion: A Systematic Review and Meta-Analysis. *Sports Med Sports Medicine.* 2015;45(7):1027-1040.
202. Broshek DK, Kaushik T, Freeman JR, Erlanger D, Webbe F, Barth JT. Sex differences in outcome following sports-related concussion. *Journal of neurosurgery.* 2005;102(5):856-863.
203. Covassin T, Schatz P, Swanik CB. Sex differences in neuropsychological function and post-concussion symptoms of concussed collegiate athletes. *Neurosurgery.* 2007;61(2):345-351.
204. Echemendia RJ, Giza CC, Kutcher JS. Developing guidelines for return to play: consensus and evidence-based approaches. *Brain Injury.* 2015;29(2):185-194.
205. DiFazio M, Silverberg ND, Kirkwood MW, Bernier R, Iverson GL. Prolonged Activity Restriction After Concussion Are We Worsening Outcomes? *Clinical pediatrics.* 2015:0009922815589914.
206. Mychasiuk R, Hehar H, Ma I, Candy S, Esser MJ. Reducing the time interval between concussion and voluntary exercise restores motor impairment, short-term memory, and alterations to gene expression. *European Journal of Neuroscience.* 2016;44(7):2407-2417.
207. Iverson GL, Gagnon I, Griesbach GS. Active rehabilitation for slow-to-recover children. *Mild traumatic brain injury in children and adolescents: From basic science to clinical management*. New York, NY: Guilford Press; US; 2012:281-302.
208. Carroll L, Cassidy JD, Peloso P, et al. Prognosis for mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *Journal of Rehabilitation Medicine.* 2004;36(0):84-105.
209. Lau BC, Collins MW, Lovell MR. Cutoff scores in neurocognitive testing and symptom clusters that predict protracted recovery from concussions in high school athletes. *Neurosurgery.* 2012;70(2):371-379.
210. Verschuren O, Maltais DB, Takken T. The 220-age equation does not predict maximum heart rate in children and adolescents. *Developmental Medicine & Child Neurology.* 2011;53(9):861-864.
211. Roemmich JN, Barkley JE, Epstein LH, Lobarinas CL, White TM, Foster JH. Validity of PCERT and OMNI walk/run ratings of perceived exertion. *Medicine and science in sports and exercise.* 2006;38(5):1014-1019.
212. Hunt AW, Paniccia M, Reed N, Keightley M. Concussion-Like Symptoms in Child and Youth Athletes at Baseline: What Is “Typical”? *Journal of athletic training.* 2016;51(10):749-757.
213. Iverson GL, Brooks BL, Collins MW, Lovell MR. Tracking neuropsychological recovery following concussion in sport. *Brain injury.* 2006;20(3):245-252.

214. Terwilliger Virginia KV. Additional Post-Concussion Impact Exposure May Affect Recovery in Adolescent Athletes. *Journal of Neurotrauma.* 2016;33(8):761.
215. Gioia GA. Multimodal Evaluation and Management of Children with Concussion: Using our heads and available evidence. *Brain injury.* 2015;29(2):195-206.
216. Iverson GL, Lovell MR, Collins MW. Interpreting change on ImPACT following sport concussion. *The Clinical Neuropsychologist.* 2003;17(4):460-467.
217. Asken BM, McCrea MA, Clugston JR, Snyder AR, Houck ZM, Bauer RM. "Playing Through It": Delayed Reporting and Removal From Athletic Activity After Concussion Predicts Prolonged Recovery. *Journal of athletic training.* 2016;51(4):329-335.
218. Elbin R, Sufrinko A, Schatz P, et al. Removal from play after concussion and recovery time. *Pediatrics.* 2016:e20160910.
219. Grool AM, Aglipay M, Momoli F, et al. Association between early participation in physical activity following acute concussion and persistent postconcussive symptoms in children and adolescents. *JAMA - Journal of the American Medical Association.* 2016;316(23):2504-2514.
220. Lishchynsky J, Palacios-Derflinger L, Toomey C, et al. The association between moderate and vigorous physical activity and time to medical clearance to return to play following sport-related concussion in youth ice-hockey players. *British Journal of Sports Medicine.* 2017;51(11):A44-A44.
221. King NS. Post-concussion syndrome: clarity amid the controversy? *The British Journal of Psychiatry.* 2003;183(4):276-278.
222. Parker TM, Osternig LR, van Donkelaar P, Chou L-S. Recovery of cognitive and dynamic motor function following concussion. *British journal of sports medicine.* 2007;41(12):868-873.
223. Fait P, Swaine B, Cantin J-F, Leblond J, McFadyen BJ. Altered integrated locomotor and cognitive function in elite athletes 30 days postconcussion: a preliminary study. *The Journal of head trauma rehabilitation.* 2013;28(4):293-301.
224. Bazarian JJ, Cernak I, Noble-Haeusslein L, Potolicchio S, Temkin N. Long-term Neurologic Outcomes After Traumatic Brain Injury. *The Journal of head trauma rehabilitation.* 2009;24(6):439-451.
225. La Fountaine MF, Heffernan KS, Gossett JD, Bauman WA, De Meersman RE. Transient suppression of heart rate complexity in concussed athletes. *Autonomic Neuroscience.* 2009;148(1):101-103.
226. De Beaumont L, Mongeon D, Tremblay S, et al. Persistent motor system abnormalities in formerly concussed athletes. *Journal of athletic training.* 2011;46(3):234.
227. McLeod TCV, Leach C. Psychometric properties of self-report concussion scales and checklists. *Journal of athletic training.* 2012;47(2):221-223.
228. Iverson GL, Zasler ND, Lange RT, Zasler N, Katz D, Zafonte R. Post-concussive disorder. *Brain injury medicine: Principles and practice.* 2007:373-405.
229. Mead GE, Morley W, Campbell P, Greig CA, McMurdo M, Lawlor DA. Exercise for depression. *The Cochrane Library.* 2009.
230. Asplund CA, McKeag DB, Olsen CH. Sport-related concussion: factors associated with prolonged return to play. *Clinical Journal of Sport Medicine.* 2004;14(6):339-343.
231. Berlin AA, Kop WJ, Deuster PA. Depressive mood symptoms and fatigue after exercise withdrawal: the potential role of decreased fitness. *Psychosomatic medicine.* 2006;68(2):224-230.
232. Vagnozzi R, Tavazzi B, Signoretti S, et al. Temporal window of metabolic brain vulnerability to concussions: mitochondrial-related impairment—part I. *Neurosurgery.* 2007;61(2):379-389.
233. Larun L, Nordheim L, Ekeland E, Hagen K, Heian F. Exercise in prevention and treatment of anxiety and de-pression among children and young people. *Cochrane Database of Systematic Reviews.* 2006;4.

234. Leddy JJ, Willer B. Use of graded exercise testing in concussion and return-to-activity management. *Current sports medicine reports.* 2013;12(6):370-376.
235. Wells EM, Goodkin HP, Griesbach GS. Challenges in determining the role of rest and exercise in the management of mild traumatic brain injury. *Journal of Child Neurology.* 2016;31(1):86-92.
236. Buckley TA, Munkasy BA, Clouse BP. Acute Cognitive and Physical Rest May Not Improve Concussion Recovery Time. *The Journal of head trauma rehabilitation.* 2015.
237. Silver JM. Effort, exaggeration and malingering after concussion. *Journal of Neurology, Neurosurgery & Psychiatry.* 2012;83(8):836-841.
238. Isaac S. *Handbook in research and evaluation; a collection of principles, methods, and strategies useful in the planning, design, and evaluation of studies in education and the behavioral sciences.* San Diego, Calif.: R.R. Knapp; 1971.
239. Hertzog MA. Considerations in determining sample size for pilot studies. *Research in nursing & health.* 2008;31(2):180-191.
240. Eldridge SM, Chan CL, Campbell MJ, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *Pilot and feasibility studies.* 2016;2(1):64.
241. Arain M, Campbell MJ, Cooper CL, Lancaster GA. What is a pilot or feasibility study? A review of current practice and editorial policy. *BMC medical research methodology.* 2010;10(1):67.
242. Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. *Journal of evaluation in clinical practice.* 2004;10(2):307-312.
243. Swanson GMG. Recruiting minorities into clinical trials: toward a participant-friendly system. *JNCI: Journal of the National Cancer Institute.* 1995;87(23):1747-1759.
244. Majerske CW, Mihalik JP, Ren D, et al. Concussion in sports: postconcussive activity levels, symptoms, and neurocognitive performance. *Journal of Athletic Training.* 2008;43(3):265.
245. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Medical care.* 2004;42(3):200-209.
246. Alla S, Sullivan SJ, McCrory P. Defining asymptomatic status following sports concussion: fact or fallacy? *British journal of sports medicine.* 2012;46(8):562-569.
247. Adamo KB, Prince SA, Tricco AC, Connor-Gorber S, Tremblay M. A comparison of indirect versus direct measures for assessing physical activity in the pediatric population: A systematic review. *jpo International Journal of Pediatric Obesity.* 2009;4(1):2-27.
248. Moor HM, Eisenhauer RC, Killian KD, et al. The relationship between adherence behaviors and recovery time in adolescents after a sports-related concussion: an observational study. *International Journal of Sports Physical Therapy.* 2015;10(2):225-233.

Appendices

Appendix 1: Email to clinicians (Manuscript II)

Dear Health Care Professional,

We are contacting you for your expertise in concussion management. We are hoping to learn more information about how clinicians, like you, provide care for youth patients experiencing persisting symptoms following a concussion.

We have prepared a brief survey with two clinical vignettes to help us understand your clinical practice strategies. The survey takes approximately 15-20 minutes. Simply click on the link for the survey.

https://surveys.mcgill.ca/ls/index.php/793585?newtest=Y&lang=en

We value your expertise. Thank you for taking the time to contribute to this research.

Appendix 2: Survey Questionnaire (Manuscript II)

*survey questions are identical for vignettes 1 and 2, they are presented only once in the appendices.

Demographics

- Female
- Male

What is your age?

- 24 years or younger
- 25-34 years old
- 35-44 years old
- 45-54 years old
- 55-64 years old
- 65- years or older

What is your highest earned academic degree?

- Bachelor's
- Master's
- Doctorate
- Other

In which province or territory do you practice?

- Alberta
- British Columbia
- Manitoba
- New Brunswick
- Newfoundland and Labrador
- Nova Scotia
- Ontario
- Prince Edward Island
- Quebec

- Saskatchewan
- Northwest Territories
- Nunavut
- Yukon

What is your primary professional designation?

- Certified Athletic Therapist
- Physical Therapist
- Occupational Therapist
- Other

How many years of experience do you have practicing in your profession? Please choose the category that best describes the total number of years you have been actively employed;

- less than 5 years
- 5-10 years
- 11-15 years
- 16-20 years
- more than 21 years

What is your primary work setting? Defined as one in which you spend 50% of your work time.

- Academic institution (post-secondary)
- Acute care hospital
- Concussion/mTBI clinic
- Health system or hospital-based outpatient facility
- Private outpatient or group practice
- Industry
- Inpatient rehabilitation facility
- School system (preschool/primary/secondary)
- National team
- Professional sports team
- Other

Is your primary work setting public or privately funded?

- Public
- Private
- Other

Do you currently work in clinical practice (i.e., providing services to patients) on average 8 h/wk. or more?

- Yes
- No

Considering your current caseload (including all diagnoses), what are the respective percentages of the age group(s) that you currently serve? The total count should add up to 100%.

  - Under 18 years
  - 18 –24 years
  - 25– 44 years
  - 45– 64 years
  - 65 years and over

How many patients have you treated for concussion in the last calendar year?

- 0 patients
- 1–12 patients
- 13–24 patients
- 24 patients
- more than 25 patients

Approximately what percentage of your caseload consists of patients with concussion?

- less than 10%
- 11-25%
- 26-50%
- 51-75%
- 76-100%

Do you work in a multidisciplinary setting?

- Yes
- No

Clinical Vignette 1

Please answer the following questions in order based on your practice habits as a clinician. At the end of the survey there will be an open text section if you wish to provide more information.

Vignette 1: A ten-year-old female soccer player sees you two weeks after a physician-diagnosed concussion. She was injured when she went to head the ball and made contact with an opposing player's head. There was no loss of consciousness upon injury. She was immediately removed from play and has been on physical rest since injury. She is seeing you today because her symptoms have not improved in two weeks.

Your assessment reveals she is still experiencing the following symptoms; headache 1/6, fatigue 4/6, sadness 3/6, nervous and anxious 3/6. She has a history of one previous concussion two years ago. She has no history of migraine headaches, learning disabilities, or mental health conditions. She has fully returned to school and by the end of the day her symptoms are the same. Her general health is excellent.

Upon exam you find no abnormalities in balance or vestibular/ocular function. Her cervical examination is normal. She has no cognitive impairment based on the sport concussion assessment tool-3.

During your appointment which of the following treatment(s) would you select? You may choose more than one.

- Manual therapy techniques
- Massage
- Acupuncture

- Education
- Exertion Testing
- Coordination drills
- Strength training
- Sleep recommendations
- Stretching
- Visualization/imagery
- Start return to play protocol
- Aerobic Exercise
- Return to learn protocol
- Goal setting
- Energy management
- Other:

What type of strength training would you prescribe?

- Body weight exercises
- Free weights
- Olympic lifting
- Other:

What type of stretching would you provide?

- Static full body
- Dynamic full body
- Upper body
- Lower body
- Neck only
- Other:

Regarding aerobic exercise: What type of exercise will you prescribe?

- Treadmill
- Stationary bicycle
- Elliptical
- Rowing machine
- Arm ergometer
- Swimming
- Other:

Regarding aerobic exercise: What is the prescribed frequency? (days/week)

- ○ 1 day per week
- ○ 2 days per week
- ○ 3 days per week
- ○ 4 days per week
- ○ 5 days per week
- ○ 6 days per week
- ○ 7 days per week
- ○ Other

Regarding aerobic exercise: How is the intensity prescribed?

- ○ Based on heart rate
- ○ Based on a perceived exertion scale
- ○ Until they sweat
- ○ Other:

Regarding the aerobic exercise intensity: What percentage of the maximum heart rate would you prescribe? (you may select a range by choosing more than 1 number)

- ○ 50%
- ○ 60%
- ○ 70%
- ○ 80%
- ○ 90%
- ○ 100%
- ○ Other:

Regarding the rate of perceived exertion of aerobic exercise: Which level reflects the intensity you would prescribe?

- ○ Very, very easy
- ○ Very easy
- ○ Easy
- ○ Just feeling a strain
- ○ Starting to get hard

- Getting quite hard
- Hard
- Very hard
- Very, very hard
- So hard I'm going to stop
- Other:

Regarding aerobic exercise: How is the duration prescribed?

- Predefined number of minutes
- Until the patient's symptoms worsen
- Until fatigue occurs
- Other:

Regarding the duration of aerobic exercise: How many minutes do you prescribe?

Regarding education; what type of information would you provide?

Would you prescribe a home program for this patient?

- Yes
- No

When would you like to see this patient again?

- 1 week
- 2 weeks
- 3 weeks
- 4 weeks
- Never - patient is discharged
- Never - patient is referred elsewhere
- Other

Would you refer this patient to another health care provider?

- Yes
- No

Who would you refer this patient to? (You can select more than one).

- Athletic Therapy
- Physiotherapy
- Kinesiology
- Massage Therapy
- Occupational Therapy
- Osteopath
- Physician
- Psychology
- Speech Language Pathology
- Other:

If you would like to provide more information about vignette 1, please type it here.

Please write your answer here:

Clinical Vignette 2

Please answer the following questions in order based on your practice habits as a clinician. At the end of the survey there will be an open text section if you wish to provide more information.

Vignette 2: An eight-year-old male hockey player sees you four weeks after a physician-diagnosed concussion. He was injured when he hit his head on the ice during the 3rd period. There was no loss of consciousness upon injury. He continued to play the rest of the game and has been on physical rest since injury. He is seeing you today because his symptoms have not improved in two weeks.

Your history reveals the following symptoms; headache 2/6, nausea 2/6, fatigue 1/6. He has no history of previous concussion, migraine headaches, learning disabilities, or mental health conditions. He has fully returned to school and by the end of the day his fatigue is 3/6.
His general health is excellent.

Upon exam you find no abnormalities in balance or vestibular/ocular function. His cervical examination is normal. He has no cognitive impairment based on the sport concussion assessment tool-3.

If you would like to provide more information about vignette 2, please type it here.

Please write your answer here:

Thank you for your participation.

Appendix 3*: Online Symptom and Activity Survey (Manuscript V)*

Information

1 What is your name? *

Please write your answer here: ___________________________________

2 How old are you?

Please choose **only one** of the following:

- ○ 13-18
- ○ 8-12
- ○ 5-7

Symptoms Before Activity

3 Select the number to describe your symptoms. How much of a problem is it?

Only answer this question if the following conditions are met: Age 13-18

Please choose the appropriate response for each item:

	0 - Not a problem	1	2	3 - moderate problem	4	5	6 - Severe problem
Headache	☐	☐	☐	☐	☐	☐	☐
Nausea	☐	☐	☐	☐	☐	☐	☐
Balance Problems	☐	☐	☐	☐	☐	☐	☐
Dizziness	☐	☐	☐	☐	☐	☐	☐

	0 - Not a problem	1	2	3 - moderate problem	4	5	6 - Severe problem
Fatigue	☐	☐	☐	☐	☐	☐	☐
Sadness	☐	☐	☐	☐	☐	☐	☐
Nervous/Anxious	☐	☐	☐	☐	☐	☐	☐

4 Select the number to describe your symptoms. How much of a problem is it?

Only answer this question if the following conditions are met: Age 8-12

Please choose the appropriate response for each item:

	0 - Not a problem	1 - a little	2 - a lot
Does your head hurt?	☐	☐	☐
Do you feel sick to your stomach?	☐	☐	☐
Do you have any balance problems like you might fall when you walk, run or stand?	☐	☐	☐
Do you feel dizzy? (like things around you are spinning or moving)	☐	☐	☐
Do you feel more tired than usual?	☐	☐	☐
Do you feel sad?	☐	☐	☐
Do you feel nervous or worried?	☐	☐	☐

5 Select the number to describe your symptoms. How much of a problem is it?

Only answer this question if the following conditions are met: Age 5-7

Please choose the appropriate response for each item:

	0 = Not a problem	1 = A little	2 = A lot
Does your head hurt?	◻	◻	◻
Do you feel sick to your stomach like you are going to throw up?	◻	◻	◻
Do you feel like you might fall when you walk, run or stand?	◻	◻	◻
Do you feel dizzy? (like things are spinning or moving)	◻	◻	◻
Do you feel more tired than usual?	◻	◻	◻
Do you feel sad?	◻	◻	◻
Do you feel nervous or worried?	◻	◻	◻

Exercise

6 Did you do your exercise home program today? *

Please choose **only one** of the following:

- ○ Yes
- ○ No

Activity Details

7 What did you choose as your activity? (e.g. bike, walk, elliptical)

Only answer this question if the following conditions are met: Exercise - yes

Please write your answer here:

8 How long did you exercise for? (in minutes)

Only answer this question if the following conditions are met: Exercise - yes

Please write your answer here:

-

9 How hard was the activity you just completed?

Only answer this question if the following conditions are met: Exercise - yes

Please choose **only one** of the following:

- ○ 1 - very, very easy
- ○ 2 - very easy
- ○ 3 - easy
- ○ 4 - just feeling a strain
- ○ 5 - starting to get hard
- ○ 6 - getting quite hard
- ○ 7 - hard
- ○ 8 - very hard
- ○ 9 - very, very hard
- ○ 10 so hard I'm going to stop

Symptoms After Activity

10 Select the number to describe your symptoms. How much of a problem is it?

Only answer this question if the following conditions are met: Age 13-18 and Exercise - yes

Please choose the appropriate response for each item:

	0 - Not a problem	1	2	3 - moderate problem	4	5	6 - Severe problem
Headache	☐	☐	☐	☐	☐	☐	☐
Nausea	☐	☐	☐	☐	☐	☐	☐

	0 - Not a problem	1	2	3 - moderate problem	4	5	6 - Severe problem
Balance Problems	□	□	□	□	□	□	□
Dizziness	□	□	□	□	□	□	□
Fatigue	□	□	□	□	□	□	□
Sadness	□	□	□	□	□	□	□
Nervous/Anxious	□	□	□	□	□	□	□

11 Select the number to describe your symptoms. How much of a problem is it?

Only answer this question if the following conditions are met: Age 8-12 and Exercise - yes

Please choose the appropriate response for each item:

	0 - Not a problem	1 - a little	2 - a lot
Does your head hurt	□	□	□
Do you feel sick to your stomach	□	□	□
Do you have any balance problems...	□	□	□
Do you feel dizzy?	□	□	□
Do you feel more tired than usual?	□	□	□
Do you feel sad?	□	□	□
Do you feel nervous or worried?	□	□	□

12 Select the number to describe your symptoms. How much of a problem is it?

Only answer this question if the following conditions are met: Age 5-7 and Exercise - yes

Please choose the appropriate response for each item:

	0 - Not a problem	1 - a little	2 - a lot
Does your head hurt?	◻	◻	◻
Do you feel sick to your stomach like you are going to throw up?	◻	◻	◻
Do you feel like you might fall when you walk, run or stand?	◻	◻	◻
Do you feel dizzy? (like things around you are spinning or moving)	◻	◻	◻
Do you feel more tired than usual?	◻	◻	◻
Do you feel sad?	◻	◻	◻
Do you feel nervous or worried?	◻	◻	◻

Comments

13 If you have anything else to tell us please write it here: