Flinders University

Return to physical activity in individuals with persistent symptoms following a mild traumatic brain injury

By

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DECLARATION

I certify that this thesis:

1. does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university

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3. to the best of my knowledge and belief, does not contain any material previously published or written by another person except where due reference is made in the text.

4. all research procedures reported in the thesis were approved by relevant ethics committees prior to the commencement of each study.

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Signed........Sally Vu........

Date........03/07/2025........

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Publications

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Vuu, S., Barr, C.J., Killington, M., Garner, J., & van den Berg, M.E.L. (2022). Physical exercise for people with mild traumatic brain injury: A systematic review of randomized controlled trials. *NeuroRehabilitation*, 51(2), 185-200, 10.3233/NRE-220044 (Q2).

Conference presentations

*Denotes presenting author

Vuu, S*. *Exploring the return to physical activity and exercise following a concussion/mild TBI.* Oral presentation accepted at Brain Injury Australia in September 2024.

This presentation included the following studies:

- Physical exercise for people with mild traumatic brain injury: A systematic review of randomized controlled trials
- Physical activity levels and factors impacting the return to physical activity in individuals following a mild traumatic brain injury
- Exploring the barriers and facilitators that adults with mild traumatic brain injury experience as they return to physical activity.

Vuu, S. *Research into head injury and activity.* Oral presentation accepted at the South Australian Sports Medicine Association in March 2024.

This presentation included the following studies:

- Physical exercise for people with mild traumatic brain injury: A systematic review of randomized controlled trials
- The Buffalo Concussion Treadmill and Bike Tests in people with mild-to-moderate traumatic brain injury: An exploratory clinical audit
- Performance and physiological response to the Buffalo Concussion Treadmill Test can identify autonomic dysfunction in the general adult population with mild traumatic brain injury: A prospective observational study
- Physical activity levels and factors impacting the return to physical activity in individuals following a mild traumatic brain injury
- Exploring the barriers and facilitators that adults with mild traumatic brain injury experience as they return to physical activity.

Vuu, S*., Barr, C.J., Killington, M., Howie, J., Hutchins, S., & van den Berg, M.E.L. *The Buffalo Concussion Treadmill and Bike Tests in people with mild-to-moderate traumatic brain injury: An exploratory clinical audit.* E-poster and oral presentation accepted at the Australian Physiotherapy Association in October 2023.

Vuu, S*., Barr, C.J., Killington, M., Garner, J., & van den Berg, M.E.L. *Physical exercise for people with mild traumatic brain Injury: A systematic review of randomized controlled trials.* Rapid 5x5 presentation accepted at the Australian Physiotherapy Association in October 2023.

Vuu, S*. *Concussion/mild traumatic brain injury*. Oral presentation accepted at Leading therapies in June 2022.

This presentation included the following studies:

- Physical exercise for people with mild traumatic brain injury: A systematic review of randomized controlled trials
- The Buffalo Concussion Treadmill and Bike Tests in people with mild-to-moderate traumatic brain injury: An exploratory clinical audit.

Vuu, S*. *Using aerobic exercise as assessment and treatment for people with mild-to-moderate traumatic brain injury.* Oral presentation accepted for the South Australian Local Health Network in October 2021.

This presentation included the following studies:

- Physical exercise for people with mild traumatic brain injury: A systematic review of randomized controlled trials

- The Buffalo Concussion Treadmill and Bike Tests in people with mild-to-moderate traumatic brain injury: An exploratory clinical audit.

Vuu, S*., Barr, C.J., Killington, M., Garner, J., & van den Berg, M. E. L. (2021). *Physical exercise for people with mild traumatic brain injury: A systematic review of randomized controlled trials*. E-poster and voice recording accepted at the World Physiotherapy Conference in April 2021.

Vuu, S*., Barr, C., Killington, M., Howie, J., Hutchins, S., & van den Berg, M. E. L. (2021). *The Buffalo Concussion Treadmill and Bike Tests in people with mild-to-moderate traumatic brain injury: An exploratory clinical audit*. E-poster and voice recording accepted at the World Physiotherapy Conference in April 2021.

Killington*, M., Howie*, J., & Hutchins*, S., & **Vuu, S*.** (2020). *Early management mild moderate traumatic brain injury.* Webinar accepted at the Australian Physiotherapy Association in October 2020.

This presentation included the following study:

- The Buffalo Concussion Treadmill and Bike Tests in people with mild-to-moderate traumatic brain injury: An exploratory clinical audit.

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ABBREVIATIONS

ANS	Autonomic nervous system
AOC	Alteration of consciousness
BCBT	Buffalo Concussion Bike Test
BCTT	Buffalo Concussion Treadmill Test
BPM	Beats per minute
COM-B	Capability, Behaviour and Motivation-Behaviour
DASS	Depression, Anxiety and Stress Scales
GCS	Glasgow Coma Scale
HR	Heart rate
HRR	Heart rate recovery
IPAQ	International Physical Activity Questionnaire
LOC	Loss of consciousness
PCD	Post-concussion disorder
PCS	Post-concussion syndrome
PTA	Post-traumatic amnesia
RCT	Randomized controlled trial
RPE	Rating of perceived exertion
RPSQ	Rivermead Post-Concussion Symptoms Questionnaire
TBI	Traumatic brain injury
TDF	Theoretical Domains Framework
VAS	Visual analogue scale

SUMMARY

There has been a shift in paradigm from “rest is best” to early return to physical activity in the initial stages following a mild traumatic brain injury (TBI). The most recent consensus statement recommends undertaking light intensity physical activity within 24 to 48 hours post-injury and exercise testing within two to 10 days post-injury. Additionally, much of the current evidence on exercise testing and exercise intervention post-mild TBI has been conducted in the acute, young and athletic population, for return-to-sport purposes. This limits generalisability to other populations and purposes. This thesis aims to assess and guide the return to physical activity in the general population with persistent symptoms following a mild TBI.

The thesis includes a series of studies including a systematic review with meta-analysis (Chapter 3), retrospective clinical audit (Chapter 4), prospective observational study (Chapter 5), survey study (Chapter 6), and qualitative study (Chapter 7).

The findings support the use of subthreshold (i.e., exercising below the threshold heart rate (HR) achieved on exercise testing) aerobic exercise for improving persistent symptoms, especially when incorporated as part of a more comprehensive intervention involving multiple modals and disciplines. This allows multiple symptoms to be targeted to enhance management of symptoms.

The findings also support the use of the Buffalo Concussion Treadmill Test (BCTT) for identifying physiological dysfunction. The inability of an individual to reach 90% of their age-predicted maximum HR indicates physiological dysfunction following a mild TBI. The test can also be used for reassessment; the closer an individual gets to 90% of their age-predicted maximum HR, the more it suggests they are nearing physiological recovery. Other measures of the BCTT such as test duration, HR recovery and perceived exertion should be interpreted with caution, as they are influenced by baseline levels of physical activity and mental health status.

Results suggest that following a mild TBI, physical activity levels are reduced, and participants experience several barriers and facilitators that influence their return to physical activity. Most notably, there was a pattern of poor mental health affecting the performance on the BCTT and recovery of symptoms. Understanding these factors could enhance clinical intervention and inform strategies to maximise recovery.

CHAPTER 1: INTRODUCTION

1.1 Introduction

Traumatic brain injury (TBI) is a major cause of death and disability worldwide (Fleminger & Ponsford, 2005), affecting approximately 69 million people (Dewan et al., 2018). Mild TBI accounts for approximately 81% of all TBIs (Dewan et al., 2018), with the reported prevalence likely being an underestimation as most people with mild TBI do not seek medical attention (Cassidy et al., 2004). There has been a recent shift in paradigm from mild TBI being seen as insignificant and short-term, to understanding that mild TBI is often more complex, with a potential for long-term sequalae (Patricios et al., 2023; Ruff, 2005). Mild TBI still remains a 'silent' epidemic (Buck, 2011), as it is not life threatening or as physically debilitating as severe TBIs, and symptoms are less specific and less understood (Karmali et al., 2022).

With up to 30% of individuals with mild TBI experiencing symptoms beyond three months (Babcock et al., 2013), physical, cognitive, emotional and behavioural symptoms (Ryan & Warden, 2003) impact an individual's ability to undertake their daily, social, leisure, domestic and vocational activities (Cooksley et al., 2018), and can reduce quality of life (Miller et al., 2014). At an individual level, care costs associated with moderate and severe TBIs are significantly higher than those for mild TBIs (Graves et al., 2015). However, due to the high prevalence of mild TBI, the overall total population-level costs far exceed those of severe TBIs, at an estimated of US $695 million in the first three months post-injury (Graves et al., 2015). This emphasises the need for prevention and early intervention strategies to mitigate the population burden of mild TBI.

1.2 Rationale for thesis

Research into mild TBI has grown over the past 20 years (Borg et al., 2004), and increasingly, there has been a shift from "rest is best" (Giza et al., 2018) to facilitating individuals to return to their usual activities through active rehabilitation. The most recent 6th consensus statement recommended that individuals with mild TBI can return to light intensity physical activity within 24 to 48 hours post-injury (Leddy et al., 2023; Patricios et al., 2023), as prolonged rest can exacerbate existing symptoms (Silverberg & Iverson, 2013), further complicating recovery. The authors recommend that, *"Healthcare professionals with access to exercise testing can prescribe subsymptom threshold aerobic exercise within 2-10 days after sport-related concussion, based on the individual's heart rate threshold that does not elicit more than mild symptom exacerbation during the exercise test"* (Patricios et al., 2023, p. 701).

However, it must be noted that the existing evidence focuses on exercise testing in acute, young, and athletic populations for return to sport purposes (Covassin & Elbin, 2011; Haider et al., 2021; Leddy & Willer, 2013; Powell et al., 2020; Schneider et al., 2017). This evidence therefore cannot be generalised to those who are older and non-athletic and continue to experience symptoms beyond expected timeframes. Therefore, the aim of this thesis is to assess and guide the return to physical activity in the general population with persistent symptoms following a mild TBI.

1.3 Research objectives

The objectives of this thesis are to:

1. Examine the impact of physical exercise interventions on persistent symptoms,
2. Investigate the use of graded exercise testing in the general adult population to assess physiological dysfunction and guide subsymptom threshold exercise interventions, and
3. Explore factors that impact return to physical activity in the general adult population.

1.4 Structure of thesis

This thesis is divided into 8 chapters. Chapters 1 and 2 provide background to the thesis as an introduction and literature review respectively. Chapters 3 to 7 report five individual studies as outlined below. Chapter 8 provides a discussion of the findings of Chapters 3 to 7, implications for clinical practice, strengths and limitations, conclusion and recommendations for future research.

Chapter 1 introduces and provides the aims and structure of the thesis. This thesis aims to assess and guide the return to physical activity in the general population with persistent symptoms following a mild TBI.

Chapter 2 provides a comprehensive literature review of the main themes throughout the thesis. This chapter provides context for Chapters 3 to 7.

Chapter 3 presents findings of a systematic review of randomized trials entitled '*Physical exercise for people with mild traumatic brain injury: A systematic review of randomized controlled trials.'* This has been adapted and published in NeuroRehabilitation.

Chapter 4 presents results of a clinical audit entitled, '*The Buffalo Concussion Treadmill and Bike Tests in people with mild-to-moderate traumatic brain injury: An exploratory clinical audit*.' This chapter has been adapted and published in the Journal of Head Trauma Rehabilitation.

Chapter 5 presents results of an observational study, '*Performance and physiological response to the Buffalo Concussion Treadmill Test can identify autonomic dysfunction in the general adult population with mild traumatic brain injury: A prospective observational study.'* This observational study compares the performance and physiological response on the Buffalo Concussion Treadmill Test between adults who had a mild TBI to age and gender matched healthy active and sedentary adults. This chapter was adapted and is under review with the Journal of Head Trauma Rehabilitation.

Chapter 6 presents survey results and is entitled, ‘*Physical activity levels and factors impacting the return to physical activity in individuals following a mild traumatic brain injury.’* This survey investigated physical activity levels, healthcare utilisation patterns, factors influencing the return to physical activity and the impact of mental health with the use of a behaviour change model in adults following mild TBI.

Chapter 7, ‘*Exploring the barriers and facilitators that adults with mild traumatic brain injury experience as they return to physical activity,’* presents results of semi-structured interviews of individuals who have experiences long-term symptoms following mild TBI. This chapter was adapted and is currently under review in the Neuropsychological Rehabilitation journal for publication.

Chapter 8 provides a discussion of the main findings of Chapters 3 to 7 of the thesis. This chapter includes the implications of clinical practice, strengths and limitations, and conclusion and recommendations for future research.

Preface

The literature review presented in Chapter 2 provides key definitions for concussion, mild traumatic brain injury (TBI) and individuals who experience persistent symptoms, as well as the overview of clinical populations and presentations that complicate recovery. Following this, mechanisms of aerobic exercise testing and interventions, and factors affecting the return to physical activity in individuals following a mild TBI are introduced.

CHAPTER 2: LITERATURE REVIEW

2.1. Traumatic brain injury severity classification

TBI is defined as *“an alteration in brain function, or other evidence of brain pathology, caused by an external force”* (Menon et al., 2010, p. 1638). Classification of initial TBI severity is important in initial assessment to estimate the risk of complications, and level of healthcare interventions required (van Baalen et al., 2009). Traditionally, TBI severity is classified as mild, moderate, or severe according to the acute injury characteristics, which include structural imaging findings, duration of loss of consciousness (LOC), duration of alteration of consciousness (AOC), duration of post-traumatic amnesia (PTA) and the Glasgow Coma Scale (GCS) score (O'Neil et al., 2013). If a patient meets the criteria in more than one severity, the higher severity level is assigned (O'Neil et al., 2013). The TBI severity classification, retrieved from the Management of Concussion/mTBI Working Group (2009) is presented in Table 2.1 to provide a clear overview of classifications.

Table 2.1 TBI severity classification

Criteria	**Mild**	**Moderate**	**Severe**
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Duration of LOC	0 to 30 minutes	>30 minutes to <24 hours	>24 hours
Duration of AOC	A moment up to 24 hours	>24 hours	>24 hours
Duration of PTA	0 to 1 day	>1 to <7 days	>7 days
GCS	13-15	9-12	<9

It is important to acknowledge the limitations associated with traditional means of TBI severity classification. Firstly, the assessment of GCS and PTA may be impacted by factors such as language barriers, poor assessment, and drug and surgical effects which can potentially affect the level of consciousness and ability to recall information (Tenovuo et al., 2021). Secondly, TBI is not a single event but a complex sequalae that presents differently at different timepoints, which traditional grading methods do not consider (Tenovuo et al., 2021). In recent years, technological advancements have allowed the integration of other methods for diagnosing TBI severity and informing clinical interventions (Dadas et al., 2022; Shenton et al., 2012; Tenovuo et al., 2021) at different timepoints. Acutely, computed tomography has been used to screen for life threatening injuries such as skull fractures and haemorrhages (Shenton et al., 2012) that require immediate medical attention. In the subacute stage, magnetic resonance imaging (MRI) has been used to assess neural activity under various conditions (Zhang et al., 2010). Biomarkers have been used at any stage of a TBI to convey the physiopathological state of the patient at that timepoint to understand the nature of the TBI, support diagnosis of TBI severity, and provide a better prediction of survival and long-term prognosis (Dadas et al., 2022). Novel methods such as advanced neuroimaging (i.e., diffusion MRI, functional MRI, structural MRI, cerebral blood flow), fluid-based biomarkers and genetic testing have shown preliminary promise for guiding diagnosis but require further research to validate their use in clinical practice (Patricios et al., 2023; Tabor et al., 2023). In addition to technological advancements in TBI diagnosis, there are a variety of clinical measures that have been validated for individuals with TBI, which aim to assess the impact of TBI on individuals. These include measures of quality of life, life satisfaction (Hawthorne et al., 2011), psychosocial status (Bay et al., 2009; McCarthy et al., 2006), functional and physical status (LeBlanc et al., 2006); all of which make an individual's life meaningful. These outcome measures support healthcare professionals to set goals that are meaningful and realistic for the individual, and direct patient-centred interventions.

Despite attempts to make TBI severity classification clearer, TBI still remains one of the most challenging conditions to classify due to the complexity of the brain and variability in presentation. As such, the distinction between mild and moderate TBI is often debated (Kristman et al., 2014). Some authors have recommended that patients with brain scan changes should be considered as complicated mild TBI or moderate TBI, and since there is a higher frequency of brain pathology in patients with a GCS of 13, the prognosis of patients with mild TBI may be similar to those with moderate TBI (Kristman et al., 2014; Williams et al., 1990). This may partially explain why much of the literature investigating moderate TBI includes populations with mild-to-moderate TBI populations (Einarsen et al., 2018). Thus, to ensure that all the relevant populations are encompassed, this thesis will include the mild-to-moderate TBI population.

2.2 Mild traumatic brain injury and concussion definitions

The terms 'mild TBI' and 'concussion' are used interchangeably (Kazl & Torres, 2019; Management of Concussion/mTBI Working Group, 2009) but at times the terms also contradict each other (Ruff et al., 2009). In the literature, the number and type of symptoms often reflect the eligibility criteria for studies, such as for an intervention or epidemiological study. This can result in variations in the severity of injuries within the participant population, potentially skewing the data. Clinically, the differences in terminology may also lead to differences in care.

For the term 'mild TBI', the World Health Organization (WHO) found 38 different definitions, 62% of which include the GCS as part of their definition (Carroll et al., 2004). For the term 'concussion', a systematic review by McCrory, Feddermann-Demont, et al. (2017) identified six consensus-based definitions with the definition by the Concussion in Sport Group being the most frequently cited. Since then, the Concussion in Sport Group has released an updated 6th consensus statement. This group defines sport-related concussion as:

> *"A TBI caused by a direct blow to the head, neck or body resulting in an impulsive force being transmitted to the brain that occurs in sports and exercise-related activities. This initiates a neurotransmitter and metabolic cascade, with possible axonal injury, blood flow*

change and inflammation affecting the brain. Symptoms and signs may present immediately, or evolve over minutes or hours, and commonly resolve within days, but may be prolonged" (Patricios et al., 2023, p. 697).

The group recognises that this definition was a conceptual definition and does not provide a diagnostic criteria (Patricios et al., 2023) but reported the Mild TBI Task Force of the American Congress of Rehabilitation Medicine (ACRM) Brain Injury Special Interest Group had recently published a diagnostic criteria (Silverberg et al., 2023). The ACRM undertook a Delphi study for expert consensus, which stated that 93.8% of expert panel members agreed that the terms concussion and mild TBI may be used interchangeably when neuroimaging is normal or not clinically indicated (Silverberg et al., 2023).

The ACRM defines mild TBI as follows:

> *"Mild TBI is diagnosed when following a biomechanically plausible mechanism of injury (Criterion 1) one or more of the criteria (i-iii) listed below are met.*
>
> *One or more clinical signs (Criterion 2) attributable to brain injury.*
>
> *At least 2 acute symptoms (Criterion 3) and at least one clinical or laboratory finding (Criterion 4) attributable to brain injury.*
>
> *Neuroimaging evidence of TBI, such as unambiguous trauma-related intracranial abnormalities on computed tomography or structural magnetic resonance imaging (Criterion 5).*
>
> *Confounding: factors do not fully account for the clinical signs (Criterion 2), acute symptoms (Criterion 3), and clinical examination and laboratory findings (Criterion 4) that are necessary for the diagnosis (Criterion 6)"* (Silverberg et al., 2023, p. 1349).

Regardless of whether the term 'mild TBI' or 'concussion' is used, the clinical signs and symptoms must not be due to (but may occur concurrently with) drugs, medications, alcohol, other injuries or other comorbidities (Patricios et al., 2023; Silverberg et al., 2023). Furthermore, much of the literature is in agreeance that concussion is a subset of a mild TBI (i.e., all concussions are mild TBIs) (Harmon et al., 2019; Kazl & Torres, 2019; McCrory et al., 2013; Ontario Neurotrauma Foundation, 2018; Rabinowitz et al., 2014) and is more mild than a mild TBI (Harmon et al., 2019; Kazl & Torres, 2019; McCrory et al., 2013; Rabinowitz et al., 2014). Additionally, the term 'concussion' is typically associated with a sport or exercise-related activity cause of injury (McCrory, Feddermann-Demont, et al., 2017; Patricios et al., 2023), whereas the term 'mild TBI' is typically associated with other causes of injury.

Therefore, to ensure that all the relevant populations are encompassed, this thesis will use the term ‘mild TBI’ to include ‘concussion’, unless referred to research studies or study participants refer to the term ‘concussion’.

2.3 Epidemiology of traumatic brain injury

Each year, approximately 69 million people worldwide are expected to suffer from a TBI, with most cases being classified as mild (81.0%), followed by moderate (11.0%) and severe (8.0%) (Dewan et al., 2018). Between the years 1990 to 2016, the age-standardised prevalence and incidence of TBI increased by 8.4% and 3.6% respectively, which was attributed to the increase in population density, ageing population, and increased use of motor vehicles (GBD 2016 Traumatic Brain Injury and Spinal Cord Injury Collaborators, 2019). Low and middle income countries experienced almost three times more cases of TBI proportionally and greater burden of disease than high income countries due to reduced quality and accessibility of healthcare (Dewan et al., 2018). Although mild TBI is estimated to affect 55.9 million people worldwide (Dewan et al., 2018), this may be an underrepresentation, as most people with mild TBI do not demonstrate life threating injuries and therefore do not present for emergency medical attention (Cassidy et al., 2004).

In Australia between 2020 to 2021, there were 406,000 emergency department presentations, 142,000 hospitalisations and 2,400 deaths resulting from head injuries, with falls and transport being the two main causes of injury (Australian Institute of Health and Welfare, 2023). Males made up two thirds of injuries, and individuals ≥65 years experienced the highest rate of head injuries (Australian Institute of Health and Welfare, 2023). Aboriginal and Torres Strait Islander people, people living in rural and remote parts of Australia, and areas of socioeconomic disadvantage were disproportionally affected by head injuries (Australian Institute of Health and Welfare, 2023). In 2008, the total cost of TBI in Australia was $8.6 billion, comprising of financial ($3.7 billion) and burden of disease costs ($4.9 billion) (Access Economics Pty Limited, 2009). The majority of TBI related costs are funded by the individual (69.4%), with the remaining being funded by State Government (19.1%) and Federal Government (11.2%) (Access Economics Pty Limited, 2009).

Regarding sport-related concussions, between 2020 to 2021, Australia recorded 3,076 hospitalisations, with 2,193 of these cases involving males and 1,624 people were under the age of 25 (Australian Institute of Health and Welfare, 2024). The most common causes of these sport-related concussions were cycling, Australian Rules Football and rugby (Australian Institute of Health and Welfare, 2024). Based on hospital admissions data from Victoria (Finch et al., 2013), it was estimated that a sport-related concussion equated to a direct health burden of around $50 million annually (Thomas et al., 2020a). However, these figures only reflect a portion of the economic impacts involved, as they do not account for those who experience symptoms but do not seek medical attention, outpatient services, comorbidities, complications that may arise, or loss of productivity in life-years (Australian Institute of Sport, 2024; Thomas et al., 2020a).

2.4 Clinical presentations

Symptoms following a moderate and severe TBI are largely related to the TBI itself, however, for mild TBI, the risk of developing persistent symptoms beyond expected timeframes are influenced by multiple factors (Iverson & Lange, 2011; Management of Concussion/mTBI Working Group, 2009). These factors include age (McCrory et al., 2004), cause of injury (Beauchamp et al., 2021), having a history of a TBI (Maestas et al., 2014) and pre-existing conditions (Karr et al., 2021).

2.4.1 Age-related presentation of mild traumatic brain injury

Age is an important factor to consider, as there are anatomical, physiological and behavioural differences between different age groups (McCrory et al., 2004). Younger children are at greater risk of sustaining a skull fracture and TBI compared to adults (Li & Kleiven, 2018; Ommaya et al., 2002) due to weaker cervical musculature, reduced skull thickness, greater head-to-neck ratio (Davis & Purcell, 2013; Muñoz-Sánchez et al., 2005; Ommaya et al., 2002), underdeveloped sutures, and insufficient calcification of the skull (Bauer & Fritz, 2004). For the same force applied, the mechanical stress is more easily transferred to the brain (Bauer & Fritz, 2004). Furthermore, a child’s brain is also still undergoing neuronal plasticity and myelination (Davis & Purcell, 2013), which increases the vulnerability of the brain to TBIs (Anderson et al., 2001; Davis & Purcell, 2013). In particular, the parietal, temporal and prefrontal regions are still maturing and undergoing myelination (Casey et al., 2005), and a TBI during this time results in greater impact on behaviour and cognition (Anderson et al., 2001; Casey et al., 2005). This translates to slowed information processing, and difficulty concentrating and forming new memories (Davis et al., 2017; Davis & Purcell, 2013), affecting their return to school and sport (Davis et al., 2017; Davis & Purcell, 2013; Patricios et al., 2023). The combination of greater mechanical stress and changes to the brain means that children require a longer timeframe of recovery compared to adults (McCrory et al., 2004).

Falls are the leading cause of TBIs and in-hospital mortality for older adults due to deterioration in balance, gait and other physical functions (Fu et al., 2017). For those who survive the TBI, older adults are at higher risk of complicated mild TBI (i.e., macrostructural changes on computed tomography scan) (Karr et al., 2020), longer hospital stays (LeBlanc et al., 2006), worse functional, cognitive and psychological outcomes, slower recovery (Gardner et al., 2018), severe disability, dependence on care (Mosenthal et al., 2004) and likelihood of never recovering (King, 2014a). This is due to the complex interactions between comorbid conditions (i.e., dementia, circulatory diseases and other neurological disorders) (Karr et al., 2020), medications, natural atrophy of cerebral tissue (Griesbach et al., 2018; Papa et al., 2012), slower and reduced healing processes (King, 2014a), frailty (Baggiani et al., 2022) and reduced functional ability (LeBlanc et al., 2006) as a result of ageing. In addition, the fall itself creates a traumatic event that increases the risk of developing psychiatric conditions such as anxiety, depression, post-traumatic stress disorder and poor coping strategies (Abdulle & van der Naalt, 2020). It can also result in physical injuries such as femur, pelvic and humerus fractures (Clement et al., 2012), which further complicate clinical presentation, rehabilitation and recovery. Early diagnosis and management are required in older adults to address the array of symptoms in hospital and following discharge (i.e., in-home rehabilitation, outpatient rehabilitation) to maximise independence and recovery (Baggiani et al., 2022).

2.4.2 Sport versus non-sport related injuries

Biomechanically, the characteristics of a sports-related injury differ from other causes of injury (Beauchamp et al., 2021; Seiger et al., 2015). The force sustained in a sport-related injury is often indirect (i.e., a force sets the head in motion without directly impacting the head) such as tripping over, being tackled or an object (i.e., ball) striking an individual on the neck or body (Delaney et al., 2006; Guskiewicz & Mihalik, 2011) rather than a direct force to the head, as seen in domestic or military assaults (Davis, 2000; Nolan, 2005). Secondly, the impact force sustained in a sport-related injury is less than that from other mechanisms of injury such as in motor vehicle or military accidents, which involve high speed forces (Davis, 2000; Nolan, 2005). Therefore, individuals that sustain a sport-related injury typically experience less physical and psychological symptoms and recover faster (Beauchamp et al., 2021; Hanlon et al., 1999; Leddy et al., 2010; Rabinowitz et al., 2014; Seiger et al., 2015). However, it should be noted that athletes may also experience prolonged symptoms if they present with risk factors such as comorbid conditions (i.e., anxiety), a history of a TBI, or sporting-related factors such as delayed reporting of their TBI or continuing to play sport after their TBI (Barnhart et al., 2021; Cuff et al., 2022; Worts et al., 2022). Faster recovery in people who sustain sport-related injuries may also be attributed to their baseline level of physical fitness (Mrazik et al., 2013), access to immediate healthcare in a sporting environment (e.g., on-field team doctors and physiotherapists) and greater motivation to adhere to intervention (Cuff et al., 2022) to return to sport (Chrisman et al., 2013). However, an athletes' pressure to return to sport may lead to an underreporting of symptoms (Chrisman et al., 2013; Davies & Bird, 2015), and delayed removal of athletes from sport participation, ultimately prolonging the time needed for safe return to play (Eagle et al., 2022; Putukian et al., 2023). Athletes that sustain a sport-related concussion must follow their team's specific return to sport protocol, which requires them to obtain medical clearance and be symptom-free before resuming participation (Australian Institute of Sport, 2024; Patricios et al., 2023).

People who sustain a mild TBI from being involved in vehicle accidents, military accidents, or domestic violence often experience a greater number and intensity of symptoms, resulting in longer recovery times (Beauchamp et al., 2021; Belanger et al., 2011; Means et al., 2022). These events create both psychological and physical trauma, which further limit recovery (Belanger et al., 2011; Mac Donald et al., 2015; Means et al., 2022). This population may experience delays in receiving healthcare due to navigating the complexities of pathways associated with third-party insurance (Harrington et al., 2015) and delays in seeking care are associated with an increased risk of experiencing persistent symptoms (Kara et al., 2020; Seiger et al., 2015). Furthermore, once individuals are treated for life-threatening injuries in hospital, and deemed medically stable, they are often discharged within two days (Australian Institute of Health and Welfare, 2021), even though symptoms may arise days after the initial injury (Patricios et al., 2023). Individuals with ongoing symptoms must then seek outpatient services for ongoing care at their own expense. Without appropriate care, which may be impacted by limited resources, finances or time (Karmali et al., 2022), individuals with mild TBI struggle to cope with their persisting psychological and physical symptoms (Loignon et al., 2020), causing a negative feedback loop of symptom exacerbation and chronicity of symptoms.

2.4.3 Complicated mild traumatic brain injury

Individuals with complicated mild TBI experience more symptoms (Voormolen, Haagsma, et al., 2019), worse functional outcomes (Karr et al., 2020) and take longer to recover (Iverson et al., 2012) compared to people with uncomplicated mild TBI. A complicated mild TBI characterised by a lower GCS score of 13 or 14, rather than 15 (Iverson et al., 2012), and neuroimaging evidence of structural intracranial injury (Iverson et al., 2012; Silverberg et al., 2023). This is often accompanied by longer duration of LOC and PTA (Dikmen et al., 2001; Williams et al., 1995). LOC refers to an unconscious paralytic state (Ommaya & Gennarelli, 1974), which is temporary in the case of a mild TBI (Marshman et al., 2013). The reticular activating system, located in the brainstem, receives input from sensory tracts and transmits this to the cortex for behaviour and arousal. The extend of functional loss can lead to either LOC or PTA (Blyth & Bazarian, 2010). PTA is characterised by changes in memory, cognition and behaviour, which can significantly affect executive function (Marshman et al., 2013).

Experiencing more than one TBI can increase the number and intensity of symptoms reported (Mannix et al., 2014) and often prolongs recovery (Guskiewicz et al., 2003), especially if they occur within a close timeframe (Longhi et al., 2005). This timeframe is known as the ‘window of vulnerability’ and may last up to 10 days (McCrea et al., 2009). Following a mild TBI, the mechanical disruption to the neuronal membranes result in the release of neurotransmitters (glutamate), influx of excitatory amino acids (sodium and calcium) and efflux of potassium (Greco et al., 2019). This ionic disequilibrium lasts up to 6 hours, triggers increased energy demands of the cell and hypermetabolism, leading to a metabolic crisis (Greco et al., 2019). This is followed by a period of metabolic depression, which is the ‘window of vulnerability’ (Giza & Hovda, 2014; Greco et al., 2019). During this period, a repeated TBI decreases glucose utilisation, particularly in the hippocampus and sensorimotor cortex, resulting in the exacerbation of cognitive and behavioural symptoms (Weil et al., 2014). In addition, repeated TBIs may induce structural changes to the brain such as cortical thinning and enlargement of the ventricles (Goddeyne et al., 2015), white matter damage (Tremblay et al., 2014) and long-term, increase risk of neurodegenerative conditions such as mild cognitive impairment, dementia and Alzheimer's disease (Guskiewicz et al., 2005; Stein et al., 2015).

Pre-existing conditions complicate recovery, particularly conditions or disorders affecting the circulatory or autonomic nervous systems (ANS) (Karr et al., 2021). Circulatory diseases such as hypertension and heart failure have been shown to alter white matter in the brain (Dufouil et al., 2001). White matter links neocortical with subcortical and limbic structures, which regulate autonomic control centres (Williamson et al., 2013). White matter anomalies present as cognitive decline such as reduced information processing speed, psychomotor speed, memory, attention, and executive function (Gunning-Dixon et al., 2009; Madden et al., 2009). Psychiatric disorders affect the ANS as does mild TBI. This includes anxiety-related disorders (i.e., anxiety, panic attacks, post-traumatic stress disorder), mood disorders (i.e., depression, bipolar disorder), schizophrenia and substance abuse disorders (i.e., alcohol, drugs) (Alvares et al., 2016). Much of the symptoms from psychiatric disorders such as pain, sleep disturbance, changes in cognition (i.e., changes to memory, attention and concentration) and mood (i.e., depression, disinhibition, irritability) overlap with the symptoms of mild TBI (Barlow, 2016; Brent & Max, 2017). Furthermore, reduced physical activity levels as a result of the sequalae of symptoms can lead to the development of circulatory diseases and psychiatric disorders (Barlow, 2016; Mercier et al., 2021). These pre-existing conditions need to be considered by clinicians for differential diagnosis and a comprehensive approach to care to ensure that both pre-existing conditions and symptoms of mild TBI are managed.

2.5 Definitions of symptoms following a mild traumatic brain injury

The terms 'concussion' and 'mild TBI' only describes the type of initial injury, not the symptoms that occur following the initial injury. Terms commonly used to describe symptoms following a concussion or mild TBI include: Post-Concussive Syndrome, Post-Concussion Disorder, Persistent Post-Concussive Symptoms (Management of Concussion/mTBI Working Group, 2009), and more recently, Persistent Post-Concussion Symptoms (Chadwick et al., 2022; Zemek et al., 2016) and persisting symptoms (Patricios et al., 2023).

Most people with mild TBI recover spontaneously, but up to 30% of people continue to experience symptoms beyond expected timeframes (Babcock et al., 2013). Symptoms following a mild TBI tend to affect physical (i.e., fatigue, headache), cognitive (i.e., poor concentration, poor memory) and behavioural/emotional (i.e., anxiety, depression, irritability) domains (Ellis et al., 2015; Ryan & Warden, 2003). These symptoms also occur in healthy people without a TBI and in other health conditions, thus, a definition to encompass symptoms following a mild TBI is required to facilitate diagnosis and management.

The two most longstanding and commonly cited definitions to describe symptoms following a mild TBI are from the American Psychiatric Association and WHO (Rose et al., 2015).

The Diagnostic and Statistical Manual, 4th edition defines 'postconcussional disorder' as,

> *'1) cognitive impairment in attention or memory, 2) at least three of eight symptoms of fatigue, sleep disturbance, headache, dizziness, irritability, affective disturbance, personality change, apathy, and 3) appearing shortly after injury and persisting for at least 3 months'* (American Psychiatric Association, 1994, p. 704).

The International Classification of Disease, 10th edition defines 'postconcussion syndrome' as,

> *'Three or more of the following symptoms: headache, dizziness, fatigue, irritability, insomnia, concentration, memory difficulty, and intolerance of stress, emotion, or alcohol occurring within 4 weeks'* (World Health Organization, 1992, pp. 63-64).

However, the terms 'syndrome' and 'disorder' are not an accurate description of symptoms following a mild TBI. Syndromes typically refer to conditions with consistent symptom linkage and symptom resolution but following a mild TBI, symptoms are not consistently linked to one another and some symptoms resolve while others linger (Arciniegas et al., 2005). Similarly, due to an array of symptoms rather than a cluster of symptoms following a mild TBI, the term disorder may not be appropriate (Ellis et al., 2015). There are a multitude of terms and definitions to denote symptoms following a mild TBI. These different definitions lead to an individual being eligible or ineligible for diagnosis in clinical practice or study inclusion in research based on their symptom endorsement, number of symptoms and duration of symptoms (Rose et al., 2015). This has been recently challenged by the 6th consensus statement on concussion in sport that has used the term, 'persisting symptoms' to not include any specific symptoms and only include a timeframe:

> '*Symptoms that persist >4 weeks across children, adolescents and adults'* (Patricios et al., 2023, p. 701).

A survey of physicians found that 55% of respondents would diagnose 'post-concussion syndrome' with only one symptom present and only 2.1% of respondents provided a diagnosis according to the American Psychiatric Association and WHO, despite the two definitions being the most commonly cited definitions (Rose et al., 2015). Additionally, the Diagnostic and Statistical Manual states explicitly that its proposed criteria are not intended for application to clinical practice but to serve as a proposed set of criteria to guide clinicians undertaking their own evaluation (American Psychiatric Association, 1994).

Due to the continued lack of consensus for a single definition for symptoms following a mild TBI, the term 'persistent symptoms' will be used throughout this thesis to denote any number and any type of symptoms experienced following a mild TBI with no minimum timeframe, unless referencing other research, whereby their terminology will be used.

2.6 Pathophysiology of mild traumatic brain injury

Mild TBI is related to temporary neuronal dysfunction rather than cell death (Giza & Hovda, 2001), as recent advanced neuroimaging has demonstrated persistent alterations that correspond to metabolic and microstructural changes (Vagnozzi et al., 2010; Wilde et al., 2008). Following a mechanical force transmitted to the brain, cellular homeostasis is disturbed, which causes the release of excitatory neurotransmitters (glutamate) and ionic fluxes (Choe et al., 2012; Giza & Hovda, 2001). Glutamate then binds to the N-methyl-D-aspartate (NMDA) receptor, which leads to further neuronal depolarization with efflux of potassium and influx of calcium (Giza & Hovda, 2001). To restore neuronal membrane potential, the sodium-potassium pump works overtime by increasing the amount of adenosine triphosphate (ATP), triggering an increase in glucose metabolism (Giza & Hovda, 2001). This hypermetabolism occurs in the presence of diminished cerebral blood flow and the discrepancy between glucose supply and demand triggers a cellular energy crisis (Giza & Hovda, 2001). Following the initial period of glucose hypermetabolism, the brain goes into a period of depressed metabolism (Giza & Hovda, 2001). This persistent increase in calcium may impair mitochondrial oxidative metabolism and worsen the energy crisis (Giza & Hovda, 2001). The accumulation of calcium may also lead to cell death, and disrupt neurofilaments and microtubules, impairing neural connectivity (Giza & Hovda, 2001). Other pathophysiological changes may include but not limited to the generation of lactic acid, free radical production, inflammatory responses and altered neurotransmission (Giza & Hovda, 2001).

These acute responses produce an array of complex signs and symptoms. However, referring to the clinical history, persistent pathophysiological alterations in specific neurological subsystems, main symptoms and physical examination findings, symptoms can be clustered into post-concussion disorders (PCDs) (Ellis et al., 2015). It is important to note that there are other causes of PCDs and PCDs can overlap, however, the clustering assists with diagnosis, prognosis and decision-making (Ellis et al., 2015). The subtypes of PCDs were retrieved from Ellis et al. (2015) and are presented in Table 2.2.

Table 2.2 Subtypes of PCDs

	Physiologic PCD	Vestibulo-ocular PCD	Cervicogenic PCD
Pathophysiology	• Persistent alterations in neuronal depolarisation, cell membrane, permeability, mitochondrial function, cellular metabolism, and cerebral blood flow	• Dysfunction of the vestibular and oculomotor systems	• Muscle trauma and inflammation • Dysfunction of cervical spine proprioception

Predominant symptoms	• Headache exacerbated by physical and cognitive activity • Nausea, intermittent vomiting, photophobia, phonophobia, dizziness, fatigue, difficulty concentrating and slowed speech	• Dizziness, vertigo, nausea, lightheadedness and postural instability at rest • Blurred or double vision, difficulty tracking objects, motion sensitivity, photophobia, eye strain and headache exacerbated by activities involving the vestibulo-ocular system	• Neck pain, stiffness, and decreased range of motion • Occipital headaches exacerbated by head movements and not physical or cognitive activity • Lightheadedness and postural imbalance
Examination findings	• No focal neurological findings • Elevated resting heart rate • Graded treadmill tests are often terminated early due to symptom exacerbation	• Impairments on balance and gait testing • Impaired vestibulo-ocular reflex, fixation, convergence, and horizontal and vertical saccades • Patients typically reach maximal exertion without symptom exacerbation on graded exercise tests	• Decreased cervical lordosis and range of motion • Paraspinal and suboccipital muscle tenderness • Impaired head-neck proprioception • Patients typically reach maximal exertion without symptom exacerbation on exercise tests

The ANS, compromising of the sympathetic and parasympathetic nervous systems (Kennedy & Ganta, 2014), functions without voluntary control and is responsible for maintaining homeostasis (Purkayastha et al., 2019). The ANS regulates cardiac and vascular functions, and also innervates cardiac and smooth muscle, and endocrine and exocrine organs, thus influencing most body systems (Esterov & Greenwald, 2017). The sympathetic nervous system is predominantly involved with cardiac and vascular regulation, particularly vasoconstriction and the release of epinephrine and norepinephrine during the “fight or flight response”, whereas the parasympathetic nervous system is involved with peripheral musculature and energy conservation during the “rest and digest response” (Esterov & Greenwald, 2017; McCorry, 2007).

Following a mild TBI, a neurometabolic cascade occurs (Giza & Hovda, 2001). In the case of a physiological dysfunction, the persistent alterations in cell membrane permeability, ion transport regulation, neurotransmitter release, cellular metabolism and cerebral blood flow causes a cerebral metabolic deficiency (Ellis et al., 2015). This results in higher sympathetic nervous system activity (King et al., 1997) rather than parasympathetic activity, and the uncoupling between the ANS and cardiovascular systems (Gall et al., 2004a) leading to an increased resting heart rate (HR) (King et al., 1997), increased HR during cognitive (Hanna-Pladdy et al., 2001) and physical exertion (Gall et al., 2004b), and decreased HR variability (Keren et al., 2005; King et al., 1997), all of which are reflective of the symptoms of a physiological PCD (Ellis et al., 2015).

2.7 Exercise testing

Subjective symptom reporting is the most common method for assessing persistent symptoms following a mild TBI (Kozlowski et al., 2013), and many self-report measures are available to aid in the diagnosis of these symptoms (Alla et al., 2009). However, these self-report measures are typically limited in terms of their psychometric properties. Many have not been developed or subjected to rigorous scientific validation, instead evolving primarily in clinical settings (Alla et al., 2009). Furthermore, the perception of subjective symptoms such as pain and fatigue following a mild TBI may be influenced by psychosocial factors. These may include negative perceptions of injury, stress, anxiety, depression and all-or-nothing behaviour (Hou et al., 2012).

Exercise testing allows for objective assessment following a mild TBI by provoking physiological markers of autonomic dysfunction that may not be evident at rest (Kozlowski et al., 2013) in a controlled and safe environment (Quatman-Yates et al., 2018). Exercise testing can occur within two to 10 days after a mild TBI (Patricios et al., 2023) provided individuals do not have contraindications to exercise testing (American College of Sports Medicine, 2021). Demonstrating exercise intolerance from the inability to exercise to one’s age-predicted maximum HR without symptom exacerbation on the test is indicative of a physiological dysfunction (Kozlowski et al., 2013). A systematic review of exercise tests for people with mild TBI reported that most exercise tests used either a treadmill or cycle ergometer as the modality, and the most common outcome measures were self-reported symptoms, HR and blood pressure (BP) (Quatman-Yates et al., 2018). However, test protocols varied across studies, including differences in initial intensity, progression parameters and criteria for test termination (Quatman-Yates et al., 2018). The authors also reported that 10 of the 12 studies reported on the Buffalo Concussion Test (Quatman-Yates et al., 2018). Both the Buffalo Concussion Treadmill Test (BCTT) and Buffalo Concussion Bike Test (BCBT) are valid and reliable graded exertion tests used to assess exercise tolerance. The tests serve multiple purposes, including diagnosing physiological dysfunction, differentiating physiological dysfunction from other diagnoses, quantifying severity and exercise capacity, and guiding aerobic exercise prescription for people following a mild TBI (Haider, Johnson, et al., 2019; Janssen et al., 2022; Leddy & Willer, 2013). The test can be performed in any facility provided a trained professional is present to administer the test (Leddy & Willer, 2013). The BCTT is more commonly used (Janssen et al., 2022; Quatman-Yates et al., 2018), due to being more functional and applicable to daily activities, and ability to elicit greater maximal exertion. Treadmill testing typically allows for higher peak exercise capacity compared to stationary cycling, as leg fatigue from increasing resistance is less of a limiting factor (American College of Sports Medicine, 2021). On the other hand, stationary cycling involves less movement of the arms and trunk, making it easier to obtain physiological measures, and allows individuals with orthopaedic or vestibular impairment to undertake an exercise test safely (American College of Sports Medicine, 2021).

The HR achieved at symptom exacerbation is used to guide exercise prescription. The rate of exercise intensity progression may vary, with some individuals needing to maintain a particular HR for longer than two weeks before progressing (Leddy & Willer, 2013). As the test requires supervision from a trained professional, a more practical and cost-effective approach may be to gradually increase the HR by 5-10 beats per minute (bpm) every two weeks for athletes, while non-athletes typically respond better to a 5 bpm increase every two to three weeks (Leddy et al., 2010; Leddy & Willer, 2013). Individuals are typically recommended a subthreshold aerobic exercise program (i.e., stationary cycling, treadmill or elliptical) for 20 minutes at 80% of the threshold HR, once per day for five to six days per week (Leddy & Willer, 2013). To ensure the individual does not exceed the prescribed HR, resulting in symptom exacerbation, a HR monitor is used (Leddy & Willer, 2013). The test can be repeated every two to three weeks to establish a new symptom-limited threshold HR until symptoms are no longer exacerbated and the individual can exercise to their age-predicted maximum HR (Leddy & Willer, 2013).

If an individual terminates the test due to symptom exacerbation before reaching their age-predicted maximum HR, they are considered to demonstrate physiological dysfunction (Leddy & Willer, 2013). The difference between the age-predicted maximum HR and the symptom-limited threshold HR provides an indication of how close an individual is to physiological recovery (Leddy & Willer, 2013). The test can be repeated periodically to assess progress towards physiological recovery. If an individual is able to exercise to their age-predicted maximum without symptom exacerbation during the test, but still reports persistent symptoms, this may indicate another underlying pathophysiology that requires further investigation (Ellis et al., 2015).

Although the BCTT or BCBT is widely used to diagnose physiological dysfunction, there are some limitations. Firstly, due to the diffuse and multifaceted nature of a mild TBI, the test should be used in conjunction with other tests to form an appropriate diagnosis (Ellis et al., 2015; Quatman-Yates et al., 2018) and to guide decisions about readiness to return to sport, school or work (Janssen et al., 2022). Secondly, the test may temporarily exacerbate symptoms, however this usually resolves within 24 hours (Leddy et al., 2018). Thirdly, some symptoms associated with physiological dysfunction also occur in healthy people, making interpretation more challenging (Gaetz & Iverson, 2009). Lastly, vestibular symptoms such as dizziness may mask as physiological dysfunction, as the head movement during treadmill testing may aggravate vestibulo-ocular symptoms (Ellis et al., 2015; Guskiewicz et al., 2001; Janssen et al., 2022). Therefore, clinicians administering the test should utilise their own clinical reasoning and judgment to differentiate between symptoms of exertion, vestibulo-ocular dysfunction, and physiological dysfunction.

2.8 Exercise intervention

2.8.1 Rest

People with mild TBI were previously recommended to rest until asymptomatic (McCrory, Meeuwisse, et al., 2017), as rest was theorised to promote recovery by reducing neurometabolic demands and symptoms (Giza & Hovda, 2001), and prevent further injury (Laurer et al., 2001). However, this approach was later recognised as unfeasible for those experiencing symptoms for extended periods, sometimes for months or years (Einarsen et al., 2018; Mosenthal et al., 2004; van Markus-Doornbosch, Peeters, Volker, et al., 2019). The concept of absolute rest was also deemed unrealistic (Kirkwood et al., 2012; Schneider et al., 2013). Rest in this context included both physical rest, such as refraining from engaging in physical activity (McCrory, Meeuwisse, et al., 2017), and cognitive rest, such as refraining from work, school and social demands, and activities requiring concentration (Valovic & Gioia, 2010).

In fact, prolonged rest following a mild TBI can lead to prolonged symptoms (Silverberg & Iverson, 2013; Thomas et al., 2020a), perception of greater symptom severity (Gibson et al., 2013; Schneider et al., 2013), poor mental health (Williamson & Shaffer, 2000), and exacerbation of comorbid conditions such as vestibular disorders, depression, post-traumatic stress disorder, chronic fatigue and pain disorders (Silverberg & Iverson, 2013). In healthy individuals without a history of a TBI, rest begins to negatively affect the cardiopulmonary and musculoskeletal systems within three days (Winkelman, 2009) and this is even sooner in athletes (Smorawiński et al., 2001). After three to six days of bed rest, healthy people often report symptoms such as headaches, restlessness and difficulty sleeping. If prolonged to a week, mood and vestibular changes may also occur (Fortney et al., 2011). Extended rest may produce symptoms that mimic mild TBI symptoms (Silverberg & Iverson, 2013) and is not an effective solution for improving persistent symptoms. In fact, physical deconditioning and avoidance of physical activity can reinforce the persistence of symptoms (Silverberg & Iverson, 2013).

The most recent consensus statement on concussion recommends relative rest for up to 48 hours after the initial injury, which includes continuing activities of daily living and reducing screen time (Leddy et al., 2023; Patricios et al., 2023). After this period, the authors recommend that clinicians should encourage return to physical activity as tolerated, such as walking or stationary cycling and systematically increase exercise intensity based on the degree of symptom exacerbation (Patricios et al., 2023). Clinicians should provide specific instructions to limit high risk activities (i.e., contact sports) while encouraging the gradual return to low risk activities, including school, work, social and daily activities (Patricios et al., 2023; Schneider et al., 2013; Silverberg & Iverson, 2013). This approach should be implemented while staying below cognitive and physical exacerbation thresholds, under the guidance of healthcare professionals (Marshall et al., 2015; Patricios et al., 2023; Schneider et al., 2017).

2.8.2 Aerobic exercise

Many non-pharmacological therapies exist for people experiencing persistent symptoms following a mild TBI (Rytter et al., 2021). These commonly include a combination of early information and advice, graded physical exercise, vestibular rehabilitation, manual treatment of the neck and upper back, oculomotor intervention and psychological intervention (Rytter et al., 2021). In the last 10 years, the amount of research into exercise interventions for people with mild TBI has increased significantly, with a particular focus on aerobic exercise, specifically symptom-limited aerobic exercise (Henke et al., 2020; Lal et al., 2018; Powell et al., 2020). Aerobic exercise at a symptom-limited level, improves persistent symptoms following a mild TBI through multiple mechanisms without exacerbating symptoms (McIntyre et al., 2020).

Prolonged sedentary behaviour following a mild TBI can lead to poor cardiorespiratory fitness, which in turn can lead to greater perceived fatigue and exercise intolerance (Chin et al., 2015; van Markus-Doornbosch, Peeters, Volker, et al., 2019). Aerobic exercise increases peak oxygen consumption, peak work rate, voluntary exhaustion, and anaerobic threshold, and decreases resting HR and HR at submaximal load due to increased stroke volume and parasympathetic activation (Carter et al., 2003; Chin et al., 2015; Mossberg et al., 2010). In addition to central adaptations, there are peripheral adaptions such as increased skeletal muscle capillary density and arteriovenous oxygen, overall enhancing the oxidative capacity of skeletal muscle (American College of Sports Medicine, 2021; Rowell, 1974). These adaptions collectively reduce perceived fatigue and improve endurance following a mild TBI (Chin et al., 2015; Mossberg et al., 2010). However, these central and peripheral adaptions are not elicited at a subthreshold intensity and are achieved when the individual can exercise to a greater intensity (i.e., when the individual is not limited by their threshold HR) and are either close to mild TBI recovery or have recovered.

The ANS, comprising the sympathetic and parasympathetic nervous system, is involved in vascular and cardiac function (Esterov & Greenwald, 2017). Following a mild TBI, autonomic dysfunction can occur, characterised by heightened sympathetic activity and blunted parasympathetic activity. This imbalance leads to decreased resting cerebral blood flow (Giza & Hovda, 2001), increased cerebral blood flow during exertion relative to workload (Clausen et al., 2016), and impaired cerebrovascular reactivity, the ability of cerebral blood vessels to constrict and/or dilate in response to vasoactive stimuli (Churchill et al., 2020). These autonomic changes are reflected in physiological responses, such as a higher resting HR, lower HR variability, and lower BP during physical and cognitive exertion and when exposed to stressors (Gall et al., 2004b; Hanna-Pladdy et al., 2001; Johnson et al., 2018; King et al., 1997). Aerobic exercise has shown to increase parasympathetic activity and decrease sympathetic activity (Carter et al., 2003). This can improve cerebral blood flow and cerebrovascular reactivity (Clausen et al., 2016) at rest and during exercise, to restore ANS function and improve physiological dysfunction symptoms following mild TBI (Goldsmith et al., 2000).

Emerging data demonstrates that aerobic exercise enhances neuroprotection and neurogenesis (Griesbach, 2011). Aerobic exercise has been shown to improve cortical connectivity and activation (Colcombe et al., 2004) through increased levels of brain-derived neurotropic factor involved in increasing hippocampal volume (Erickson et al., 2011). Aerobic exercise also increases proliferation of neuronal stem cells, and reduces neuronal degeneration, reactive astrocytes and apoptotic cell death around the damaged area (Itoh et al., 2011). The release of endorphins, monoamines and serotonin, and reduction in cortisol levels through aerobic exercise, further enhances neurogenesis (Chen, 2013; Klempin et al., 2013), therefore, aerobic exercise can improve memory, cognitive and mood (Erickson et al., 2011; Klempin et al., 2013) symptoms following a mild TBI.

2.8.3 Vestibular exercise

The vestibular system is a complex sensorimotor system responsible for motion detection and body positioning, multisensory integration, and coordinating motor responses related to movement and balance (Hain, 2011). Vestibular impairments can be classified as peripheral or central (D. A. Murray et al., 2017). Peripheral impairment occurs in the presence of damage to the labyrinth and/or eighth vestibular nerve, whereas central impairment occurs when there is damage to the brain (D. A. Murray et al., 2017). The most common vestibular impairments following a mild TBI include benign paroxysmal positional vertigo, vestibulo-ocular reflex impairment, visual motion sensitivity and balance impairment (Mucha et al., 2018). Due to the multisensory integration of the vestibular system, symptoms are worsened by visual, somatosensory and auditory stimuli (Keshner et al., 2004).

Vestibular rehabilitation is recommended for individuals experiencing dizziness, neck pain and/or headaches for >10 days (Patricios et al., 2023; Schneider et al., 2023). Vestibular rehabilitation can be used as a standalone or multimodal intervention, potentially involving manual therapy, strength training, symptom-limited aerobic exercise, occupational tasks, counselling and/or medication use (D. A. Murray et al., 2017; Patricios et al., 2023). The gold standard for vestibular rehabilitation is to provide an individualised program based on the identified impairments and progress the exercises in a functional manner as symptoms improve (Alsalaheen et al., 2013; Ellis et al., 2015; D. A. Murray et al., 2017). Vestibular rehabilitation exercises typically involve a combination of manoeuvres and exercises such as canalith repositioning manoeuvres for benign paroxysmal positional vertigo, habituation exercises for impaired motion sensitivity, adaption or gaze stabilisation exercises for deficits in the vesitublo-ocular reflex, substitution exercises to facilitate central programming of eye movement, and balance and aerobic exercises to improve balance and walking (Aligene & Lin, 2013). Exercise progression often follows a pattern from sitting to standing, gradually increasing difficulty with more challenging stances, dynamic balance and ambulation. Further challenges may involve unstable surfaces, movement of the head, arm or trunk, and the addition of visual input or cognitive dual tasks (Alsalaheen et al., 2013). Although vestibular rehabilitation should be individualised to target specific impairments, the most commonly prescribed exercises following a mild TBI include eye-head coordination exercises, static balance and ambulation exercises (Alsalaheen et al., 2013).

2.9 Barriers and facilitators to returning to physical activity following a mild traumatic brain injury

The Australian healthcare system consists of both public and private hospitals, with the private sector including hospitals, medical practices, and allied health practices (Thorne et al., 2022). Individuals that sustain a moderate to severe TBI typically receive inpatient and outpatient care through the public health sector (Helps et al., 2008; O'Callaghan et al., 2010), However, those with mild TBI often do not seek immediate medical attention at an emergency department (Cassidy et al., 2004) or receive follow-up outpatient care. Some individuals with mild TBI do not recognise that they have sustained a TBI (Delaney et al., 2005), while others recognise the symptoms but consider them subtle and not alarming enough to warrant medical attention (Buck, 2011). Individuals may also be reluctant to report their TBI, especially in a sporting or domestic violence setting for fear of repercussions (Cusimano et al., 2017; Zieman et al., 2017). Even when individuals seek medical attention at an emergency department, they are often discharged within two days after being screened for life-threatening injuries with patients diagnosed with mild TBI experiencing the shortest hospital length of stay compared to other types of TBI (Australian Institute of Health and Welfare, 2021). Upon hospital discharge, most patients do not receive mild TBI specific education (Koval et al., 2020), as education is not sufficiently standardised, varying in terms of content and delivery (Eliyahu et al., 2016) leading to differences in effectiveness of the education provided. For individuals that experience the persistence of symptoms, accessing healthcare services outside of the hospital may be influenced by other factors such as their socioeconomic status and level of education (Thorne et al., 2022).

The persistence of physical, cognitive, emotional and/or behavioural symptoms following a mild TBI (Ryan & Warden, 2003) can significantly reduce the ability to undertake physical activity (Huber et al., 2019; Mercier et al., 2021). While evidence-based guidelines exist to facilitate a graded approach to returning to school, sport (Patricios et al., 2023), and to a lesser extent, work (Karmali et al., 2022), individuals continue to experience reduced physical activity levels (Thomas et al., 2020a) and quality of life (Mercier et al., 2021), indicating that there are other factors to consider when implementing interventions.

Barriers and facilitators to physical activity are defined as factors that hinder or encourage the engagement in physical activity respectively (Kosteli et al., 2017). The identification of perceived barriers and facilitators to physical activity is important for understanding the factors that influence physical activity participation. This understanding allows for the development and enhancement of strategies and interventions that facilitate behaviour change and encourage individuals to return to prior physical activities. Since different patient populations experience unique barriers and facilitators, employing a validated behaviour change framework or model provides a systematic approach to identifying these factors (Atkins et al., 2017; Michie et al., 2011).

One such model is the Capability, Opportunity and Motivation-Behaviour (COM-B) model, an evidence-based behaviour change model, which has been widely used by policy makers, researchers and health professionals as a framework to implement interventions, understand behaviour and conduct motivational interviewing to enhance health outcomes (Atkins et al., 2017; Michie et al., 2011; Willmott et al., 2021). The model recognises that behaviour arises from the interaction of three key components: capability, opportunity and motivation. Modifying any of these factors can lead to changes in behaviour (Michie et al., 2011). Capability refers to the psychological and physical capacity of an individual to engage in the behaviour; opportunity (physical and social) refers to all factors that lie outside of the individual that enable the behaviour; and motivation (reflective and automatic) includes the reflective and automatic processes, both conscious and subconscious, that drive behaviour (Michie et al., 2011). In particular, the COM-B model has been utilised by researchers to understand behaviour change, guide intervention delivery, and design behaviour change strategies across various patient populations, including individuals following a TBI (Christie et al., 2024; Drattel et al., 2025; Knight et al., 2024).

Preface

The 3rd consensus statement on concussion published in 2009 recommends physical and cognitive rest for up to 48 hours (McCrory et al., 2009), whereas the most recent 6th consensus statement recommends light intensity physical activity within the first 24 to 48 hours following a concussion (Patricios et al., 2023). This shift from longer periods of rest to relative rest has been met with an upsurge of exercise-based interventions. To understand the effect of these interventions, a systematic review of randomized controlled trials (RCTs) was carried out to answer the question, *'What is the effect of physical exercise on persistent symptoms in people who have experienced a mild traumatic brain injury (TBI)'*? This chapter presents systematic review findings which have been modified and published in NeuroRehabilitation journal (Appendix 1).

Publication

Vuu, S., Barr, C.J., Killington, M., Garner, J., & van den Berg, M. E. L. (2022). Physical exercise for people with mild traumatic brain injury: A systematic review of randomized controlled trials. *NeuroRehabilitation*, 51(2), 185-200. http://doi.org/10.3233/NRE-220044

CHAPTER 3: PHYSICAL EXERCISE FOR PEOPLE WITH MILD TRAUMATIC BRAIN INJURY: A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS

3.1 Introduction

The latest consensus statements recognise that there is insufficient evidence to prescribe strict rest and instead recommend that following a relative rest period during the acute phase (i.e., 24–48 hours) of recovery, people with mild TBI should be encouraged to become gradually more active while staying below their cognitive and physical exacerbation threshold (McCrory, Meeuwisse, et al., 2017; Patricios et al., 2023). Traditionally, a physical and cognitive rest period, as well as activity restriction, was prescribed as treatment for people with mild TBI (Leddy et al., 2012; McCrory, Meeuwisse, et al., 2017). This approach was intended to ease discomfort, and prevent repeated injury and exacerbation of symptoms (McCrory, Meeuwisse, et al., 2017; McCrory et al., 2013), without consensus on the optimal amount and duration of rest (Leddy et al., 2012; McCrory et al., 2013). However, evidence suggests that prolonged rest beyond 48 hours (Patricios et al., 2023) can lead to secondary complications such as deconditioning, anxiety, depression, and irritability; all of which are commonly reported symptoms following a mild TBI (Schneider et al., 2013). Most people with mild TBI recover spontaneously but up to 30% continue to experience symptoms beyond three months post-injury (Babcock et al., 2013).

The terminologies, ‘concussion’ and ‘mild TBI’, both described as *“an acute neurophysiological event related to blunt impact or other mechanical energy applied to the head, neck or body (with transmitting forces to the brain)”* are often used interchangeably (Ontario Neurotrauma Foundation, 2018, p. 1). As most people following a mild TBI do not have structural changes on their brain scan (O'Neil et al., 2013), functional changes rather than structural changes result in an array of somatic, cognitive, physical, and behavioural symptoms (McCrory, Meeuwisse, et al., 2017). The most reported symptoms in the first 12 weeks following a mild TBI include headache, dizziness, poor attention, poor memory, irritability and depression (Levin & Diaz-Arrastia, 2015). The extent of these symptoms is influenced by psychological and physiological factors (McCrory, Meeuwisse, et al., 2017), complications of the TBI itself, past medical history and current comorbidities (Marshall et al., 2015). This collection of non-specific post-traumatic symptoms is commonly identified as Post-Concussion Syndrome (PCS) (McIntyre et al., 2020), Post-Concussion Disorder (PCD) (Ellis et al., 2015), or Persistent Symptoms (Makdissi et al., 2013). The use of these terms are ambiguous due to the complexities with, and inconsistent use of, diagnostic criteria, including experienced symptoms, their onset and duration (Dwyer & Katz, 2018).

Recent systematic reviews have found preliminary evidence for the effectiveness of physical exercise for improving persistent symptoms following mild TBI (Baker et al., 2020; Henke et al., 2020; Lal et al., 2018; Langevin et al., 2020; McIntyre et al., 2020; Shen et al., 2021). However, these reviews had various limitations. Some focused specific exercise types (Lal et al., 2018; McIntyre et al., 2020), populations, such as adolescents (Henke et al., 2020; Shen et al., 2021), or injury context, such as sport-related injuries (Baker et al., 2020; Henke et al., 2020; Langevin et al., 2020). Others restricted their scope to interventions with a narrow timeframe (Lal et al., 2018; McIntyre et al., 2020), or included studies with various study designs (Henke et al., 2020; Lal et al., 2018; McIntyre et al., 2020), thereby incorporating low level evidence such as from studies without a comparison group, increasing risk of bias. To address these limitations, a comprehensive systematic review was conducted to examine the effect of physical exercise on persistent symptoms in individuals with mild TBI. This review aimed to be more inclusive by not restricting based on age, injury cause, or time since injury. Additionally, it focused solely on RCTs to ensure a higher level of evidence. This approach allowed for a more robust evaluation of the effectiveness of physical exercise interventions across a broader spectrum of the mild TBI population, providing more generalisable findings.

3.2 Methods

This systematic review was completed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). The protocol was registered with the International Prospective Register for Systematic Reviews (PROSPERO) (CRD4201913703) (Centre for Reviews and Dissemination, n.d.) (Appendix 2). No modifications were made following protocol registration.

3.2.1 Literature search and selection criteria

The databases, CINAHL, Cochrane Library, Embase, MEDLINE, SPORTDiscus, and Web of Science were searched using a combination of Medical Subject Headings and keywords for mild TBI, concussion, post-concussion syndrome, exercise, and RCTs. The search strategies for the databases were undertaken with a research librarian, and are presented in Table 3.1. The search was restricted to the English language, human trials, and articles published between 2010 to the 13th of January 2021 when the search was conducted to update the literature. Reference lists of included studies and relevant reviews were hand searched for additional articles.

Table 3.1 Search strategies on databases

Database	Search strategy	
CINAHL	S13	Limiters – Published Date: 20100101-20210113; English Language
	S12	S3 AND S8 AND S11
	S11	S9 OR S10
	S10	(MH "Stratified Random Sample") OR (MH "Systematic Random Sample") OR (MH "Simple Random Sample") OR (MH "Random Sample") OR (MH "Random Assignment")
	S9	T1 (trial* OR random* OR clinical* OR control* OR assign* OR placebo* OR blind* OR mask*)
	S8	S4 OR S5 OR S6 OR S7
	S7	(MH "Exercise") OR (MH "Resistance Training") OR (MH "Exercise Positions") OR (MH "Abdominal Exercises") OR (MH "Therapeutic Exercise") OR (MH "Group Exercise") OR (MH "Sport Specific Training")
	S6	(MH "Muscle Strength") OR (MH "Exercise Test, Muscular") OR (MH "Athletic Training Programs") OR (MH "Resistance Training") OR (MH "Muscle Strengthening")
	S5	(MH "Cardiorespiratory Fitness") OR (MH "Physical Fitness") OR (MH "Walking") OR (MH "Athletic Training Programs") OR (MH "Exercise Equipment and Supplies")
	S4	T1 (exercis* OR aerobic OR anaerobic OR conditioning OR fit* OR strength* OR resist* OR balanc* OR vestibular OR endurance OR walk* OR run* OR jog* OR swim* OR cycl* OR "aqua therapy" OR hydrotherapy OR gym* OR treadmill OR ergomet* OR “physical activity” OR yoga OR “tai chi” or "activit*")
	S3	S1 OR S2
	S2	(MH "Brain Concussion") OR (MH "Postconcussion Syndrome") OR (MH "Brain Injuries")
	S1	T1 ("mild traumatic brain injury" OR MTBI OR "mild TBI" OR "mild brain injury" OR concuss* OR "post concuss*" OR post-concuss* OR "PCS")
Cochrane Library	1	"mild traumatic brain injury" OR MTBI OR "mild TBI" OR "mild brain injury" OR concuss* OR "post concuss*" OR post-concuss* OR "PCS"
	2	exercis* OR aerobic OR anaerobic OR conditioning OR fit* OR strength* OR resist* OR balanc* OR vestibular OR endurance OR walk* OR run* OR jog* OR swim* OR cycl* OR "aqua therapy" OR hydrotherapy OR gym* OR treadmill OR ergomet* OR “physical activity” OR yoga OR “tai chi” or "activit*"
	3	trial* OR random* OR clinical* OR control* OR assign* OR placebo* OR blind* OR mask*
	4	Cochrane Library Publication Date: Between Jan 2010 and Jan 2021
Embase	1	("mild traumatic brain injury" OR MTBI OR "mild TBI" OR "mild brain injury" OR concuss* OR "post concuss*" OR post-concuss* OR "PCS").mp
	2	Brain concussion/ or concussion/
	3	1 or 2
	4	(exercis* OR aerobic OR anaerobic OR conditioning OR fit* OR strength* OR resist* OR balanc* OR vestibular OR endurance OR walk* OR run* OR jog* OR swim* OR cycl* OR "aqua therapy" OR hydrotherapy OR gym* OR treadmill OR ergomet* OR “physical activity” OR yoga OR “tai chi” or "activit*").mp
	5	Exercise/
	6	4 or 5
	7	(trial* OR random* OR clinical* OR control* OR assign* OR placebo* OR blind* OR mask*).mp
	8	/random sample

	9	7 or 8
	10	3 and 6 and 9
	11	Limit 10 to yr="2010 – 2021"
MEDLINE	1	("mild traumatic brain injury" OR MTBI OR "mild TBI" OR "mild brain injury" OR concuss* OR "post concuss*" OR post-concuss* or PCS).tw.kf.
	2	Brain Concussion/
	3	Contrecoup Injury/
	4	Post-Concussion Syndrome/
	5	1 or 2 or 3 or 4
	6	(exercis* OR aerobic OR anaerobic OR conditioning OR fit* OR strength* OR resist* OR balanc* OR vestibular OR endurance OR walk* OR run* OR jog* OR swim* OR cycl* OR "aqua therapy" OR hydrotherapy OR gym* OR treadmill OR ergomet* OR "physical activity" OR yoga OR "tai chi" or "activit*").tw.kf.
	7	Exercise/ or Circuit-Based Exercise/ or Exercise Movement Techniques/ or Plyometric Exercise/ or Exercise Therapy/
	8	Physical Fitness/ or Physical Conditioning, Human/ or Physical Functional Performance/ or Physical Endurance/
	9	6 or 7 or 8 or 9
	10	(trial* OR random* OR clinical* OR control* OR assign* OR placebo* OR blind* OR mask*).tw.kf.
	11	Randomized Controlled Trial/
	12	10 or 11
	13	5 and 9 and 12
	14	limit 13 to yr="2010-current"
SportDiscus	S5	S1 AND S2 AND S3 Limiters – Published Date: 20100101-20210113
	S4	S1 AND S2 AND S3
	S3	TI=(trial* OR random* OR clinical* OR control* OR assign* OR placebo* OR blind* OR mask*)
	S2	TI=(exercis* OR aerobic OR anaerobic OR conditioning OR fit* OR strength* OR resist* OR balanc* OR vestibular OR endurance OR walk* O R run* OR jog* OR swim* OR cycl* OR "aqua therapy" OR hydrotherapy OR gym* OR treadmill OR ergomet* OR "physical activity" OR yoga OR "tai chi" or "activit*")
	S1	TI=("mild traumatic brain injury" OR MTBI OR "mild TBI" OR "mild brain injury" OR concuss* OR "post concuss*" OR post-concuss* or PCS)
Web of Science	#10	(#9 and #8 and #7) AND LANGUAGE: (English) AND TIMESPAN: (2010-2021)
	#9	#6 OR #5
	#8	#4 OR #3
	#7	#2 OR #1
	#6	TI=(trial* OR random* OR clinical* OR control* OR assign* OR placebo* OR blind* OR mask*)
	#5	TS=(trial* OR random* OR clinical* OR control* OR assign* OR placebo* OR blind* OR mask*)
	#4	TS=(exercis* OR aerobic OR anaerobic OR conditioning OR fit* OR strength* OR resist* OR balanc* OR vestibular OR endurance OR walk* OR run* OR jog* OR swim* OR cycl* OR "aqua therapy" OR hydrotherapy OR gym* OR treadmill OR ergomet* OR "physical activity" OR yoga OR "tai chi" or "activit*")
	#3	TI=(exercis* OR aerobic OR anaerobic OR conditioning OR fit* OR strength* OR resist* OR balanc* OR vestibular OR endurance OR walk* OR run* OR jog* OR swim* OR cycl* OR "aqua therapy" OR hydrotherapy OR gym* OR treadmill OR ergomet* OR "physical activity" OR yoga OR "tai chi" or "activit*")
	#2	TI=("mild traumatic brain injury" OR MTBI OR "mild TBI" OR "mild brain injury" OR concuss* OR "post concuss*" OR post-concuss* or PCS)
	#1	TS=("mild traumatic brain injury" OR MTBI OR "mild TBI" OR "mild brain injury" OR concuss* OR "post concuss*" OR post-concuss* OR "PCS")

Studies that referred to their study population as those having experienced a mild TBI, mild-to-moderate TBI, concussion, or post-concussion syndrome were considered eligible for inclusion, see Table 3.2. Studies including people with moderate or moderate-to-severe TBI and mixed populations, where results for those with mild TBI were not reported separately, were excluded. The study intervention type involved physical exercise interventions (e.g., cycling, running) regardless of delivery mode and setting, and the comparator intervention included usual care (e.g., education, multidisciplinary intervention), or other physical intervention (e.g., stretching exercises, relaxation exercises). There were no limitations regarding the study population or intervention, to capture all studies that investigated exercise for people following a mild TBI. The primary study outcome was experienced persistent symptoms, defined as any symptoms experienced following a mild TBI. All other clinical outcomes were considered as secondary study outcomes.

Table 3.2 Inclusion criteria

	Inclusion criteria
Population	• mild TBI • mild-to-moderate TBI • concussion • PCS
Intervention	• Any physical exercise intervention regardless of delivery mode (e.g., individual, group) and setting (inpatient, outpatient, home, community)
Comparator	• Usual care (e.g., education, multidisciplinary intervention) • Other physical intervention (e.g., stretching exercises, relaxation exercises)
Outcome	• Primary: persistent symptoms • Secondary: all other clinical outcomes

All studies were uploaded to Covidence and duplicates were removed (Covidence systematic review software, 2023). Title and abstract screenings were independently screened by two reviewers (SV and JG). Following title and abstract screening, all remaining full texts were obtained and screened independently by the same reviewers (SV and JG). Any conflicts were resolved through discussion in consultation with a third reviewer (MV). All studies meeting the inclusion criteria were reported and studies of which no full-text could be obtained were excluded.

Data were extracted using an Excel pro-forma that included the following outcomes: study characteristics (sample size, setting), participants' characteristics (age, gender, time since injury, cause of injury), intervention characteristics (type, key descriptors, intensity, frequency, duration), and reported outcomes (key findings, between-group means, 95% confidence intervals (CIs), effect sizes). Data of all studies was extracted by author one (SV). A second author independently checked for accuracy and extracted data from 20% of the included studies (MV) demonstrating an agreement of more than 80% (Shea et al., 2017).

A narrative synthesis was conducted for all data. Standard mean differences and 95% CIs were used to analyse continuous data. Due to the heterogeneity of the available data, a meta-analysis, performed using the Review Manager 5.3 software (Review Manager (RevMan), 2014), was possible only to calculate the effect size of aerobic exercise using the change in persistent symptoms from immediately pre to post for aerobic exercise intervention compared to usual care.

3.2.2 Quality assessment

A risk of bias assessment was completed using a modified version of the Critical Appraisal Skills Program (CASP) (Critical Appraisal Skills Programme, 2018). A modified version was undertaken to include the descriptors for rating 'Yes', 'No' and 'Can't tell'. Studies scoring ≤3/6, 4/6, or ≥ 5/6 were judged of low, moderate, or high quality respectively. Studies were not excluded from the review based on their quality. CASP items deemed as critical value included appropriateness of randomisation and blinding, whether groups were treated equally, whether participants were lost to follow-up, and the amount of detail provided for the population, intervention, and comparator. To assess the completeness of intervention reporting, the Template for Intervention Description and Replication (TIDieR) was used (Hoffman et al., 2014). Quality of evidence was assessed using the Grade of Recommendations Assessment, Development and Evaluation (GRADE) tool based on the risk of bias, inconsistency, indirectness, imprecision, and publication bias of the studies. Due to the heterogeneity of the available study data, analysis with GRADEpro GDT could only be undertaken for those studies that were included in the meta-analysis (GRADEpro GDT, 2024).

3.3 Results

3.3.1 Search results and study characteristics

A PRISMA flow diagram depicting the study selection process is presented in Figure 3.1. Of the 11,083 citations retrieved in the systematic search, 96 studies were reviewed in full-text of which 11 met the inclusion criteria and reported the effect of an exercise intervention on persistent symptoms in people with mild TBI (Bailey et al., 2019; Chan et al., 2018; Dobney et al., 2020; Kleffelgaard et al., 2019; Kurowski et al., 2017; Leddy et al., 2012; Maerlender et al., 2015; Micay et al., 2018; Reneker et al., 2017; Rytter et al., 2019; Schneider et al., 2014). Six studies reported on a population aged 18 years old or under (Bailey et al., 2019; Chan et al., 2018; Dobney et al., 2020; Kurowski et al., 2017; Leddy, Haider, Ellis, et al., 2019; Micay et al., 2018). Time since injury ranged from five days (Micay et al., 2018) to six months post-injury (Rytter et al., 2019), and one study did not specify (Maerlender et al., 2015). Cause of injury included sport-related injuries (Chan et al., 2018; Leddy, Haider, Ellis, et al., 2019; Maerlender et al., 2015; Micay et al., 2018; Reneker et al., 2017; Schneider et al., 2014), mixed aetiologies (Bailey et al., 2019; Kleffelgaard et al., 2019; Kurowski et al., 2017; Rytter et al., 2019), and one did not specify (Dobney et al., 2020). The sample size ranged from 15 (Micay et al., 2018) to 113 (Leddy, Haider, Ellis, et al., 2019) and the total number of participants included in this review was 467. The study characteristics are presented in Table 3.3.

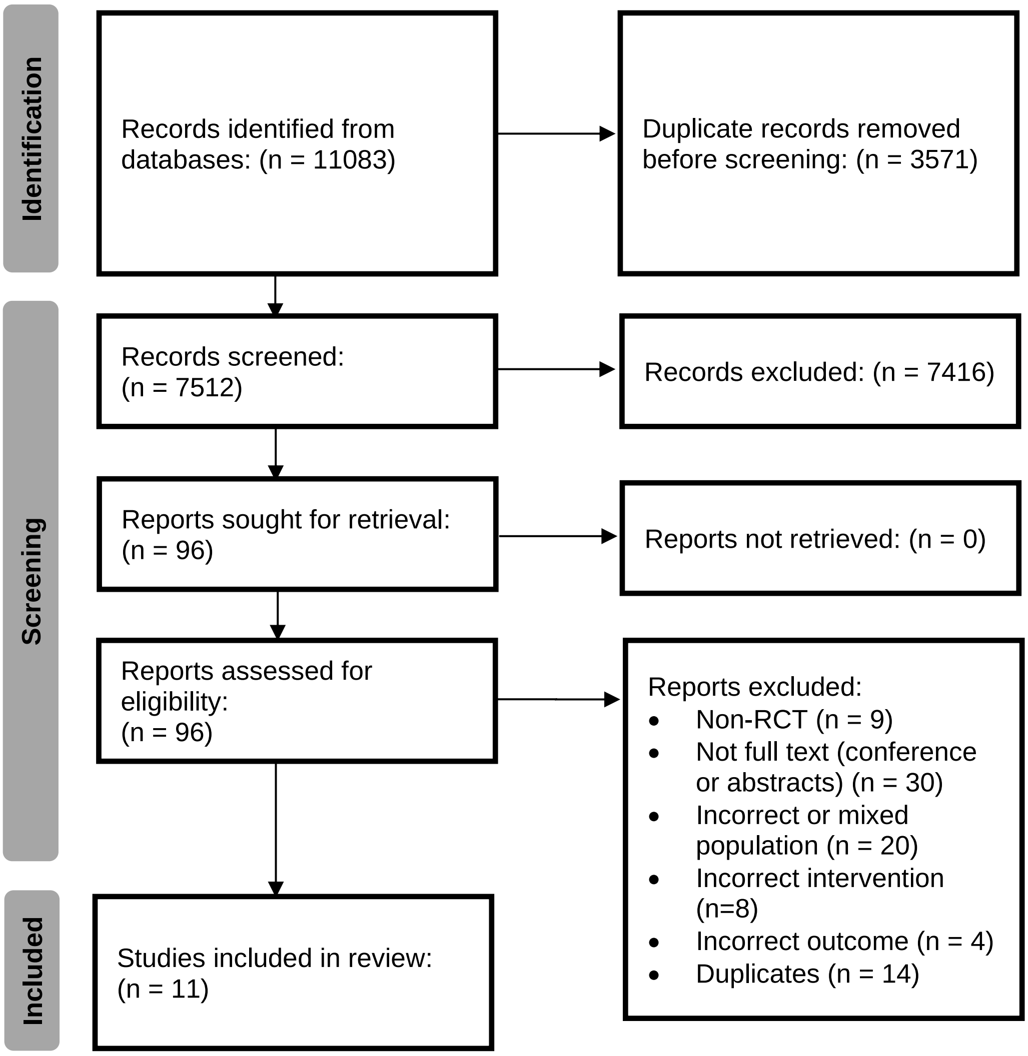

Figure 3.1 PRISMA flow diagram

Table 3.3 Study characteristics

Study	Country	Setting	Diagnosis	Cause of injury	Time since injury	Age (years)	Gender	Type of exercise	CASP score
Bailey et al. (2019)	USA	Hospital	Post- concussion symptoms	Mixed	≥4 weeks	14-18	9 males 7 females	Aerobic	Low
Chan et al., (2018)	Canada	Concussion clinic	Post-concussion symptoms	Sport	≥4 weeks	12-18	5 males 14 females	Aerobic	Medium
Dobney et al., (2018)	Canada	Hospital	Post-concussion symptoms	Unknown	≥2 weeks	9-17	12 males 8 females	Aerobic	Medium
Kleffelgaard et al., (2019)	Norway	Hospital	Dizziness following a mild-to-moderate TBI	Mixed	≥4 weeks	16-60	20 males 45 females	Vestibular	Medium
Kurowski et al., (2017)	USA	Clinic, community, and hospital	Post-concussion symptoms	Mixed	≥4 weeks	12-17	13 males 17 females	Aerobic	Medium
Leddy et al., (2019)	Canada	Concussion clinic	Concussion	Sport	≤10 days	13-18	65 males 48 females	Aerobic	High
Maerlender et al., (2015)	USA	Not reported	Recently concussed	Sport	Recently concussed	Not reported	8 males 20 females	Aerobic	Low
Micay et al., (2018)	Canada	Sport medicine centre	Symptomatic following sport-related concussion	Sport	≤10 days	14-18	15 males 0 females	Aerobic	High
Reneker et al., (2017)	USA	Sport medicine centre	Post-concussion symptoms in the migraine cluster	Sport	≥10 days	10-23	25 males 16 females	Vestibular	High
Rytter et al., (2019)	Denmark	Hospital	Post-concussion symptoms in attention and/or memory	Mixed	>6 months	18-65	30 males 59 males	Strength and aerobic	High
Schneider et al., (2014)	Canada	Medical centre	Post-concussion symptoms of dizziness, neck pain and/or headache	Sport	≥10 days	12-30	18 males 13 females	Vestibular	High

3.3.2 Quality assessment

Table 3.4 presented the scoring on a modified version of the CASP. Two studies were rated low (Bailey et al., 2019; Maerlender et al., 2015), four medium (Chan et al., 2018; Dobney et al., 2020; Kleffelgaard et al., 2019; Kurowski et al., 2017) and five were rated as high (Leddy, Haider, Ellis, et al., 2019; Micay et al., 2018; Reneker et al., 2017; Rytter et al., 2019; Schneider et al., 2014) quality.

Assessment of intervention reporting using the TIDieR checklist indicated that all studies provided a rationale for the intervention and outlined the intervention procedures. Most studies also appropriately described the mode of intervention delivery (9/11), where the intervention occurred (8/11) and intervention dosage (10/11). Only 3/11 studies provided sufficient information about the intervention provider. The TIDieR assessment of intervention groups is shown in Table 3.5.

A summary of the key findings using the GRADE assessment for the studies included in the meta-analysis is provided in Table 3.6. Certainty of evidence for the effect of aerobic exercise intervention on persistent symptoms was moderate, and risk of bias was serious due to one of three studies having inadequate blinding (Chan et al., 2018; Maerlender et al., 2015; Rytter et al., 2019).

Table 3.4 Analysis of bias using a modified CASP

	1. Did the trial address a clearly focussed issue? **N: No PICO** **CT: Missing at least 1 PICO** **Y: All PICO**	**2. Was the assignment of patients to treatments randomized?** **N: Non-RCT** **CT: Unsuitable randomisation** **Yes: Suitable randomisation**	**3. Were all of the patients who entered the trial properly accounted for at its conclusion?** **N: Not accounted** **CT: Not specified** **Y: ITT completed or no drop-outs**	**4. Were patients, health workers and study personnel 'blind' to treatment?** **N: No blinding** **CT: Incomplete blinding** **Y: Assessor blinded**	**5. Were the groups similar at the start of the trial?** **N: ≥1 difference in baseline characteristics** **CT: Baseline characteristics not specified** **Y: No difference in baseline characteristics**	**6. Aside from the experimental intervention, were the groups treated equally?** **N: Not treated equally** **CT: Mostly treated equally** **Y: Treated equally**	**TOTAL** **Low: ≤3/6 'Yes'** **Medium: 4/6 'Yes'** **High: ≥5/6 'Yes'**
Bailey et al., (2019)	Y	Y	N n=1 in the CG withdrew after baseline	N	CT	Y	Low
Chan et al., (2018)	Y	Y	Y	Y	CT	CT n=1 in the CG received follow-up support from the occupational therapist for mental health	Medium
Dobney et al., (2018)	Y	Y	N n=2 in the IG were excluded from symptom analysis	N	Y	Y	Medium
Kleffelgaard et al., (2019)	Y	Y	N n=6 in the IG and n=4 in the CG were lost at second follow-up	Y	Y	N Those in the CG who had positive positioning tests were treated with repositioning manoeuvres	Medium
Kurowski et al., (2017)	Y	Y	N n=3 in the IG and n=1 in the CG did not complete the final assessment	Y	N Mechanism of injury was significant between groups	Y	Medium

Leddy et al., (2019)	Y	Y	N n=5 in the IG and n=5 in the CG were excluded from the analysis	Y	Y	Y	High
Maerlender et al., (2015)	CT Missing participant age	Y	N n=1 in the CG were excluded from analysis	N	Y	Y	Low
Micay et al., (2018)	Y	Y	N N=2 in the CG were excluded from analysis	Y	Y	Y	High
Reneker et al., (2017)	Y	Y	Y	Y	Y	Y	High
Rytter et al., (2019)	Y	Y	Y	Y	Y	Y	High
Schneider et al., (2014)	Y	Y	Y	Y	CT	Y	High

Y=Yes N=No CT=Can't tell
IG=Intervention group CG=Control group

Table 3.5 Analysis of intervention groups using the TIDieR

	1. Brief name	2. Why	3. What: materials	4. What: procedures	5. Provider	6. How	7. Where	8. When and how much	9. Tailoring	10. Modifications	11. How well: planned	12: How well: actually
Bailey et al., (2019)	Y	Y	N	Y	N	Y	Y	Y	N	N	N	N
Chan et al., (2018)	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Y
Dobney et al., (2018)	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	N
Kleffelgaard et al., (2019)	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y
Kurowski et al., (2017)	Y	Y	N	Y	N	Y	Y	Y	Y	N	Y	Y
Leddy et al., (2019))	Y	Y	Y	Y	N	Y	Y	Y	N	N	N	N
Maerlender et al., (2015)	N	Y	N	Y	N	N	N	N	N	N	N	N
Micay et al., (2018)	Y	Y	N	Y	N	N	N	Y	N	N	Y	Y
Reneker et al., (2017)	N	Y	Y	Y	Y	Y	N	Y	Y	Y	N	N
Rytter et al., (2019)	Y	Y	Y	Y	N	Y	Y	Y	Y	N	N	N
Schneider et al., (2014)	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y

Y=Yes
N=No

Table 3.6 GRADE for aerobic exercise compared to usual care for people with mild TBI

Authors: Chan et al., (2018), Maerlender et al., (2015) and Rytter et al., (2019)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Aerobic exercise**	**Usual care**	**Relative (95% CI)**	**Absolute (95% CI)**		
Post-concussion symptoms (assessed with: Post-Concussion Symptom Scale, Immediate Post-Concussion Assessment and Cognitive Test, Rivermead Post-concussion Symptom Questionnaire)												
3	randomised trials	serious[a]	not serious	not serious	not serious	none	68	68	-	SMD -0.39 (-0.73 to -0.05)	⨁⨁⨁ MODERATE	IMPORTANT

SMD: Standardised mean difference

Explanations: a) One study had inadequate blinding and follow-up of patients

3.3.3 Primary study results: the effect of physical exercise on persistent symptoms

All 11 included studies reported on the effect of exercise on persistent symptoms. Five studies compared a physical exercise intervention, all involving aerobic exercise, to usual care (Chan et al., 2018; Dobney et al., 2020; Maerlender et al., 2015; Micay et al., 2018; Rytter et al., 2019). A total of six studies compared an exercise intervention to another physical intervention, of these three compared an aerobic exercise intervention to another physical intervention (Bailey et al., 2019; Kurowski et al., 2017; Leddy, Haider, Ellis, et al., 2019), and three compared a vestibular exercise intervention to another physical intervention (Kleffelgaard et al., 2019; Reneker et al., 2017; Schneider et al., 2014). Five of the 11 studies reported a positive effect on persistent symptoms in favour of the physical exercise intervention (Bailey et al., 2019; Kurowski et al., 2017; Leddy, Haider, Ellis, et al., 2019; Reneker et al., 2017; Rytter et al., 2019), five reported no significant between-group differences (Chan et al., 2018; Kleffelgaard et al., 2019; Maerlender et al., 2015; Micay et al., 2018; Schneider et al., 2014), and one provided descriptive data with no statistical analysis (Dobney et al., 2020). A summary of the intervention characteristics is provided in Table 3.7.

Table 3.7 Intervention characteristics

Study	Intervention components	Outcomes	Results
Bailey et al., (2019)	IG: Aerobic exercise 80% of threshold heart rate (HR) on a treadmill in the clinic and at home Social modelling, focusing on positive experiences and interpreting symptoms Duration: 20 mins, frequency: daily, duration: 6 weeks. CG: Other physical intervention Stretching exercises for the first 3 weeks, walking for the next 3 weeks Time: 20mins, frequency: daily, duration: 6 weeks.	Primary • Post-Concussion Symptom Scale	The IG (mean % change: -63.3 (17.4)) improved more than the CG (mean % change: -56.8 (27.8)) on the Post-Concussion Symptom Scale when adjusted for depression scores (p<0.05).
Chan et al., (2018)	IG: Aerobic exercise 60% of age-predicted maximum HR on a treadmill or stationary bike, used with a gaming system, 15 mins Coordination exercises of the individual's main activity/sport, 10 mins Visualisation of the individual's main sport/activity, 5-10 mins Education about recovery, coping strategies and returning to sport/school CG intervention Duration: 35 mins, frequency: daily, duration: 6 weeks. CG: Usual care 1x session with the occupational therapist about symptom management and returning to sport 1x session with a hospital-affiliated teacher for returning to school 1x session with psychiatrist for medication prescription and referral to allied health Time: not reported, frequency: 3 sessions, duration: 6 weeks.	Primary • Post-Concussion Symptom Scale • Immediate Post-Concussion Assessment and Cognitive Test Secondary • Patient-Reported Outcomes Measurement Information System • Beck Depression Inventory • Pediatric Quality of Life Multidimensional Fatigue Scale • Balance Error Scoring System	The mean (SD) change on Post-Concussion Symptom Scale from baseline to follow-up was -24.7 (19.1) and -15.8 (12.5) in the IG and CG respectively, which was associated with a Cohen's d treatment effect size (ES) of 0.55, however, no p-value was reported. Between group differences were not reported for all other outcomes.
Dobney et al., (2018)	IG: Aerobic exercise Commencing 2 weeks post-mild TBI 60% of age-predicted maximum HR on a treadmill or stationary bike, 15 mins Coordination exercises of the individual's main sport/activity, 10 mins	Primary • Post-Concussion Symptom Inventory	Median (range) scores on the Post-Concussion Symptom Inventory for youths at weeks 2 and 4 were 21 (4-59) and 3 (0-49) in the IG, and 25 (6-35) and 11 (0-35) for the CG. Separate data were reported for the two participants classified as "child" in the CG with scores transformed.

	Visualisation of the individual’s main sport/activity, 5-10 mins Education about recovery, coping strategies and returning to sport/school Home exercise program (HEP) as above If symptom-free for 1 week at rest, advised to start the stepwise protocol for return to sport Time: 35 mins, frequency: daily, duration: 8 weeks. CG: Usual care Commenced the intervention 4 weeks post-mild TBI.		Between group difference was not reported for the Post-Concussion Symptom Inventory.
Kleffelgaard et al., (2019)	IG: Vestibular exercise Group-based vestibular exercises of Brandt-Daroff, habituation, gaze stabilisation (adaptation and substitution) and balance exercises HEP of 2-5 individualized exercises and general physical activity, with tracking via an exercise diary Education about social modelling, focussing on positive experiences and interpreting symptoms CG intervention Time: Not reported, frequency: 2xweekly, duration: 8 weeks. CG: Other physical intervention Multidisciplinary outpatient rehabilitation Individuals with a positive Dix-Hallpike and Roll Test were treated with Epley and Bar-B-Que Roll manoeuvres Time: Not reported, frequency: not reported, duration: 8 weeks.	Primary • Rivermead Post-concussion Symptoms Questionnaire Secondary • Dizziness Handicap Inventory • High-Level Mobility Assessment Tool • Vertigo Symptom Scale • Hospital Anxiety and Depression Scale • Balance Error Scoring System	First follow-up: Rivermead Post-concussion Symptoms Questionnaire, Vertigo Symptom Scale, Hospital Anxiety Depression Scale and Balance Error Scoring System reported non-significant between-group differences (p>0.05). Mean difference between the IG and CG on the Dizziness Handicap Inventory was -8.7 (-16.6 to -0.9), which was significant (p=0.03). Mean difference between the IG and CG on the High-Level Mobility Assessment Tool was 3.7 (1.4 to 6.0), which was significant (p=0.002). Second follow-up: Non-significant between-group differences for all outcomes (p>0.05).
Kurowski et al., (2017)	IG: Aerobic exercise 80% of threshold HR on a stationary bike, adjusted weekly Time: Not reported, frequency: 5-6xweekly, duration: >6 weeks, additional 1-2 weeks for those who had not recovered. CG: Other physical intervention Stretching exercises of the upper and lower body, and trunk New stretches fortnightly	Primary • Self-reported Post-Concussion Symptom Inventory • Parent-reported Post-Concussion Symptom Inventory	Intervention was complete at week 7 but data were not reported until follow-up. Self-reported Post-Concussion Symptom Inventory was provided at final assessment, which was after 9 weeks, demonstrated an improved rate of recovery in the IG compared to the CG (p=0.036) but not for the Parent-reported Post-Concussion Symptom Inventory (p=0.50).

	Time: Not reported, frequency: 5-6xweekly, duration: >6 weeks, additional 1-2 weeks for those who had not recovered.		
Leddy et al., (2019)	IG: Aerobic exercise 80% of threshold HR of walking, jogging, stationary cycling or treadmill in the home or gym under supervision, 20 mins or earlier if symptoms increase by ≥2-points from pre-exercise levels New HR determined by weekly clinic visits for as long as the individual remained symptomatic Instructed not to stretch or participate in other sports/activities that exacerbate symptoms and limit the use of technology Time: 20 mins, frequency: daily, duration: until asymptomatic. CG: Other physical intervention Gentle, whole-body progressive stretching, advanced weekly Time: 20 mins, frequency: daily, duration: until asymptomatic.	Primary • Days from injury to recovery	The IG recovered in a median of 13 (IQR: 10-18.5) days, whereas the CG recovered in 17 (IQR: 13-23) days (p=0.009).
Maerlender et al., (2015)	IG: Aerobic exercise Mild-to-moderate exertion on a stationary bike Time: 20 mins, frequency: daily, duration: not reported. CG: Usual care Instructed not to engage in exertion beyond normal activities required for school Time: Not reported, frequency: not reported, duration: not reported.	Primary • Immediate Post-Concussion Assessment and Cognitive Test	Median number of days to recovery on the Immediate Post-Concussion Assessment and Cognitive Test was no different by group (p=0.705).
Micay et al., (2018)	IG: Aerobic exercise First session, stationary cycling session at 60% of the age-predicted maximum HR, 10 mins Intensity maintained at the next session, 20 mins Subsequently, intensity increased by 5% until 70% was reached, maintained for remaining sessions All sessions included 5 mins of warm-up and cool-down Time: 30 mins, frequency: 8 sessions, duration: 11 days. CG: Usual care	Primary • Post-Concussion Symptom Scale • Time to Medical Clearance for Return-to-Play	No significant difference between groups in mean Time to Medical Clearance for Return-to-Play, which was 36.1±18.5 for the IG and 29.6±15.8 for the CG (p=0.87). Between group difference on the Post-Concussion Symptom Scale was not reported. Intervention was complete at day 11 but data were not presented until after day 21.

	Physician consultation for the stepwise progressive return-to-sport protocol Time: not reported, frequency: not reported, duration: 11 days.		
Reneker et al., (2017)	IG: Vestibular exercise Habituation, adaptation, oculomotor, neuromotor and balance exercises, with individualised dosage and progression Manual therapy including soft tissue release, mobilisation and/or thrust manipulations HEP of the above exercises Time: 30-60 mins, frequency: 2xweekly, duration: 4 weeks or until Medical Clearance for Return-to-Play. CG: Other physical intervention Physiotherapist provided sham, subtherapeutic and minimally progressive techniques HEP of cervical isometric, gentle cervical range of motion, vestibulo-ocular reflex, and cancellation exercises Time: 30-60 mins, frequency: 2xweekly, duration: 4 weeks or until Medical Clearance for Return-to-Play.	Primary • Post-Concussion Symptom Scale • Time to Medical Clearance for Return-to-Play	Median number of days to symptomatic recovery on the Post-Concussion Symptom Scale in the IG was 13.5 days and CG was 17 days (log-rank=0.13). The IG demonstrated a HR of 1.99 (95% CI: 0.95, 4.15) compared to the CG. Median number of days for Medical Clearance for Return-to-Play in the IG was 15.5 days and CG was 26 days (log-rank=0.18). The IG demonstrated a HR of 2.91 (95% CI: 1.01, 8.43) compared to the CG.
Rytter et al., (2019)	IG: Aerobic exercise Module 1, 12 weeks 12-14 individual sessions with a neuropsychologist (1-2 hours/week) 24 hours group psychoeducation sessions with small exercise and conversation (2 hours/week) 33 hours of individual exercise sessions with a physiotherapist (2-3 hours/week) Module 2, 10 weeks 10 individual sessions with a neuropsychologist (1 hour/week) 16 hours of group exercises and conversation (1.5 hours/week) 10.5 hours of individual exercise sessions with a physiotherapist (1 hour/week) 1 meeting with a case manager	Primary • Rivermead Post-concussion Symptoms Questionnaire	Post-intervention: Rivermead Post-concussion Symptoms Questionnaire showed a significant reduction in the IG (32.29 (14.18)) compared to the CG (37.50 (8.48)) (p=0.013, ES=0.29). Headache Impact Test showed a significant reduction in the IG (16.49 (11.29)) compared to the CG (61.73 (7.45)) (p=0.039, ES=0.38). Multidimensional Depression Inventory did not show significant difference between the IG and CG (p=0.281). Multidimensional Fatigue Inventory mental fatigue domain showed a significant reduction in the IG (65.11 (16.36) compared to the CG (72.16 (17.23) (p=0.019, ES=0.42). Short Form Health Survey role functioning/physical and social functioning domains showed a significant reduction in the IG compared to the CG (p<0.05).

	2 meetings with an existing or potential employer Exercise sessions involved riding on a stationary bike for 5-30 mins at a subthreshold level, and weight-lifting machines starting with low weights and repetitions, gradually increasing. Time: as above, frequency: as above, duration: 22 weeks. CG: Usual care Standard care through the public health system Time: not reported, frequency: not reported, duration: 22 weeks.	Secondary • Headache Impact Test • Major Depression Inventory • Multidimensional Fatigue Inventory Short Form Health Survey	6 month follow-up: Rivermead Post-concussion Symptoms Questionnaire showed a significant reduction in the IG (29.69 (12.92)) compared to the CG (35.30 (7.57)) (p=0.005, ES=0.26). Headache Impact Test showed a significant reduction in the IG (57.11 (8.99)) compared to the CG (61.77 (6.89)) (p=0.004, ES=0.68). Major Depression Inventory showed a significant reduction in the IG (13.7 (9.27)) compared to the CG (18.52 (10.29)) (p=0.008, ES=0.40). Multidimensional Fatigue Inventory general fatigue, reduced activities and mental fatigue domains demonstrated a significant reduction in the IG compared to the CG (p<0.05). Short Form Health Survey did not show a significant difference between the IG and CG (p>0.05).
Schneider et al., (2014)	IG: Vestibular exercise Habituation, gaze stabilisation, adaptation, balance, canalith repositioning, cervical neuromotor and sensorimotor retraining exercises Manual therapy of the cervical and thoracic spine CG intervention Time: not reported, frequency: 1xweekly, duration: 8 weeks or until Medical Clearance for Return-to-Play.	Primary • Medical Clearance for Return-to-Play • Sport Concussion Assessment Tool	The IG was 3.91 (95% CI: 1.34 to 11.34) times more likely to be medically cleared by 8 weeks compared to the CG. No between group differences were provided for other outcomes.
	CG: Other physical intervention Range of motion and stretching exercises Postural education Time: not reported, frequency: 1xweekly, duration: 8 weeks or until Medical Clearance for Return-to-Play.	Secondary • Balance Confidence Scale • Dizziness Handicap Index • Dynamic Visual Acuity • Head Thrust Test • Motion Sensitivity Test • Functional Gait Assessment • Cervical Flexor Endurance Joint Position Error	

HR=Heart rate HEP=Home exercise program ES=Effect size
IG=Intervention group CG=Control group

Comparison 1: physical exercise intervention versus usual care

Aerobic exercise versus usual care

All five studies assessing the effect of a physical exercise intervention on persistent symptoms, compared to usual care, used an aerobic exercise intervention (Chan et al., 2018; Dobney et al., 2020; Maerlender et al., 2015; Micay et al., 2018; Rytter et al., 2019). Only one study reported positive study findings. Utilising a 22 week aerobic and strength program a significant improvement was observed in the Rivermead Post-concussion Symptoms Questionnaire score for the intervention group compared to the usual care group (p=0.013, ES=0.29) in an adult population with injury due to mixed aetiology and over 10 days post-injury (Rytter et al., 2019).

Of the other four studies that did not find a significant effect of aerobic exercise intervention compared to usual care, two studies utilised a stationary cycling program (Maerlender et al., 2015; Micay et al., 2018). One studied a cohort aged 18 years or under who suffered a sports injury and received an 11 day intervention, initiated earlier than 10 days post-injury, and reported on the Post-Concussion Symptom Scale (Micay et al., 2018). The other studied a cohort of unreported ages, with unreported time since a sport-related injury, and an intervention of unreported duration, and reported on the Immediate Post-Concussion Assessment and Cognitive Test (Maerlender et al., 2015).

Finally, the last two studies utilised a treadmill or stationary bike based intervention in those aged 18 years or under, commencing at least 10 days post-injury (Chan et al., 2018; Dobney et al., 2020). One study only reported descriptive data for aerobic exercise compared to a delayed start usual care group at the 2 week intervention stage, 4 weeks post-injury, suggesting improvements with exercise on the Post-Concussion Symptom Inventory with no statistical analysis performed (Dobney et al., 2020). The other second study assessed the effects of a 6 week intervention, however, failed to demonstrate an interaction effect of group by time on the Post-Concussion Symptom Scale (Chan et al., 2018).

Three of the five studies provided sufficient information to be included in a meta-analysis comparing aerobic exercise to usual care (Chan et al., 2018; Maerlender et al., 2015; Rytter et al., 2019). The results demonstrated a statistically significant improvement in persistent symptoms due to the aerobic exercise (SMD -0.39, 95% CI: -0.73 to -0.05, p=0.03) when compared with usual care (Figure 3.2). The other two studies were not included in the meta-analysis because they reported data only after a follow-up period (Micay et al., 2018) or did not report mean and SD results (Dobney et al., 2020).

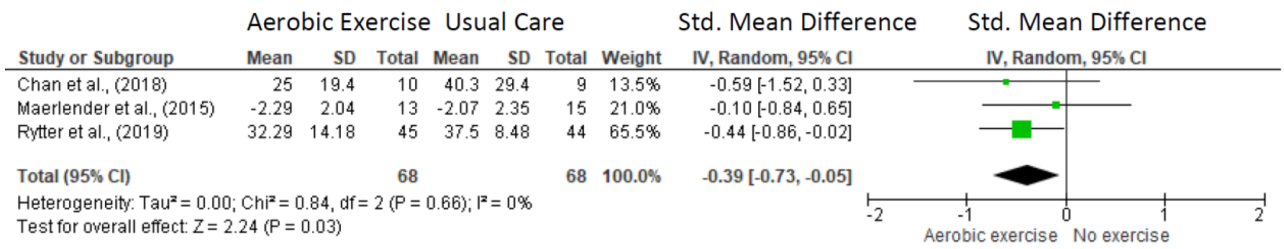

Figure 3.2 Effects of aerobic exercise on persistent symptoms

Comparison 2: physical exercise intervention versus other physical intervention

Aerobic exercise versus other physical intervention

Three studies compared the effect of aerobic exercise, on a stationary bike (Kurowski et al., 2017), treadmill (Bailey et al., 2019) or multiple modes (Leddy, Haider, Ellis, et al., 2019) with another physical intervention such as stretching or walking, on persistent symptoms. All three studies were in a population aged 18 years or under, two began the intervention more than 10 days post-injury of mixed cause (Bailey et al., 2019; Kurowski et al., 2017) and one began the intervention within 10 days of a sport-related injury (Leddy, Haider, Ellis, et al., 2019). One study continued the intervention until symptom resolution and reported a significantly shorter time to symptom resolution for the aerobic exercise group (Leddy, Haider, Ellis, et al., 2019). Two studies conducted a 6 week intervention, with the aerobic exercise group in one study having a significantly greater improvement on the Post-Concussion Symptom Scale, however, only when adjusted for baseline levels of depression (Bailey et al., 2019). The other study reported significantly greater improvements in the aerobic exercise group for the Post-Concussion Symptom Inventory immediately post-intervention, however, data were only provided for a follow-up period by which the difference was no longer significant (Kurowski et al., 2017).

Vestibular exercise versus other physical intervention

Three studies assessed the effect of vestibular exercise interventions on persistent symptoms when compared to another physical intervention (Kleffelgaard et al., 2019; Reneker et al., 2017; Schneider et al., 2014), in a mixed age group who were more than 10 days post-injury. Two studies included only people recovering from a sport-related injury (Reneker et al., 2017; Schneider et al., 2014) and one study included people with mixed aetiologies (Kleffelgaard et al., 2019). One study reported a significant between-group difference in days to symptomatic recovery, as assessed by the Post-Concussion Symptom Scale after a 4 week program, favouring the vestibular intervention group compared to a subtherapeutic sham intervention group (median: 13.5 days versus 17 days, HR=1.99) (Reneker et al., 2017). Two studies incorporating an 8 week vestibular intervention did not report any significant differences between the vestibular exercise and comparison groups on either the Sports Concussion Assessment Tool (Schneider et al., 2014) or the Rivermead Post-concussion Symptoms Questionnaire (Kleffelgaard et al., 2019).

3.3.4 Secondary study results: other clinical measures

Included studies reported on a range of secondary measures, including physical and psychological performance, quality of life, medical clearance, and other secondary outcomes.

Physical performance

One study measured the effect of an 8 week group-based vestibular exercise program compared to usual care, and demonstrated a significant between-group difference in favour of the vestibular group on the High-Level Mobility Assessment Tool (mean difference: 3.7, 95% CI: 1.4 to 6.0, p=0.002), however, did not find any significant between-group difference on the Balance Error Scoring System (Kleffelgaard et al., 2019).

Psychological performance

One study comparing the effects of a combined aerobic exercise, strength and psychoeducation intervention with usual care found a significant mean difference on the Major Depression Inventory at the 6 month follow-up period (p=0.008, ES=0.40) in favour of the intervention group (Rytter et al., 2019), whereas another study comparing the effect of an aerobic exercise program with usual care did not find any between-group differences for psychological outcomes (Chan et al., 2018). Comparing a vestibular exercise program to usual care, one study (8 weeks/2xweekly) reported no between-group difference on the Hospital Anxiety Depression Scale at post-intervention and follow-up (Kleffelgaard et al., 2019).

Quality of life

One study compared a 22 week aerobic and muscle strength program to usual care and found significant improvement on domains of the Short Form Survey post-intervention and at the 6 month follow-up (p<0.05) in favour of the aerobic exercise group (Rytter et al., 2019). Another study comparing a submaximal aerobic exercise to a usual care intervention over 6 weeks did not report any between-group differences on the Pediatric Quality of Life Multidimensional Fatigue Scale (Chan et al., 2018).

Medical clearance

One study comparing an aerobic exercise intervention to usual care reported no significant difference for Time to Medical Clearance for Return-to-Play (p=0.87) (Micay et al., 2018). Two studies compared vestibular exercise interventions to another physical intervention (Reneker et al., 2017; Schneider et al., 2014), of which the first study reported Time to Medical Clearance was 10.5 days sooner in the vestibular exercise group (median: 15.5 days) compared to the sham intervention group (median: 26 days, log-rank=0.18) (Reneker et al., 2017). The second study reported that the vestibular exercise group was 3.91 (95% CI: 1.34 to 11.34) times more likely to be medically cleared within 8 weeks compared to a stretching exercise group (Schneider et al., 2014).

Other secondary outcomes

An 8 week group-based vestibular exercise program found dizziness significantly improved on the Dizziness Handicap Inventory (mean difference: -8.7, 95% CI: -16 to -0.9, p=0.03) but not on the Vertigo Symptom Scale, when compared to usual care (Kleffelgaard et al., 2019). A study comparing a 22 week aerobic and strength program to usual care reported significant improvements on some domains on the Multidimensional Fatigue Inventory and Headache Impact Test, post-intervention and at the 6 month follow-up period (p<0.05) (Rytter et al., 2019). Lastly, a study comparing a vestibular exercise program (8 weeks/1xweekly) to a stretching intervention did not detail the between-group difference for outcomes of dizziness, vestibulo-ocular reflex, cervical proprioception, and cervical strength (Schneider et al., 2014).

3.4 Discussion

This study aimed to determine the effect of physical exercise on persistent symptoms in people with mild TBI. Physical exercise interventions in the included studies were broadly considered as aerobic or vestibular. A meta-analysis of three studies demonstrated that aerobic exercise interventions significantly improved persistent symptoms in people with mild TBI compared to usual care. A narrative analysis revealed limited evidence for the efficacy of vestibular interventions for improving persistent symptoms. Effects of aerobic and vestibular interventions on secondary clinical outcomes were unclear due to the heterogeneity of the outcome measures used.

Signs and symptoms following a mild TBI may vary considerably between individuals due to biomechanical, pathophysiological and neurobehavioural factors (Kirkwood et al., 2006; McIntyre et al., 2020). However, symptom characteristics can be subtyped into physiological, vestibulo-ocular and cervicogenic PCD (Ellis et al., 2015).

The proposed pathophysiology of physiological PCD are the alterations in cerebral blood flow and metabolism (Ellis, Leddy, et al., 2016; Leddy & Willer, 2013), resulting in symptoms such as headache, dizziness, nausea, fatigue, light and sound sensitivity, irritability and symptoms exacerbated by physical or cognitive exertion (Ellis, Leddy, et al., 2016; Ellis et al., 2015). Aerobic exercise stimulates the autonomic nervous system through increased cardiac output, cerebral blood flow, cerebral metabolism, and neuroplasticity, which improves symptoms and exercise tolerance (Leddy & Willer, 2013; Tan et al., 2014). Aerobic exercise has also been shown to increase activity of the frontal and parietal lobes, and hippocampus, therefore improve cognitive symptoms such as memory and problem solving (Colcombe et al., 2004; Erickson et al., 2009). Three studies in our review assessing the effects of aerobic exercise versus usual care were conducted in people aged 18 years or under (Chan et al., 2018; Dobney et al., 2020; Micay et al., 2018), two of which were in sporting related injuries (Chan et al., 2018; Micay et al., 2018) and two started the intervention at least 10 days post-injury (Chan et al., 2018; Dobney et al., 2020). None of the three studies demonstrated any beneficial effect of aerobic exercise on symptom recovery. Three studies comparing aerobic exercise to other physical interventions in people 18 years or younger all found that the aerobic intervention was statistically beneficial compared to light exercise involving mostly stretching (Bailey et al., 2019; Kurowski et al., 2017; Leddy, Haider, Ellis, et al., 2019) but these were significant either in time to symptom resolution (Leddy, Haider, Ellis, et al., 2019), when adjusted for depression (Bailey et al., 2019) or did not maintain a significant effect as early as one week post-intervention (Kurowski et al., 2017).

In our review, all aerobic exercise interventions used either subthreshold (exercising below symptom exacerbation) or submaximal (exercising to a percentage of the age-predicted maximum HR) intensity with treadmill running and stationary cycling being the most common modalities. Undertaking aerobic exercise at a subthreshold or submaximal intensity stresses physiological systems within the body's autoregulatory capabilities, to gradually restore autonomic control to normal. This allows people with mild TBI to experience the benefits of aerobic exercise without the exacerbation of symptoms (Ellis, Leddy, et al., 2016; Kleffelgaard et al., 2019). Aerobic exercise intervention programs of studies that reported improvement in persistent symptoms were generally of greater intensity (i.e., 80% of subthreshold HR) and longer duration (i.e., ≥6 weeks). This is supported by literature indicating that improvements from aerobic exercise are seen 6 to 8 weeks after training (Katch et al., 2014; McIntyre et al., 2020) and that too light of an aerobic intensity may not result in improvements (Garber et al., 2011). Our results further confirm this, showing relative success of aerobic exercise when compared to light exercise interventions in the short-term. While high intensity exercise may exacerbate symptoms, particularly within the first three days post-injury (Gurley et al., 2013; Lischynsky et al., 2019; Majerske et al., 2008), the studies included in our review that engaged in early exercise did not report worsening symptoms, as none of these studies implemented a vigorous aerobic exercise intervention.

The proposed pathophysiology of vestibulo-ocular PCD involves dysfunction of the vestibulo-ocular system, while cervicogenic PCD is associated with muscle trauma, inflammation, and impaired proprioception of the cervical spine. These conditions result in an array of vestibular and cervical symptoms that tend to overlap (Ellis, Leddy, et al., 2016; Ellis et al., 2015). Of the three studies applying a vestibular exercise intervention (Kleffelgaard et al., 2019; Reneker et al., 2017; Schneider et al., 2014), only one demonstrated a significant effect of the intervention after four weeks (Reneker et al., 2017) with the other two studies showing no difference between the intervention and control group after eight weeks (Kleffelgaard et al., 2019; Schneider et al., 2014). All three vestibular interventions were initiated at least 10 days post-injury (Kleffelgaard et al., 2019; Reneker et al., 2017; Schneider et al., 2014). The vestibular interventions included a combination of canalith repositioning manoeuvres, habituation, gaze stabilisation, adaptation, substitution, balance, and mobility exercises, which reintegrate and restore the somatosensory visual and vestibular systems (Ellis, Leddy, et al., 2016). The gold standard approach to vestibular rehabilitation involves identifying functional limitations and subsequently prescribing an individualised program (Herdman & Clendaniel, 2014). The addition of manual therapy for the treatment of cervical pain and cervicogenic headaches can provide additional benefits (Schneider et al., 2017). This approach was utilised in two of three studies that implemented a vestibular exercise intervention. Due to the small number of studies and variations in vestibular exercise intervention approaches, conclusions about the optimal intervention dosage and frequency could not be drawn.

In our review, time since injury ranged from less than a week to greater than six months. Only two studies (Leddy, Haider, Ellis, et al., 2019; Micay et al., 2018) started an intervention within 10 days post-injury. Both studies involved participants aged 18 years and under with a sport-related injury and employed an aerobic intervention, with one study reporting greater improvement in the intervention group compared to the control group (Leddy, Haider, Ellis, et al., 2019). Time since injury is an important factor to consider when prescribing exercise, as adults are generally expected to recover within two weeks, compared to within four weeks in children (McCrory, Meeuwisse, et al., 2017). This difference is partly due to the fact that children require two to three times greater impact force to exhibit clinical symptoms compared to adults (McCrory et al., 2004). Additionally, individuals who do not receive intervention for persistent symptoms within the first three months are at risk of developing chronic symptoms, maladaptive coping strategies, and mood disorders (Rytter et al., 2019; Schneider et al., 2017). Addressing these comorbidities and secondary problems may require additional interventions (Rabinowitz et al., 2014).

Another factor that may influence exercise prescription is the cause of injury. Six studies in the review focused on sport-related injuries (Chan et al., 2018; Leddy, Haider, Ellis, et al., 2019; Maerlender et al., 2015; Micay et al., 2018; Reneker et al., 2017; Schneider et al., 2014), with four employing aerobic exercise interventions (Chan et al., 2018; Leddy, Haider, Ellis, et al., 2019; Maerlender et al., 2015; Micay et al., 2018) and two utilising vestibular exercises (Reneker et al., 2017; Schneider et al., 2014). Sport-related injuries typically result in less physical and psychological trauma compared to other causes of mild TBI, such as vehicular accidents, falls or assaults (Rabinowitz et al., 2014), and therefore are expected to recover faster. Additionally, greater levels of aerobic fitness in athletes may play a protective role in persistent symptoms (Kontos et al., 2006).

Symptoms following a mild TBI include physical, cognitive, emotional, and psychological aspects and therefore require a multidisciplinary approach to care. In our review, three studies used a multidisciplinary approach to care (Chan et al., 2018; Kleffelgaard et al., 2019; Rytter et al., 2019), two of which reported favourable effects on persistent symptoms (Chan et al., 2018; Rytter et al., 2019). This is further supported by a systematic review indicating that individualised multidisciplinary care in an individual or group-based setting is beneficial for improving persistent symptoms, especially when psychological interventions are included (Moore et al., 2024). Although multidisciplinary interventions comprise of several intervention components, making it difficult to identify the core driver of the intervention effect (Pérez et al., 2016), it is reflective of real-life clinical practice (Brasure et al., 2013).

The studies in the review were rated as medium to high quality (Chan et al., 2018; Dobney et al., 2020; Kleffelgaard et al., 2019; Kurowski et al., 2017; Leddy, Haider, Ellis, et al., 2019; Micay et al., 2018; Reneker et al., 2017; Rytter et al., 2019; Schneider et al., 2014), except for two studies due to lacking intention-to-treat analysis and inadequate blinding (Bailey et al., 2019; Maerlender et al., 2015), indicating the individual RCTs were of good quality. When the results were pooled together for a GRADE assessment (Chan et al., 2018; Maerlender et al., 2015; Rytter et al., 2019), there was moderate certainty of evidence for aerobic exercise compared to usual care for improving persistent symptoms.

The main strength of this systematic review is the systematic and transparent method used for the identification of eligible research studies, and appraisal of study quality and reporting, as well as evidence certainty rating. Another strength of this review is the fact that it included RCTs only, without limitations based on demographic characteristics. Since the conduct of this review, multiple reviews have been published (Baker et al., 2020; Langevin et al., 2020; Miutz et al., 2022; Powell et al., 2020; Shen et al., 2021). Whilst these reviews agreed with our findings that aerobic exercise can improve persistent symptoms (Baker et al., 2020; Langevin et al., 2020; Miutz et al., 2022; Powell et al., 2020; Reid et al., 2022; Shen et al., 2021), all reviews included sport-related concussions and aerobic exercise (Baker et al., 2020; Langevin et al., 2020; Miutz et al., 2022; Powell et al., 2020; Shen et al., 2021) and one included any type of study design (Baker et al., 2020). This makes it difficult to generalise the findings of these reviews to people with other causes of injuries and receiving other types of exercise interventions.

Some limitations should be considered too. Firstly, due to the lack of a widely accepted definition of mild TBI, study populations were defined differently in all studies, which may have confounded the results, as people may have had varying severity of mild TBI. Secondly, studies generally had small sample sizes and effect sizes, however, this issue was partially addressed by the conduct of a meta-analysis for the effect of aerobic exercise on persistent symptoms. Thirdly, the heterogeneity of the outcome measures used in the individual studies hindered the completion of a meta-analysis and GRADE assessment for vestibular exercise on persistent symptoms. Lastly, intervention characteristics varied across studies making it difficult to draw conclusions with regards to optimal exercise prescription.

3.5 Conclusion

The systematic review demonstrated that the main types of physical exercise interventions used in people with mild TBI were aerobic and vestibular exercise. The results of the meta-analysis were in favour of aerobic exercise intervention compared to usual care, yet there was limited evidence for the use of vestibular exercise for improving persistent symptoms in people with mild TBI. Future studies should target the intervention to be specific to the type of disorder (i.e., physiological, vestibulo-ocular, cervicogenic PCD), presenting evidence for appropriate interventions based on the key characteristics of age (<18 years, ≥18 years), cause of injury (sport-related injury, falls, other cause of injuries) and time since injury (acute, subacute, chronic). Lastly, more robust study methodologies and the establishment of a consistent outcome measure for reporting persistent symptoms are needed to reduce risk of bias.

Preface

The findings from Chapter 3 have demonstrated symptom improvement from aerobic exercise, specifically at a subthreshold aerobic exercise level. One way to obtain this subthreshold aerobic exercise intensity is through exercise testing. However, it remains unclear whether such exercise tests are feasible for individuals with more complex injuries (i.e., those who have sustained a mild-to-moderate traumatic brain injury (TBI) from a non-sport related injury and who are older). The aim of this chapter is to '*assess the performance of the Buffalo Concussion Treadmill Test (BCTT) and Buffalo Concussion Bike Test (BCBT) in non-athletic people following a mild-to-moderate TBI'* using retrospective data from an outpatient rehabilitation service. The findings from this chapter are published in the Journal of Head Trauma Rehabilitation (Appendix 3).

Publication

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CHAPTER 4: THE BUFFALO CONCUSSION TREADMILL AND BIKE TESTS IN PEOPLE WITH MILD-TO-MODERATE TRAUMATIC BRAIN INJURY: AN EXPLORATORY CLINICAL AUDIT

4.1 Introduction

Graded physical exertion tests are used to assess physiological dysfunction (Leddy et al., 2007; Leddy & Willer, 2013) in people with mild TBI, by provoking markers of physiological dysfunction that may not be evident at rest (Ellis et al., 2015; Kozlowski et al., 2013; Leddy et al., 2011). One such graded exertion test is the BCTT, or the alternative BCBT, during which individuals are asked to complete an incremental exercise test until symptom exacerbation or maximum exertion (Ellis et al., 2015). These tests, which have shown to be a safe and reliable way of assessing physiological dysfunction in people following a mild TBI, can be used to differentiate physiological dysfunction from other diagnoses, to quantify severity, and guide prescription of aerobic exercise (Leddy & Willer, 2013; Leslie & Craton, 2013). Individuals who can exercise to 85-90% of their age-predicted maximum heart rate (HR) without exacerbation of their symptoms are thought to be less likely to have a physiological cause compared to individuals who are limited by symptoms in reaching this HR (Leddy & Willer, 2013).

Although most people with mild TBI recover within four weeks, 10% to 30% of individuals experience persistent symptoms beyond this time (Babcock et al., 2013; McCrory et al., 2013). Post-Concussion Syndrome (PCS) is a widely accepted term used to describe a set of non-specific symptoms reported following a mild TBI, which persists beyond the expected timeframe of recovery (Broshek et al., 2015). Ellis and colleagues (2015) have categorised PCS by pathophysiology, symptom presentation and physical exam findings broadly into physiological, vestibulo-ocular or cervicogenic post-concussion disorders (PCDs), and to a lesser degree, post-traumatic mood disorders or migraine headache type PCDs, recognising however that other PCDs and disorders may overlap (Ellis et al., 2015). There has been a debate as to whether “PCS” is a true syndrome or disorder (Iverson & Lange, 2011).

Most studies utilising the BCTT or BCBT have been conducted for return-to-sport purposes in young and athletic study populations with acute mild TBI (Chrisman et al., 2019; Haider, Johnson, et al., 2019; Haider, Leddy, et al., 2019; Leddy, Haider, Ellis, et al., 2019; Leddy, Haider, Hinds, et al., 2019). This makes it challenging to generalise the findings of these studies to older or non-athletic individuals, or to those with a non-acute mild TBI. It is unclear if people with a mild TBI in the general population can safely undertake a graded exercise test, and if the test can in turn be used to identify physiological dysfunction.

To address this gap in the literature, this study will present BCTT and BCBT data from a rehabilitation outpatient clinic providing multidisciplinary services to individuals who have experienced a mild TBI. Within this clinic, the principles of graded exercise testing to prescribe rehabilitation exercises to people with mild TBI were followed irrespective of the cause of injury or base fitness levels. A clinical audit was conducted to assess performance on the BCTT or BCBT in this non-athletic clinical population. The objectives were to: 1) explore performance outcomes on the BCTT or BCBT; 2) describe the differences in patient demographics and performance outcomes on the BCTT or BCBT between patients who terminated the test due to symptom exacerbation and patients who terminated the test due to other reasons; and 3) explore the relationships between self-reported symptoms post-TBI, and performance outcomes on the BCTT or BCBT.

4.2 Methods

4.2.1 Study design

A retrospective clinical audit methodology was adopted that involved review of clinical notes of patients with mild-to-moderate TBI attending the Early Management of Mild Brain Injury Rehabilitation Service (EMMBIRS), of the South Australia Brain Injury Rehabilitation Service (SABIRS) between the years 2018 to 2020. EMMBIRS provided interdisciplinary rehabilitation services, for up to six months, to individuals following a mild or moderate TBI. Services included physiotherapy, occupational therapy, social work, psychology, speech pathology and a medical specialist review. EMMBIRS received direct referrals from a range of settings such as hospitals, medical and allied health clinics, and services, as well as indirect referrals through the SABIRS' pre-existing Concussion Clinic, a transdisciplinary phone rehabilitation service providing telephone assessment, education, information, and strategy support.

4.2.2 Buffalo Concussion Treadmill or Bike Test protocol

In EMMBIRS, the BCTT or BCBT were routinely conducted to test for physiological dysfunction following a mild-to-moderate TBI and to guide aerobic exercise prescription. The treating clinician deemed patients eligible for the BCTT or BCBT if they, 1) did not have contraindications to exercise testing according to the American Heart Association guidelines, 2) had precautions to exercise testing (Gibbons et al., 1997) and were cleared by the medical specialist and 3) consented to completing the test.

The BCTT was primarily conducted to avoid leg fatigue, however, the BCBT was completed if patients had significant orthopaedic, balance or vestibular issues that limited their ability to safely exercise on a treadmill, or the patient had a strong preference for the bike test. The treating clinician followed the protocol by Leddy and colleagues for both the BCTT (Leddy et al., 2020b) and BCBT (Leddy et al., 2020a).

Buffalo Concussion Treadmill Test

The starting setting for the BCTT was 3.2 mph (5.1 km/h) for patients up to 5'10" (165 cm) and 3.6 mph (5.8 km/h) for patients 5'10" (165 cm) and above at 0% incline. After each minute, the treadmill was increased by 1% incline until 15% was reached. When 15 minutes was reached, the speed was increased by 0.4 mph (0.6 km/h) for each minute until test termination. After the termination of the test, patients continued the on the treadmill for an additional 2 minutes at 2.5 mph (4.0 km/h) and 0% incline for a cool-down. Starting speed, increment increase, and speed increase was adjusted at the discretion of the treating clinician to suit the patient's athletic status, height, and comfort, taking into consideration their safety.

Buffalo Concussion Bike Test

When performing the BCBT, patients were instructed to pedal at a rate of 60±5 repetitions per minute with no resistance. After two minutes, the power output was increased by one stage (one stage every two minutes) until test termination. The power output at each stage was dependent on the weight of the patient. The power output was higher for heavier patients and for each successive stage. After the termination of the test, the power output was reduced to no resistance for a 2 minute cool-down at approximately 30 repetitions per minute.

For both the Buffalo Concussion Treadmill or Bike Test

For both versions of the test, self-reported subjective measures of effort and symptoms were recorded at each minute during the test using the Borg Rating of Perceived Exertion (RPE) and Visual Analogue Scale (VAS) respectively. The Borg RPE, a valid and reliable psycho-physical tool assesses and monitors subjective perception of effort during exercise, has a scale of 6-20 with higher scores indicating greater RPE (Chen et al., 2002; Scherr et al., 2013). The VAS, a valid and reliable Likert scale, measures the patient's overall symptom severity on a scale of 0-10 with higher scores indicating greater symptom severity (Kahl & Cleland, 2005).

The test was terminated due to either (1) the patient experiencing symptom exacerbation (defined as a 3-point or greater increase in the symptom severity scale for patients with ≤5/10 for baseline VAS or a 1-point increase for those who rated >5/10 on the scale prior to test commencement), or (2) other reasons including reporting an exertion level of ≥19/20 on the Borg RPE; reaching ≥90% of their age-predicted maximum HR; or the patient wishing to stop. The test was also terminated if the treating clinician deemed continuing a health risk to the patient.

4.2.3 Data collection

Data extracted from the clinical notes included demographic information (i.e., age and gender), brain injury specific information (i.e., cause of injury, time since injury, scan changes, post-traumatic amnesia, loss of consciousness, and Glasgow Coma Scale), and demographic information (i.e., history of a TBI, history of psychological condition, and past medical history). Self-reported depression, anxiety, stress, and severity of symptoms, as scored with the Depression Anxiety Stress Scale (DASS) and Rivermead Post-Concussion Symptoms Questionnaire (RPSQ), were also recorded. The DASS is a valid and reliable measure of mental health, contains domains of depression, anxiety and stress, and rates items on a 4-point scale (0-3) with higher scores indicating greater mental health severity (Brown et al., 1997; Henry & Crawford, 2005; Lovibond & Lovibond, 1995). The RPSQ, is a valid and reliable measure of post-concussion symptoms, has domains of 'early symptom clusters' and 'late symptom clusters', and consists of 16 post-concussion symptom items rated on a 5-point scale (0-4) with higher scores indicating greater symptom severity (Eyres et al., 2005; King et al., 1995; Potter et al., 2006).

Performance outcomes on the BCTT or BCBT including HR (resting and threshold), Borg RPE (resting and termination), symptom severity on the VAS (resting and termination), reason for test termination and test duration were also collected.

4.2.4 Statistical analysis

Data were extracted according to an Excel proforma. All statistical analysis was performed using IBM SPSS Statistics 25. Descriptive summary statistics were presented as mean (SD) for data that were normally distributed, as frequency (%) for categorical data, and as median (IQR) for ordinal data and descriptive data that were not normally distributed.

Participant data were grouped according to their reason for test termination (i.e., due to symptom exacerbation or for other reasons), test modality (i.e., BCTT or BCBT) and history of mental health (i.e., those who had a history of a psychological condition or those who did not). Independent sample t-tests were performed to determine differences in performance outcomes for patients who undertook the BCTT versus patients who undertook BCBT, and patients who reported a history of mental health versus patients who did not for data that were normally distributed. For data that were not normally distributed, a Welch's t-test was used.

Bivariate correlations were undertaken to assess the relationship between Borg RPE and threshold HR. The relationship between outcomes on the self-reported measures (RPSQ and DASS) and BCTT or BCBT performance outcomes was also assessed, controlling for time since injury with alpha corrected to 0.01 due to multiple comparisons.

4.3 Results

4.3.1 Patient demographics

Demographic and clinical data of all 49 patients who attended the clinic between 2018 and 2020 were reviewed and analysed. Patients' mean (SD) age was 33.7 (13.0) years, 29 (59.2%) were males, and the mean (SD) time since injury was 56.2 (36.4) days which is considered chronic. Most patients had post-traumatic amnesia for <24 hours (41.7%), loss of consciousness for ≤30 minutes (45.2%), and a Glasgow Coma Score of 13-15, indicative of a mild TBI (95.4%). Brain scan results were normal for most patients (63.0%). Fourteen (28.6%) patients reported a history of TBI and 26 (53.1%) reported having at least one past medical condition, of which 16 (32.7%) reported having a psychological condition of either anxiety or depression.

Baseline RPSQ early symptom (mean (SD): 4.7 (2.7)) and late symptom (mean (SD): 21.0 (10.3)) clusters scores revealed that participants experienced various post-concussion symptoms up to a moderate severity. Early symptom clusters scores were associated with headaches, dizziness, nausea and/or vomiting, whereas late symptom clusters score was associated with impact on participation, psychosocial functioning, and lifestyle. For the DASS domains, depression was rated as mild (mean (SD) :12.6 (12.4)), anxiety as moderate (mean (SD): 11.8 (10.5)) and stress as mild (mean (SD): 17.3 (12.1)). Further patient demographics are presented in Table 4.1.

Table 4.1 Patient demographics

Patient demographics	n	Results for all participants	n	Results of patients who terminated the test due to symptom exacerbation	n	Results of patients who terminated the test due to other reasons
Age (years), mean±SD (range)	49	33.7±13.0 (16-63)	14	34.8±11.7 (19-55)	35	33.3±13.7 (16-63)
Gender, n (%) • Male • Female	49	 29 (59.2) 20 (40.8)	14	 6 (42.9) 8 (57.1)	35	 23 (65.7) 12 (34.3)
Cause of injury, n (%) • Motor vehicle accident • Motor bike accident • Cycling accident • Other sports • Pedestrian hit by motor vehicle	49	 20 (40.8) 8 (16.3) 13 (26.5) 4 (8.2) 4 (8.2)	14	 6 (42.9) 3 (21.4) 1 (7.1) 2 (14.3) 2 (14.3)	35	 14 (40.0) 5 (14.3) 12 (34.3) 2 (5.7) 2 (5.7)
History of TBI, n (%) • Yes • No	49	 14 (28.6) 35 (71.4)	14	 4 (28.6) 10 (71.4)	35	 10 (28.6) 25 (71.4)
History of psychological condition, n (%) • Yes • No	49	 16 (32.7) 33 (67.3)	14	 3 (21.4) 11 (78.6)	35	 13 (37.1) 22 (62.9)
Past medical history, n – patients may have reported on more than one • Nil • Psychological condition • Vestibular condition • Musculoskeletal condition • Neurological condition • Other medical condition	49	 23 (46.9) 16 (32.7) 2 (4.1) 5 (10.2) 4 (8.2) 7 (14.3)	14	 9 (64.3) 3 (21.4) 0 (0.0) 2 (14.3) 0 (0.0) 3 (21.4)	35	 14 (40.0) 13 (37.1) 2 (5.7) 3 (8.6) 4 (11.4) 4 (11.4)
Time since injury (days), mean±SD (range)	49	56.2±36.4 (14-211)	14	71.1±55.1 (22-211)	35	49.9±23.7 (14-113)
Scan changes, n (%) • Yes • No	46	 17 (37.0) 29 (63.0)	13	 4 (30.8) 9 (69.2)	33	 13 (39.4) 20 (60.6)
Post-traumatic amnesia, n (%) • Nil • <24 hours • 1-7 days • >1 week	49	 13 (27.1) 20 (41.7) 13 (27.1) 2 (4.2)	13	 4 (30.8) 7 (53.8) 2 (15.4) 0 (0.0)	35	 9 (25.7) 13 (37.1) 11 (31.4) 2 (5.7)
Loss of consciousness, n (%) • Nil	42	 15 (35.7)	11	 3 (27.3)	31	 12 (38.7)

• Yes, but unknown • Yes, ≤30 minutes		8 (19.0) 19 (45.2)		2 (18.2) 6 (54.5)		6 (19.4) 13 (41.9)
Glasgow Coma Score, n (%) • 15 • 14 • 13 • 10 • 8	44	 35 (79.5) 6 (13.6) 1 (2.3) 1 (2.3) 1 (2.3)	12	 9 (75.0) 2 (16.7) 0 (0.0) 0 (0.0) 1 (8.3)	32	 26 (81.3) 4 (12.5) 1 (3.1) 1 (3.1) 0 (0.0)
Self-reported measures • RPSQ, mean±SD (range) ○ Early symptom clusters (0-12) ○ Late symptom clusters (0-52) • DASS (0-63), mean±SD (range) ○ Depression (0-21) ○ Anxiety (0-21) ○ Stress (0-21)	 49 47	 4.7±2.7 (0-11) 21.0±10.3 (1-46) 12.6±12.4 (0-42) 11.8±10.5 (0-38) 17.3±12.1 (0-42)	 14 13	 5.7±2.5 (2-11) 28.4±10.0 (18-46) 8.2±7.6 (1-21) 6.9±6.2 (1-19) 9.7±6.8 (0-21)	 35 34	 4.3±2.8 (0-11) 18.0±9.0 (1-34) 5.6±5.6 (0-21) 5.5±4.8 (0-18) 8.4±5.8 (0-19)
Reported symptoms pre-BCTT or BCBT, n – patients may have reported on more than one • Nil • Dizziness, light headedness • Haziness, fogginess • Headache, pressure around head • Fatigue • Musculoskeletal pain • Balance dysfunction • Visual dysfunction • Nausea	49	 15 (30.6) 11 (22.4) 3 (6.1) 29 (40.8) 8 (16.3) 6 (12.2) 1 (2.0) 2 (4.1) 2 (4.1)	14	 1 (7.1) 5 (35.7) 1 (7.1) 7 (50.0) 3 (21.4) 1 (7.1) 1 (7.1) 1 (7.1) 2 (14.3)	35	 14 (40.0) 6 (17.1) 2 (5.7) 13 (37.1) 5 (14.3) 5 (14.3) 0 (0.0) 1 (2.9) 0 (0.0)

BCBT=Buffalo Concussion Bike Test
BCTT=Buffalo Concussion Treadmill Test
DASS=Depression, Anxiety and Stress Scales
RPSQ=Rivermead Post-Concussion Symptoms Questionnaire
TBI=Traumatic brain injury

4.3.2 Performance outcomes

Forty-two out of 49 patients completed the BCTT, the remaining seven completed the BCBT. No adverse events were documented. On average, patients lasted 11.9 (5.3) minutes on the test and rated their highest perceived exertion at test termination as 15.8 (3.0), classified as 'hard' on the Borg RPE scale. Patients' mean (SD) resting HR was 79.3 (9.1) beats per minute (bpm), which increased to 148.0 (23.6) bpm at test termination, reaching 79.7% (13.5%) of the age-predicted maximum HR. On average, baseline symptom severity, as measured with the VAS, was 1.4 (1.7) points and increased to 2.6 (2.2) points at test termination, indicative of mild symptom exacerbation. Headache/pressure around the head was the most frequently reported symptom (40.8%).

Significant differences in performance outcomes were observed between those who terminated the test due to symptom exacerbation (n=14) and those who terminated the test due to other reasons (n=35). Compared to those who terminated the test due to other reasons, individuals who terminated the test due to symptom exacerbation, on average scored 2.8-points (95% CI: 1.9 to 3.8, p=0.01) higher on the VAS for symptom severity at test termination, reached an 11.1% (95% CI -18.5 to -3.6, p=0.01) lower age-predicted threshold HR, had a 3.3-point (95% CI: -4.8 to -1.8, p=0.01) lower Borg RPE rating at test termination, and completed the test with a 5.6 minute (95% CI: -8.5 to 2.8, p=0.01) shorter test duration. Performance outcomes of the BCTT and BCBT are presented in Table 4.2.

The reasons for test termination and average test duration times are presented in Table 4.3. Fourteen (28.6%) patients stopped due to symptom exacerbation and 35 (71.4%) stopped for other reasons. Of the 14 patients that stopped due to symptom exacerbation, 12 stopped due to a ≥3-point increase in symptom severity on the VAS. Two patients who rated at least a 5 or greater on the scale prior to test commencement stopped due to a 1-point increase. The shortest average test duration (4.0±0.1 minutes) was observed in those patients who had a VAS at baseline was >5/10 and terminated the test upon a 1-point increase, as per protocol. This was followed by patients unwilling to continue due to unrelated symptoms such as musculoskeletal pain and leg fatigue (9.2±6.1 minutes). Nine patients terminated the test due to reaching 90% of their age-predicted maximum HR (14.0±4.0 minutes), of which 3 experienced symptom exacerbation during the test but not sufficient to warrant test termination (i.e., less than 3-point change for ≤5/10 baseline VAS or 1-point change for >5/10 baseline VAS). Patients whose test was terminated by the therapist (deeming continuing a health risk) had the longest average test duration (18.0±2.8 minutes).

Six of the seven patients who completed the BCBT terminated the test due to reaching 90% of age-predicted maximum HR, while the remaining patient terminated due to reporting ≥19/20 on the Borg RPE. There were significant differences between the BCTT and BCBT groups for both threshold HR and age-predicted threshold HR with higher HRs observed in the BCBT group (p<0.05). There were also significant differences in both resting and termination VAS scores with higher scores in the BCTT compared to BCBT group (p<0.05). Differences in performance outcomes between the BCTT and BCBT are presented in Table 4.4.

A significant difference was observed between patients who reported a history of a psychological condition and those who did not, where patients who reported a history of a psychological condition reported 1.1-points (95% CI: -0.12 to 2.07, p=0.03) higher for baseline initial symptom severity on the VAS.

No significant relationship was found between threshold HR and Borg RPE at test termination (r=0.37, p=0.19) in patients who terminated the test due to symptom exacerbation. However, in patients who terminated the test due to other reasons (such as reporting ≥19/20 on the Borg RPE, reaching ≥90% of age-predicted maximum HR, patient unwilling to continue due to unrelated symptoms, and therapist perceived safety), analysis revealed a significant moderate relationship between threshold HR and Borg RPE at test termination (r=0.38, p=0.02), where an increase in Borg RPE was associated with an increase in threshold HR.

When exploring the relationship between baseline RPSQ scores and test performance outcomes, and baseline DASS scores and test performance outcomes, a shorter test duration was associated with higher scores on both self-reported depression (r=-0.41, p<0.01) and late symptom clusters on the RPSQ (r=-0.40, p<0.01). Higher self-reported depression was also associated with a higher score on the VAS for symptom severity (r=0.41, p<0.01) as seen in Table 4.5.

Table 4.2 Performance outcomes on the BCTT and BCBT

Outcomes	n	Results for all participants	n	Results for patients who terminated the test due to symptom exacerbation	n	Results for patients who terminated the test due to other reasons	Mean difference (95% CI), p-value
Test duration (mins), mean±SD (range)	46	11.9±5.3 (2-20)	13	8.1±4.5 (3-16)	33	14.0±4.7 (5-20)	-5.6 (95% CI: -8.5 to 2.8) p=0.01
Borg RPE (/20), mean±SD (range)	49	15.8±3.0 (9-19.5)	14	13.4±2.2 (11-17)	35	17.0±2.5 (12-20)	-3.3 (95% CI: -4.8 to -1.8), p=0.01
HR (bpm), mean±SD (range)							
• Rest	47	79.3±9.1 (62-93)	12	78.6±9.8 (63-85)	35	79.8±8.8 (61-96)	-0.3 (95% CI: -6.0 to 5.4), p=0.91
• Threshold	49	148.0±23.6 (100-185)	14	135.5±25.8 (107-185)	35	154.6±19.6 (110-177)	-19.1 (95% CI: -32.2 to -5.9), p=0.01
Age-predicted HR (%), mean±SD (range)							
• Rest	47	42.6±5.7 (30-56)	12	42.3±6.1 (37-52)	35	42.8±5.6 (30-56)	-0.4 (95% CI: -4.3 to 3.4), p=0.81
• Threshold	49	79.7±13.5 (53-111)	14	72.9±12.4 (58-92)	35	83.3±12.8 (59-109)	-11.1 (95% CI: -18.5 to -3.6), p=0.01
VAS of symptoms, mean±SD (range)							
• Rest	47	1.4±1.7 (0-7)	14	2.1±2.1 (0-7)	35	1.1±1.2 (0-2)	0.9 (95% CI: -0.3 to 2.0), p=0.12
• Termination	49	2.6±2.2 (0-8)	14	4.7±1.4 (3-8)	35	1.5±1.6 (0-4)	2.8 (95% CI: 1.9 to 3.8), p=0.01

BPM=Beats per minute
HR=Heart rate
RPE=Rating of Perceived Exertion
VAS=Visual Analogue Scale

Table 4.3 Reasons for test termination

Reason for test termination, n (%)	n (%)	Test duration (mins)
Patients who terminated the test due to symptom exacerbation		
• ≥3-points increase on the VAS for patients who rated ≤5/10	12 (24.5)	9.7±4.3 (3-16)
• 1-point increase on the VAS for patients who rated >5/10	2 (4.1)	4.0±0.1 (4-4)
Patients who terminated the test due to other reasons		
• Reporting ≥19/20 on the Borg RPE	14 (28.6)	14.5±4.4 (5-19)
• Reaching ≥90% of age-predicted maximum HR	9 (18.4)	14.0±4.0 (7-18)
• Patient unwilling to due to unrelated symptoms such as musculoskeletal pain and leg fatigue	10 (20.4)	9.2±6.1 (7-20)
• Therapist ceased due to perceived safety	2 (4.1)	18.0±2.8 (16-20)

HR=Heart rate
RPE=Rating of Perceived Exertion
VAS=Visual Analogue Scale

Table 4.4 Differences in performance outcomes between the BCTT and BCBT

Outcomes	n	Results for people who undertook the BCTT	n	Results for people who undertook the BCBT	Mean difference (95% CI), p-value
Test duration (mins), mean±SD (range)	40	11.7±5.5	6	13.3±3.8	-1.6 (95% CI: -5.7 to 2.4, p=0.4)
Borg RPE (/20), mean±SD (range)	42	15.7±3.1	7	16.1±2.2	-0.5 (95% CI: -2.6 to 1.7, p=0.6)
HR (bpm), mean±SD (range)					
• Rest	40	78.6±8.7	7	83.7±10.5	-5.1 (95% CI: -15.0 to 4.7, p=0.3)
• Threshold	42	145.3±23.8	7	164.1±15.0	-18.8 (95% CI: -33.6 to -4.1, p=0.02)
Age-predicted HR (%), mean±SD (range)					
• Rest	40	41.8±5.1	7	47.7±6.4	-6.0 (95% CI: -12.0 to 0.05, p=0.05)
• Threshold	42	77.4±12.6	7	93.6±10.3	-16.2 (95% CI: -25.9 to -6.4, p=0.004)
VAS of symptoms, mean±SD (range)					
• Rest	42	1.6±1.7	7	0.3±0.5	1.3 (95% CI: 0.6 to 1.9, p<0.001)
• Termination	42	3.0±2.1	7	0.6±0.9	2.3 (95% CI: 1.3 to 3.4, p<0.001)
Patients who terminated the test due to symptom exacerbation, n (%)	42		7		
• ≥3-points increase on the VAS for patients who rated ≤5/10		12 (28.6)		0 (0.0)	
• 1-point increase on the VAS for patients who rated >5/10		2 (4.8)		0 (0.0)	
Patients who terminated the test due to other reasons, n (%)					
• Reporting ≥19/20 on the Borg RPE		13 (31.0)		1 (14.3)	
• Reaching ≥90% of age-predicted maximum HR		3 (7.1)		6 (85.7)	
• Patient unwilling to due to unrelated symptoms such as musculoskeletal pain and leg fatigue		10 (23.8)		0 (0.0)	
• Therapist ceased due to perceived safety		2 (4.8)		0 (0.0)	

BCBT=Buffalo Concussion Bike Test
BCTT=Buffalo Concussion Treadmill Test
BPM=Beats per minute
HR=Heart rate
RPE=Rating of Perceived Exertion
VAS=Visual Analogue Scale

Table 4.5 Correlations between the RPSQ, DASS and performance outcomes on the BCTT and BCBT

	Resting HR (bpm)	**Age-predicted threshold HR (%)**	**Termination Borg RPE**	**Resting VAS**	**Termination VAS**	**Test duration (mins)**
RPSQ early symptom clusters	-0.11	-0.16	-0.13	0.35	0.29	-0.05
RPSQ late symptom clusters	0.15	-0.30	-0.16	0.38	0.38	-0.40*
DASS depression	0.10	-0.17	-0.03	0.31	0.41*	-0.41*
DASS anxiety	0.25	-0.36	-0.07	0.31	0.31	-0.37
DASS stress	0.13	-0.19	0.12	0.36	0.33	-0.28

BPM=Beats per minute
DASS=Depression, Anxiety and Stress Scales
HR=Heart rate
RPE=Rating of Perceived Exertion
RPSQ=Rivermead Post-Concussion Symptoms Questionnaire
*P<0.01

4.4 Discussion

This study retrospectively reviewed the BCTT and BCBT performance of 49 patients with mild-to-moderate TBI attending a multidisciplinary rehabilitation service. Fourteen patients stopped the test due to symptom exacerbation. Of those who stopped the test for other reasons, 23 reached maximum exercise thresholds as defined by either maximum HR or RPE. No relationship between HR and RPE was observed in those who stopped due to symptom exacerbation. Regardless of the reason for stopping, baseline post-concussion symptom severity, and depression and anxiety levels were negatively associated with test performance, including increased symptom severity, test termination at a lower HR, and shorter test duration. No adverse events were documented, indicating the test is safe in the clinical setting.

In the present study, 14 of 49 patients stopped the test due to symptom exacerbation, similar to previous study results which showed that symptom exacerbation was observed before maximum exercise thresholds were reached in people with mild TBI (Chizuk et al., 2021; Morissette et al., 2020; Rutschmann et al., 2021). The most common symptom reported was headache or pressure around the head, which is consistent with previous studies (Graham et al., 2021; Leddy et al., 2011). Patients who report an increase in symptoms during the test, preventing them from exercising to their age-predicted maximum HR, are more likely to have physiological PCD than those who can exercise to their age-predicted maximum (Ellis et al., 2015; Kozlowski et al., 2013; Leddy & Willer, 2013). While our study evaluated a single BCTT or BCBT performance, the test can be used to reassess physiological recovery, with physiological resolution being defined as the ability to exercise at 85-90% of age-predicted maximum HR without symptom exacerbation for 20 minutes (Leddy et al., 2010). Comparison of HR at the point of symptom exacerbation to the individual's age-predicted maximum HR provides an indication of how close an individual is to physiological recovery (Leddy et al., 2011). Multiple studies have found that individuals with physiological PCD tend to reach 5-15 minutes on the test, compared to those with a vestibulo-ocular or cervicogenic PCD or healthy participants that were able to exercise for 15-25 minutes without symptom exacerbation (Ellis, Leddy, et al., 2016; Kozlowski et al., 2013). This was supported by our study, which found that patients who terminated the test due to symptom exacerbation had a 5.6 minute shorter test duration compared to patients who terminated due to other reasons.

In our study, patients that completed the BCBT reported significantly less symptom severity at baseline and test termination, which may explain why none of the patients in the BCBT group terminated the test due to symptom exacerbation and on average reached 90% of their age-predicted maximum HR. The BCBT was used for patients who experienced significant vestibular or orthopaedic issues, preventing them from undertaking the BCTT safely, or if the patient had a strong preference for the BCBT. This finding may also be attributed to the treadmill version challenging the vestibular system and exacerbating symptoms more than the bike version (Graham et al., 2021).

The latest consensus statement on concussion in sport recommends that after a brief period of relative rest up to 48 hours after injury, people with mild TBI should gradually return to activity such as work, school or sport (McCrory, Meeuwisse, et al., 2017; Patricios et al., 2023). Prolonged rest can reduce cerebral blood flow, exacerbating physiological PCD, and which is associated with persisting symptoms (Albalawi et al., 2017; Ellis et al., 2015; Esterov & Greenwald, 2017). For patients who stopped exercising due to symptom exacerbation, the HR achieved at test termination can be used to prescribe individualised subthreshold aerobic exercise (Ellis et al., 2015; Leddy, Haider, Ellis, et al., 2019; Leddy, Haider, Hinds, et al., 2019). The most used protocol involves prescription of aerobic exercise at 80-90% (Leddy et al., 2021) of threshold HR for 20 minutes, 5 to 6 days per week (McIntyre et al., 2020). However the frequency, intensity (training HR), and duration of the exercise sessions can be modified according to individual tolerance and to the degree of symptom exacerbation experienced during the exercise bouts (Leddy et al., 2016; Leddy & Willer, 2013). Systematic reviews have found that exercise at a subthreshold level is beneficial for improving persistent symptoms after a mild TBI (Lal et al., 2018; Langevin et al., 2020; Vuu et al., 2022) by increasing cardiac output, cerebral blood flow, cerebral vasodilation, brain metabolism and overall autonomic function (Secher et al., 2008; Smith & Ainslie, 2017). Patients who stop a treadmill or cycle test early should be prescribed exercise treatment at 80% to 90% of the intensity (HR threshold) at which they terminated exercise due to symptom exacerbation. Subthreshold aerobic exercise can be combined with other interventions to ensure multiple symptoms are addressed (Bailey et al., 2019; Ellis, Leddy, et al., 2016).

Subjective symptom reporting is the most common method of measuring recovery following a TBI (Kozlowski et al., 2013), however the validity and reliability of self-reported measures has been questioned (van der Scheer et al., 2018). The importance of this was highlighted in our results, as no relationship was observed between RPE and threshold HR for patients who terminated the test due to symptom exacerbation, unlike patients who terminated the test due to other reasons. Patients who terminate the test due to symptom exacerbation may therefore be unable to accurately perceive their level of exertion, which is consistent with a prior observation (Hinds et al., 2016). Graded exercise testing, such as the BCTT and BCBT incorporates objective physiological measures meaning there is not a sole reliance on subjective symptom reporting alone (Kozlowski et al., 2013). The results of our study indicate the importance of using a graded exercise test to assess the degree of exercise tolerance by determining the symptom-limited exercise intensity. This approach allows for individualised subsymptom exacerbation threshold exercise prescriptions, which if repeated may be used to monitor physiological recovery (Leddy & Willer, 2013). Completing the test does not guarantee recovery is complete, only that the physiological dysfunction is no longer an issue. Completion of the test with some symptoms means that there are issues (i.e., ongoing dysfunction of the cervicogenic or vestibulo-ocular subsystems) (Ellis et al., 2015) that require further clinical investigations. In our study, differential diagnosis was not undertaken, however, of the nine patients who terminated the test due to reaching 90% of their age-predicted HR, three experienced symptom exacerbation during the test, four had a history of a psychological condition and two had a history of a neurological condition. By using the BCTT or BCBT in conjunction with other tests, differential diagnosis can be achieved (Ellis et al., 2015).

In our study, 71% of patients terminated the test due to reasons other than symptom exacerbation, as recorded by the treating clinician. One such reason for test termination was musculoskeletal or leg pain deemed unrelated to symptoms previously reported by the patient. Mean test duration for those stopping due to non-symptom related pain was 9.2 minutes, comparable to the 8.1 minutes for patients who terminated the test due to symptom exacerbation. The shortest test duration was observed in those who increased in symptoms by 1/10 on the VAS for those who had a resting VAS of 5/10 or greater. This is to be expected due to the lower relative change acceptable before terminating the test. Of the 10 patients who stopped due to a non-symptom related change, two had a history of a musculoskeletal injury but whether this was due to the TBI itself or not is unknown. As expected, patients who terminated the test due to reporting ≥19/20 on Borg RPE, or ≥90% of age-predicted maximum HR, had comparable test durations of 14.5 and 14.0 minutes respectively. Notably, patients who ceased the test due to therapist perceived safety issues had an average test duration of 18 minutes, similar to that seen in the athletic population (Rutschmann et al., 2021). One potential explanation is that this subgroup of patients may have been significantly fitter. However, as they did not reach HR or Borg RPE limits, it may instead have been indicative of autonomic dysfunction. As the HR response was not representative of the intensity of exercise being performed, these patients who terminated exercise for other reasons may in fact have displayed symptomatic responses to exercise testing and been unable to accurately perceive exertion. Our study results showed that whilst there was no relationship between maximum HR and RPE for those who stopped due to symptom exacerbation, a significant moderate relationship ($r=0.38$ $p=0.02$) existed for those who stopped due to other reasons. Whilst it is expected to see a relationship between HR and RPE, perceived exertion should more closely represent actual physical effort, and thus it appears that for some participants there may have been a disconnect between the two measures. It is likely that for those who stopped for other reasons, some were not recognised as symptom related, whereas others stopped due to genuinely reaching peak performance levels but may not have reported a peak effort. Further work is needed to identify symptom-related reasons for termination of exercise testing, to ensure the correct support and advice is provided to patients regarding their recovery post-mild TBI.

One limitation of the clinical use of the BCTT or BCBT in people with mild TBI is that the clinical manifestations of PCD and mood disorders overlap (Ellis et al., 2015). Autonomic nervous system dysfunction occurs in psychological conditions such as anxiety, depression, schizophrenia, panic disorders, cognitive impairment, and sleep disturbances (Alvares et al., 2016; Purkayastha et al., 2019). This is supported by a study that exposed patients with mild TBI to a stressful condition involving challenging cognitive tasks found that their symptom reports and autonomic arousal increased (Hanna-Pladdy et al., 2001). In our study, we found that patients who reported a history of a mental health condition, and higher self-reported depression scores at admission to the clinic, also reported increased symptom severity, resulting in shorter test duration. This is consistent with the literature reporting that people with psychological conditions tend to catastrophise pain (Gilliam et al., 2019), considering a history of a psychological condition as a risk factor for developing chronic pain following a mild TBI (Lavigne et al., 2015). When testing and prescribing exercise intervention in people with mild TBI, consideration should be given to the impact of existing psychological conditions on symptoms experienced during the test and the implications for exercise prescription.

This study has several limitations that should be acknowledged. The first is the retrospective nature of the study. Only full clinical data sets could be included in the analysis, and the clinical judgement of reasons for test termination may have impacted the data grouping and subsequent analysis. Secondly, the physical fitness of the patients prior to mild TBI was not assessed. Assumptions were made that the population in the study was not as physically fit as the athletic population studied in much of the literature, making comparison to published data difficult. Thirdly, differential diagnosis was not undertaken to determine if patients were experiencing a subtype of a PCD, and future studies should consider including this data to help guide clinical decision-making when using the BCTT and BCBT. Additionally, there were unequal group sizes between the BCTT and BCBT groups for comparison of performance outcomes. Although this was partially addressed by the conduct of a Welch's t-test for data that were not normally distributed, type 1 error may have occurred due to the small sample size. Finally, the extent and impact of other contributing factors to performance on the BCTT or BCBT including mental health issues are not fully understood.

4.5 Conclusion

The data from this clinical audit suggests that it is safe to use the BCTT and BCBT in a non-athletic population with mild TBI. Patients who terminated the test due to symptom exacerbation demonstrated shorter test duration and lower threshold HR compared to patients who terminated the test due to other reasons. The average test duration of those who terminated for other reasons suggests that in some cases, mild TBI-related issues may have impacted on the test performance and further investigation is warranted. Those who terminated due to symptom exacerbation were unable to accurately perceive their exertion. Lastly, study results indicate that there is a relationship between mental health and test performance in people with mild TBI.

Preface

The clinical audit findings from Chapter 4 indicated that the Buffalo Concussion Treadmill Test (BCTT) and Buffalo Concussion Bike Test can be safely used to identify physiological dysfunction within a non-athletic population with mild traumatic brain injury (TBI). However, it was unclear if baseline levels of physical fitness affected the performance outcomes of the test. To address this issue, Chapter 5 *'explores the underlying mechanisms impacting the BCTT in a general adult population with mild TBI in comparison to age and gender matched healthy active and sedentary adults'*. This study with minor changes to the methods, results and discussion was submitted to the Journal of Head Trauma Rehabilitation.

Publication

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CHAPTER 5: PERFORMANCE AND PHYSIOLOGICAL RESPONSE TO THE BUFFALO CONCUSSION TREADMILL TEST CAN IDENTIFY AUTONOMIC DYSFUNCTION IN THE GENERAL ADULT POPULATION WITH MILD TRAUMATIC BRAIN INJURY: A PROSPECTIVE OBSERVATIONAL STUDY

5.1 Introduction

More than 50 million people worldwide experience a TBI each year (Maas et al., 2017) and up to 31% of those affected will experience persistent symptoms three to six months post-injury (Cancelliere et al., 2023). With the most recent consensus statement on concussion/mild TBI recommending a gradual return to physical activity following 24 to 48 hours of relative rest (Patricios et al., 2023), exercise testing has been recognised as an important assessment tool for diagnosing exercise intolerance as a result of physiological dysfunction (Leddy et al., 2018; Quatman-Yates et al., 2018). Physiological dysfunction causes a range of symptoms, which are exacerbated by physical or cognitive exertion, and therefore can be diagnosed using exercise testing (Ellis et al., 2015).

The BCTT is one of the most common exercise intolerance or graded exertion tests available (Quatman-Yates et al., 2018). The BCTT is a safe and reliable method for diagnosing, quantifying and monitoring physiological dysfunction (Leddy et al., 2011; Leddy et al., 2010), and guiding aerobic exercise prescription following a mild TBI (Janssen et al., 2022; Leddy, Haider, Ellis, et al., 2019; Leddy & Willer, 2013). A systematic review by Haider et al. (2023) found that graded exercise testing within two weeks of a mild TBI has excellent sensitivity for confirming or ruling out exercise intolerance in athletes following a sport-related concussion. However, the authors noted that “because all the included studies evaluated athletes, our results may not generalize to non-athletes” (Haider et al., 2023). More recently, studies have been conducted to investigate the use of the BCTT in non-athletic populations, demonstrating that the test can elicit symptom exacerbation before individuals reach their maximum heart rates (HRs) (DeGroot et al., 2024; Galea et al., 2023; Janssen et al., 2022). Since athletic individuals may perform better on exercise tests, as achieving longer test durations and higher HRs compared to sedentary people, further investigation is warranted to determine whether physical activity levels influence performance outcomes, particularly symptom exacerbation.

There are multiple components of an exercise test that can be used to determine physiological dysfunction. Exercise intolerance is one measure of physiological dysfunction, which occurs when the test is terminated early due to symptom exacerbation. A reduction in test duration due to symptom exacerbation in people with Persistent Post-concussion Symptoms (PPCS) has been reported in both the athletic (Clausen et al., 2016) and sedentary (Kozlowski et al., 2013) populations when compared to their healthy counterparts. In exercise testing, physiological dysfunction can also be indicted using measures of HR, including resting, maximum (threshold) (Clausen et al., 2016; Kozlowski et al., 2013), and age-predicted maximum HR (Leddy & Willer, 2013; McIntyre et al., 2020; Vuu et al., 2022). Other measures that are used to measure physiological dysfunction include blood pressure (BP) and rating of perceived exertion (RPE), however these do not consistently discriminate between those with PPCS and those without during graded exercise tests (Clausen et al., 2016; Kozlowski et al., 2013; Leddy et al., 2010).

In summary, there is evidence to support the use of exercise testing to diagnose exercise induced physiological dysfunction and incomplete recovery in people with mild TBI. However, most studies to date have been conducted in an athletic population and it is unknown whether test results may be impacted by individuals' physical activity levels. Therefore, the aim of this study was to explore underlying mechanisms impacting BCTT performance in a general adult population with mild TBI. Specifically, we intended to (1) describe BCTT performance in adults with a mild TBI, healthy active adults and healthy sedentary adults, and (2) explore if between-group differences in physiological response during the BCTT are the result of autonomic dysfunction or levels of physical activity.

5.2 Methods

A prospective observational study was conducted comparing three groups: adults with mild TBI, healthy active adults and healthy sedentary adults. This study was approved by the Southern Adelaide Local Health Network Ethics Committee on the 10/03/2020 (HREC/19/SAC/286) and site-specific approval by the Central Adelaide Local Health Network Ethics Committee on the 25/08/2020 (governance reference number: 13581). Due to the COVID-19 pandemic restrictions and construction works at the original testing site, an amendment was granted to add Flinders University as a recruitment site. The study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies (von Elm et al., 2007).

5.2.1 Participants

Adults with mild TBI who experienced ongoing symptoms were recruited from a local outpatient interdisciplinary rehabilitation service between January 2021 to September 2021. The service included patients with both mild TBI and complex mild TBI. Mild TBI was defined by the service as the presence of problematic symptoms, formal post-traumatic amnesia of <24 hours, self-reported post-traumatic amnesia of <24 hours and no abnormal radiology findings. Complex mild TBI was defined using the same criteria as mild TBI, with the addition of at least one red flag. Red flags included post-injury headaches, dizziness, or memory difficulties impacting daily activities; as well as having a history a formal mental health diagnosis (i.e., depression) or a previous TBI with residual symptoms/impairments at the time of injury. Patients scheduled to complete the BCTT for the first time as part of usual clinical care were informed about the study by their treating clinician. If the patient was interested in participating, the clinician gained verbal consent to provide the research team with their contact details. The research team contacted the patient within a week to provide further study details and obtain written consent (see Appendix 4 for amended participant information sheet/consent form to include the Flinders University recruitment site). The clinician excluded patients from study participation if they had contraindications or precautions to exercise testing and were not cleared by their treating physician according to the American Heart Association guidelines (Gibbons et al., 1997).

Healthy active and sedentary adults were recruited through flyers placed at universities, sports, and allied health centres, and via social media until early 2023 (see Appendix 5 for recruitment flyer). Healthy adults were categorised as active if they reported undertaking moderate intensity aerobic physical activity for a minimum of 30 minutes, five times per week, or vigorous intensity aerobic exercise for a minimum of 20 minutes, three times per week (American College of Sports Medicine, 2021). Healthy adults were categorised as sedentary if they reported activity levels below these thresholds. Healthy active and sedentary adults were deemed ineligible for study participation if they had a history of TBI, or self-reported contraindications or precautions to exercise testing in accordance with the American Heart Association guidelines (Gibbons et al., 1997). Where possible, healthy adult participants were matched to the adults with mild TBI group by age and gender.

5.2.2 Protocol

All participants were asked to participate in a one-off data collection session during which they completed the same BCTT protocol (Leddy et al., 2020b), as per the usual care protocol for participants with mild TBI (Appendices 6 and 7 for the protocol for adults with mild TBI and healthy active and sedentary adults respectively).

The starting setting for the BCTT was 3.2 mph (5.1 km/h) for participants up to 5’10” (165 cm) and 3.6mph (5.8 km/h) for participants ≥5’10” (165 cm) at 0 degree incline. After each minute, the treadmill was increased by 1 degree incline until 15 degrees was reached. When 15 degrees was reached, the speed was increased by 0.4 mph (0.6km/h) for each minute until test termination. Upon termination of the test, participants continued to walk on the treadmill for an additional 2 minutes at 2.5mph (4.0 km/h) and 0 degree incline to cool-down. Participants were then asked to sit down for five minutes. Starting speed, increment increase, and speed increase were adjusted to suit the athletic status, height, and comfort of the participant, taking into consideration their safety (Leddy et al., 2020b).

The test was terminated if the participant reached ≥90% of their age-predicted maximum HR, rated their perceived exertion as ≥19/20 on the Borg RPE, the treating clinician or researcher felt it was unsafe for the participant to continue, or the participant wished to stop. In addition, for adults with mild TBI, the test was terminated if the participant experienced symptom exacerbation, defined as a 3-point increase in symptom severity on the Visual Analogue Scale (VAS) for those who rated ≤5/10 for baseline VAS, or a 1-point increase for those who rated >5/10 for baseline VAS.

Test duration and reason for test termination were recorded alongside HR and Borg RPE at baseline, each minute during the test and each minute after the test for a duration of five minutes. In the mild TBI group, symptom severity was measured using the VAS at baseline, each minute during the test and each minute after the test for a duration of five minutes. BP was measured immediately before and after the test while participants were seated, following the 2-minute cool-down on the treadmill, as the BP monitor could not be used in a standing position. Collection of blood lactate was optional and, for those who participated was also measured immediately before and after the test while seated post treadmill (i.e., after the 2-minute cool-down), as it was considered unsafe to complete a finger prick in standing.

HR was measured using the Polar Verity Sense, an armband worn HR monitor (Polar Electro, 2023). The age-predicted maximum HR was calculated as 220-age (Fox 3rd et al., 1971; Shookster et al., 2020). Resting HR was measured after one minute of seated rest prior to the exercise test. Threshold HR was defined as the HR at termination of exercise. The resting HR and threshold HR reached during exercise was expressed as a percentage of age-predicted maximum HR. HR was then measured one and five minutes post exercise whilst seated. Heart rate recovery (HRR) at both one minute and five minutes post exercise was obtained by subtracting the threshold HR to define the HRR fast phase and HRR slow phase respectively (Barak et al., 2011; Tulumen et al., 2011). RPE was measured using the Borg RPE on a 6-20 scale with higher scores indicating greater perceived exertion (Borg, 1982). A 0-10 VAS scale was used to measure symptom severity, with higher scores indicating greater symptom severity (Lee & Kieckhefer, 1989). Blood lactate was measured before and post exercise using the Accutrend Plus (F. Hoffmann-La Roche Ltd, 2023), via a finger prick sample.

5.2.3 Data collection

Participants self-reported their levels of activity for the week prior to testing, including frequency per week, intensity (light, moderate, vigorous or combination) and duration for each exercise modality (structured or incidental) or physical activity (i.e., gardening, commuting). Participants were then categorised as active or sedentary based on the American College of Sports Medicine (2021) definition. Participants completed the following self-reported questionnaires: the Depression, Anxiety and Stress Scale (DASS); and the Montreal Cognitive Assessment (MoCA). The DASS is a valid and reliable measure of emotional symptoms, containing domains of depression, anxiety and stress, and rates items on a 4-point scale (0-3), with higher scores indicating greater severity of emotional symptoms (Brown et al., 1997; Henry & Crawford, 2005; Lovibond & Lovibond, 1995). The MoCA, a valid and reliable measure of cognition, takes approximately 10 minutes to complete, and has a total score of 30 with ≥26 being classified as normal (Nasreddine et al., 2005).

For adults with mild TBI, demographic and clinical characteristics were collected from clinical records, including age and gender, brain injury specific information (i.e., time since injury, cause of injury, Glasgow Coma Scale, duration of loss of consciousness, duration of post-traumatic amnesia and scan changes (yes to denote abnormal scan results; no to denote normal scan results)), and past medical history. Healthy active and sedentary adults were asked for a self-reported medical history.

5.2.4 Statistical analysis

All statistical analysis was performed using IBM SPSS Statistics 29. Descriptive summary statistics were presented as mean±standard deviation (SD) for data that were normally distributed and as frequency (%) for categorical data. A one-way Analysis of Variance (ANOVA) was conducted to explore the differences between the three groups (i.e., adults with mild TBI, healthy active adults, and healthy sedentary adults) for demographic characteristics and test outcomes.

Initial analysis indicated that physical activity levels varied largely within the adults with mild TBI group, therefore a post-hoc analysis was undertaken with minutes of physical activity per week as the covariate for all test outcome measures.

Furthermore, to explore the data, the adults with mild TBI group was recategorized into an active and a sedentary group using the definitions by the American College of Sports Medicine. A Least Significant Difference (LSD) post-hoc analysis was undertaken for four groups (i.e., active adults with mild TBI, sedentary adults with mild TBI, healthy active adults and healthy sedentary adults). A one-way ANOVA was repeated, with minutes of physical activity per week as covariate, to account for the wide range of physical activity levels reported within the groups, and to explore the differences between the four groups.

5.3 Results

5.3.1 Participant demographics

Twenty-one participants with mild TBI, 17 healthy active adults and 14 healthy sedentary adults were recruited. Thirty-one (60.8%) participants were male, and the mean age was 37.8±14.6 years. For participants with mild TBI, the average time since injury was 36.1±24.7 days (range: 7 to 105 days), most injuries were sustained from a bicycle accident (10 (47.6%)) and 13 (61.9%) reported a history of prior TBI. The healthy sedentary group were significantly ($p<0.05$) less active

(45.4±53.9 mins) over the seven days prior to testing than both the healthy active group (677.7±538.4 mins) and the adults with mild TBI group (412.6±388.9 mins). Emotional symptoms identified with the DASS were significantly worse in the adults with mild TBI group (16.63±10.9) compared to healthy active (7.9±6.8) and sedentary (7.1±4.6) groups ($p<0.05$). Two participants in the healthy sedentary group did not complete the MoCA. No significant differences were found in cognition across the three groups (see Table 5.1).

5.3.2 Baseline measures

Mean resting HR was significantly different between all three groups ($p<0.05$) and was lowest in healthy active adults (65.3±11.4 beats per minute (bpm)), followed by adults with mild TBI (74.8±14.8 bpm) and highest in healthy sedentary adults (84.1±11.1 bpm). There were no other significant differences between the three groups for baseline measures of RPE, BP, and blood lactate (see Table 5.2).

5.3.3 Test duration and reason for test termination

The adults with mild TBI group demonstrated a significantly shorter test duration (10.8±5.7 mins) compared to both the healthy active (14.1±2.9 mins) and healthy sedentary (11.6±3.0 mins) groups ($p<0.05$). In all three groups, most participants stopped due to reaching 90% of their age-predicted maximum HR (adults with mild TBI group: 14 (66.7%), healthy active group: 17 (100%), healthy sedentary group: 13 (92.9%)). In the adults with mild TBI group, seven people (38.1%) terminated the test due to symptom exacerbation. At test termination, adults with mild TBI had a mean VAS score of 2.9±0.9 and the most common symptoms were headache (66.7%), dizziness (47.6%) and light-headedness (47.6%). The mean age-predicted maximum HR reached at test termination was significantly lower in the adults with mild TBI group (84.3±9.8%) compared to the healthy active (90.0±0.2%) and sedentary (89.3±2.8%) groups ($p<0.05$). However, all three groups had a similar RPE at cessation of the test (adults with mild TBI: 15.6±2.3, healthy active adults: 16.0±2.4, healthy sedentary adults: 15.1±2.4). At the end of the exercise test, fast and slow phase HRR were significantly better in the healthy active group (fast: 69.6±18.2 bpm, slow: 79.0±13.8 bpm) compared to both the mild TBI (fast: 44.5±18.7 bpm, slow: 61.1±20.4 bpm) and healthy sedentary (fast 49.6±20.1 bpm, slow 63.0±11.7 bpm) groups ($p<0.05$) with no significant difference between the adults with mild TBI and healthy sedentary groups.

Blood lactate was collected post test termination from 17, 14 and 10 participants in the adults with mild TBI, healthy active, and healthy sedentary groups respectively, and was significantly lower in the adults with mild TBI group (2.9±0.9 mmol/L) compared to both the healthy active (4.4±1.8 mmol/L) and sedentary (4.3±1.7 mmol/L) groups ($p<0.05$) (see Table 5.2).

5.3.4 Post-hoc analysis

When including levels of physical activity as a covariate, there were no changes in the results for test duration, age-predicted maximum HR at test termination, RPE, or blood lactate measures. Also, a significant difference was still found between the adults with mild TBI and healthy active groups in both fast and slow HRR. However, there was no longer a detectable significant difference between the healthy active and sedentary groups.

5.3.5 Analysis of the four groups

Of the 21 adults with mild TBI, 13 were classified as active and eight as sedentary based on their 7-day self-reported physical activity levels (642.3±3.12.7 mins versus 39.4±85.2 mins, $p<0.05$). Besides this, there were no other significant differences in patient demographics between active and sedentary adults with mild TBI (see Table 5.3).

With regards to performance outcomes, the active adults with mild TBI group (12.5±5.7 mins) lasted significantly longer on the BCTT compared to the sedentary adults with mild TBI group (8.0±4.8 mins). There were no other significant differences between active and sedentary adults with mild TBI (see Table 5.4).

Including levels of physical activity as a covariate for the four groups did not alter the results reported between active and sedentary people with mild TBI for performance outcomes.

Table 5.1 Participant demographics

	n	Adults with mild TBI (n=21)	N	Healthy active adults (n=17)	n	Healthy sedentary adults (n=14)
Age (years), mean±SD	21	39.1±14.4	17	37.4±15.3	14	36.4±15.0
Gender, n (%)	21		17		14	
• Male		14 (66.7)		10 (58.8)		7 (50.0)
• Female		7 (33.3)		7 (41.2)		7 (50.0)
Self-reported minutes of physical activity in the past 7 days, mean±SD	21	412.6±388.9[ab]	17	677.7±538.4[c]	14	45.4±53.9
Modality of physical activity in the 7 days – participants may have reported more than one, n (%)	21		17		14	
• Nil		6 (28.6)		0 (0.0)		9 (64.3)
• Running		5 (23.8)		6 (35.3)		1 (7.1)
• Cycling		9 (42.9)		3 (17.7)		2 (14.3)
• Hiking		0 (0.00)		1 (5.9)		0 (0.0)
• Gym		5 (23.8)		14 (82.4)		3 (21.4)
• Climbing		0 (0.0)		3 (17.7)		0 (0.0)
• Martial arts		1 (4.8)		2 (11.8)		0 (0.0)
• Hockey		0 (0.0)		1 (5.9)		0 (0.0)
• Rowing		1 (4.8)		1 (5.9)		0 (0.0)
• Swimming		0 (0.0)		1 (5.9)		0 (0.0)
• Surfing		1 (4.8)		0 (0.00)		0 (0.0)
• Soccer		0 (0.0)		1 (5.9)		0 (0.0)
• Basketball		0 (0.0)		1 (5.9)		0 (0.0)
• Netball		0 (0.0)		2 (11.8)		0 (0.0)
• Football		0 (0.0)		1 (5.9)		0 (0.0)
• Gymnastics		0 (0.0)		1 (5.9)		0 (0.0)
DASS total (0-63), mean±SD	19	16.6±10.9[ab]	17	7.9±6.8	14	7.1±4.6
DASS depression (0-21), mean±SD	19	5.6±5.2[ab]	17	2.3±2.6	14	2.4±3.0
DASS anxiety (0-21), mean±SD	19	4.2±3.2[ab]	17	1.6±2.0	14	1.4±1.7
DASS stress (0-21), mean±SD	19	6.8±3.4[ab]	17	4.1±3.2	14	3.3±2.0
MoCA (0-30), mean±SD	21	28.1±1.3	17	27.9±2.3	12	27.0±2.0
Past medical history – participants may have reported more than one, n (%)	21		17		14	
• Nil		10 (47.6)		6 (35.3)		4 (28.6)
• Musculoskeletal conditions		1 (4.8)		6 (25.3)		3 (21.4)
• Orthopaedic conditions		2 (9.5)		3 (17.7)		1 (7.1)
• Respiratory conditions		2 (9.5)		1 (5.9)		2 (14.3)
• Cardiovascular conditions		0 (0.0)		1 (5.9)		4 (28.8)

• Psychological conditions		6 (28.6)		1 (5.9)		1 (7.1)
• Neurological conditions		3 (14.3)		2 (11.8)		1 (7.1)
• Autoimmune conditions		1 (4.8)		0 (0.0)		1 (7.1)
• Gastrointestinal conditions		0 (0.0)		0 (0.0)		2 (14.3)
• Other conditions		2 (9.5)		0 (0.0)		1 (7.1)
Time since injury (days), mean±SD	21	36.1±24.7				
Cause of injury, n (%)	21					
• Bicycle accident		10 (47.6)				
• Motor bike accident		5 (23.8)				
• Water sport accident		2 (9.5)				
• Equestrian accident		3 (14.3)				
• Fall		1 (4.8)				
Glasgow Coma Scale (3-15), n (%)	15					
• 14		7 (46.7)				
• 15		8 (53.3)				
Duration of loss of consciousness, n (%)	19					
• Nil		10 (52.6)				
• Yes but unknown duration		5 (26.3)				
• Yes ≤30 mins		4 (21.1)				
Duration of post-traumatic amnesia, n (%)	21					
• Nil		8 (38.1)				
• <24 hours		11 (52.4)				
• 1-7 days		2 (9.5)				
Scan changes, n (%),	20					
• Yes		5 (25.0)				
• No		15 (75.0)				
History of TBI, n (%)	21					
• Yes		13 (61.9)				
• No		8 (38.1)				

DASS=Depression, Anxiety and Stress Scales
MoCA=Montreal Cognitive Assessment
TBI=Traumatic brain injury
a $p<0.05$ between adults with mild TBI and healthy active adults
b $p<0.05$ between adults with mild TBI and healthy sedentary adults
c $p<0.05$ between healthy active adults and healthy sedentary adults

Table 5.2 Baseline measures and performance outcomes on the BCTT

	n	Adults with mild TBI (n=21)	n	Healthy active adults (n=17)	n	Healthy sedentary adults (n=14)
Test duration (mins), mean±SD	21	10.8±5.7[a]	17	14.1±2.9	14	11.6±3.0
Reason for test termination, participants may have reported more than one, n (%)	21		17		14	
• Reaching 90% of age-predicted maximum HR		14 (66.7)		17 (100.0)		13 (92.9)
• Reporting ≥19/20 on the Borg RPE		2 (9.5)		2 (11.8)		1 (7.1)
• 3-point change from initial VAS for participants who rated ≤5/10		7 (33.3)		0 (0.0)		0 (0.0)
• 1-point change from initial VAS for patients who rated >5/10		1 (4.8)		0 (0.0)		0 (0.0)
• Calf fatigue		1 (4.8)		1 (5.9)		0 (0.0)
Resting HR (bpm), mean±SD	21	74.8±14.8[ab]	17	65.3±11.4[c]	14	84.1±11.1
Threshold HR (bpm), mean±SD	21	153.0±24.6	17	164.4±13.9	14	163.9±14.2
Resting HR as a percentage of the age-predicted maximum HR (%), mean±SD	21	41.5±8.9[a]	17	36.1±7.3[c]	14	45.8±4.9
Threshold HR as a percentage of the age-predicted maximum HR (%), mean±SD	21	84.3±9.8[ab]	17	90.0±0.2	14	89.3±2.8
HRR 1 min post exercise (fast phase) (bpm), mean±SD	21	44.5±18.7[a]	17	69.6±18.2[c]	14	49.6±20.1
HRR 5 mins post exercise (slow phase) (bpm), mean±SD	21	61.1±20.4[a]	17	79.0±13.8[c]	14	63.0±11.7
Resting RPE (6-20), mean±SD	21	6.3±0.7	17	6.0±0.0	14	6.0±0.0
Final RPE (6-20), mean±SD	21	15.6±2.3	17	16.0±2.4	14	15.1±2.4
Resting VAS (0-10), mean±SD	21	1.2±1.3				
Final VAS (0-10), mean±SD	21	2.9±0.9				
Reported symptoms, participants may have reported more than one, n (%)	21					
• Nil		1 (4.8)				
• Dizziness		10 (47.6)				
• Headache		14 (66.7)				
• Light-headedness		10 (47.6)				
• Nausea		2 (9.5)				
• Fogginess		7 (33.3)				
• Changes to vision		3 (14.3)				
• Fatigue		2 (9.5)				
• Unsteady		2 (9.5)				
Resting systolic BP (mmHg), mean±SD	21	128.9±15.3	17	128.8±16.0	14	135.9±25.6
Post-BCTT systolic BP (mmHg), mean±SD	21	139.4±17.1	17	132.9±15.9	14	138.0±21.7

Resting diastolic BP (mmHg), mean±SD	21	81.1±10.5	17	76.1±7.7	14	83.3±11.7
Post-BCTT diastolic BP (mmHg), mean±SD	21	81.3±8.4	17	76.8±7.5	14	83.4±11.4
Resting blood lactate (mmol/L), mean±SD	19	1.7±0.6	15	2.0±0.6	10	1.8±0.5
Post-BCTT blood lactate (mmol/L), mean±SD	17	2.9±0.9[ab]	14	4.4±1.8	10	4.3±1.7

BCTT=Buffalo Concussion Treadmill Test
BPM=Beats per minute
BP=Blood pressure
HR=Heart rate
HRR=Heart rate recovery
RPE=Rating of Perceived Exertion
VAS=Visual Analogue Scale
a $p<0.05$ between adults with mild TBI and healthy active adults
b $p<0.05$ between adults with mild TBI and healthy sedentary adults
c $p<0.05$ between healthy active adults and healthy sedentary adults

Table 5.3 Participant demographics for the 4 groups

	n	Active adults with mild TBI (n=13)	n	Sedentary adults with mild TBI (n=8)	n	Healthy active adults (n=17)	n	Healthy sedentary adults (n=14)
Age (years), mean±SD	13	39.7±17.5	8	38.0±8.3	17	37.4±15.3	14	36.4±15.0
Gender, n (%)	13		8		17		14	
• Male		10±76.9		4±50.0		10±58.8		7±50.0
• Female		3±23.1		4±50.0		7±41.2		7±50.0
Self-reported minutes of physical activity in the 7 days, mean±SD	13	642.3±312.7[ac]	8	39.4±85.2[e]	17	677.7±538.4[f]	14	45.4±54.0
Modality of physical activity in the past 7 days – participants may have reported more than one, n (%)	13		8		17		14	
• Nil		0 (0.0)		6 (75.0)		0 (0.0)		9 (64.3)
• Running		4 (30.8)		1 (12.5)		6 (35.3)		1 (7.1)
• Cycling		8 (61.5)		1 (12.5)		3 (17.7)		2 (14.3)
• Hiking		0 (0.0)		0 (0.0)		1 (5.9)		0 (0.0)
• Gym		5 (38.5)		0 (0.0)		14 (82.4)		3 (21.4)
• Climbing		0 (0.0)		0 (0.0)		3 (17.7)		0 (0.0)
• Martial arts		1 (7.7)		0 (0.0)		2 (11.8)		0 (0.0)
• Hockey		0 (0.0)		0 (0.0)		1 (5.9)		0 (0.0)
• Rowing		1 (7.7)		0 (0.0)		1 (5.9)		0 (0.0)
• Swimming		1 (7.7)		0 (0.0)		1 (5.9)		0 (0.0)
• Surfing		1 (7.7)		0 (0.0)		0 (0.0)		0 (0.0)
• Soccer		0 (0.0)		0 (0.0)		1 (5.9)		0 (0.0)
• Basketball		0 (0.0)		0 (0.0)		1 (5.9)		0 (0.0)
• Netball		0 (0.0)		0 (0.0)		2 (11.8)		0 (0.0)
• Football		0 (0.0)		0 (0.0)		1 (5.9)		0 (0.0)
• Gymnastics		0 (0.0)		0 (0.0)		1 (5.9)		0 (0.0)
DASS total (0-63), mean±SD	12	16.7±10.9[bc]	7	16.6±11.8[de]	17	7.9±6.8	14	7.1±4.6
DASS depression (0-21), mean±SD	12	5.3±5.0[b]	7	6.1±5.9d[e]	17	2.3±2.6	14	2.4±3.0
DASS anxiety (0-21), mean±SD	12	4.5±3.7[bc]	7	3.7±2.6	17	1.6±2.0	14	1.4±1.7
DASS stress (0-21), mean±SD	12	6.8±2.9[bc]	7	6.7±4.5[d]	17	4.1±3.2	14	3.3±2.0
MoCA (0-30), mean±SD	13	28.4±1.3[c]	8	27.8±1.3	17	27.9±2.3	1	27.0±2.0
Past medical history – participants may have reported more than one, n (%)	13		8		17		14	
• Nil		5 (38.5)		5 (62.5)		6 (35.3)		4 (28.6)
• Musculoskeletal conditions		1 (7.7)		0 (0.0)		6 (25.3)		3 (21.4)
• Orthopaedic conditions		2 (15.4)		0 (0.0)		3 (17.7)		1 (7.1)
• Respiratory conditions		1 (7.7)		1 (12.5)		1 (5.9)		2 (14.3)

• Cardiovascular conditions		0 (0.0)		0 (0.0)		1 (5.9)		4 (28.6)
• Psychological conditions		4 (30.8)		2 (25.0)		1 (5.9)		1 (7.1)
• Neurological conditions		2 (15.4)		1 (12.5)		2 (11.8)		1 (7.1)
• Autoimmune conditions		1 (7.7)		0 (0.0)		0 (0.0)		1 (7.1)
• Gastrointestinal conditions		0 (0.0)		0 (0.0)		0 (0.0)		1 (7.1)
• Other conditions		2 (15.4)		0 (0.0)		0 (0.0)		1 (7.1)
Time since injury (days), mean±SD	13	31.6±18.9	8	43.5±32.1				
Cause of injury, n (%)	13		8					
• Biking accident		8 (61.5)		2 (25.0)				
• Motor bike accident		3 (23.1)		2 (25.0)				
• Water sport accident		1 (7.7)		1 (12.5)				
• Equestrian accident		1 (7.7)		2 (25.0)				
• Fall		0 (0.0)		1 (12.5)				
Glasgow Coma Scale (3-15), n (%)	10		5					
• 14		5 (50.0)		2 (40.0)				
• 15		5 (50.0)		3 (60.0)				
Loss of consciousness, n (%),	12		7					
• Nil		6 (50.0)		4 (57.1)				
• Yes but unknown duration		3 (25.0)		2 (28.6)				
• Yes ≤30 mins		3 (25.0)		1 (14.3)				
Post traumatic amnesia, n (%)	13		8					
• Nil		5 (38.5)		3 (37.5)				
• <24 hours		7 (53.9)		4 (50.0)				
• 1-7 days		1 (7.7)		1 (12.5)				
Scan changes, n (%)	13		7					
• Yes		4 (30.8)		1 (14.3)				
• No		9 (69.2)		6 (85.7)				
History of TBI, n (%)	13		8					
• Yes		9 (69.2)		4 (50.0)				
• No		4 (30.8)		4 (50.0)				

DASS=Depression, Anxiety and Stress Scales
MoCA=Montreal Cognitive Assessment
TBI=Traumatic brain injury
a $p<0.05$ between active adults with mild TBI and sedentary people with mild TBI
b $p<0.05$ between active adults with mild TBI and healthy active adults
c $p<0.05$ between active adults with mild TBI and healthy sedentary adults
d $p<0.05$ between sedentary adults with mild TBI and healthy sedentary adults
e $p<0.05$ between sedentary adults with mild TBI and healthy active adults
f $p<0.05$ between healthy active adults and healthy sedentary adults

Table 5.4 Baseline measures and performance outcomes with physical activity as a covariate for the 4 groups

	N	Active adults with mild TBI (n=13)	n	Sedentary adults with mild TBI (n=8)	n	Healthy active adults (n=17)	n	Healthy sedentary adults (n=14)
Test duration (mins), mean±SD	13	12.5 ±5.7[a]	8	8.0±4.8[e]	17	14.1±2.9	14	11.6±3.0
Reason for test termination, participants may have reported more than one, n (%)	13		8		17		14	
• Reaching 90% of age-predicted maximum HR		9 (69.2)		5 (62.5)		17 (100.0)		13 (92.9)
• Reporting ≥19/20 on the Borg RPE		1 (7.7)		1 (12.5)		2 (11.8)		1 (7.1)
• 3-point change from initial VAS for patients who rated ≤5/10		4 (30.8)		3 (37.5)		0 (0.0)		0 (0.0)
• 1-point change from initial VAS for patients who rated >5/10		1 (7.7)		0 (0.0)		0 (0.0)		0 (0.0)
• Calf fatigue		0 (0.0)		1 (12.5)		1 (5.9)		0 (0.0)
Resting HR (bpm), mean±SD	13	71.0±9.2[c]	8	81±20.6[e]	17	65.3±11.4[f]	14	84.1±11.1
Threshold HR (bpm), mean (SD)	13	155.2±22.6	8	149.5±28.7	17	164.4±13.9	14	163.9±14.2
Resting HR as a percentage of the age-predicted maximum HR (%), mean±SD	13	39.5±4.9[c]	8	44.7±11.7[e]	17	36.1±7.3[f]	14	45.8±4.9
Age-predicted maximum HR (%), mean±SD	13	85.8±7.1	8	81.7±13.3[de]	17	90.0±0.2	14	89.3±2.8
HRR 1 min post exercise (fast phase) (bpm), mean±SD	13	47.4±17.5[b]	8	39.9±20.9[e]	17	69.6±18.2[f]	14	49.6±12.4
HRR 5 mins post exercise (slow phase) (bpm), mean±SD	13	65.9±18.9[b]	8	53.3±21.6[e]	17	79.0±13.8[f]	17	63.0±11.7
Resting RPE (6-20), mean±SD	13	6.5±0.9[bc]	8	6.1 ±0.4	17	6.0±0.0	14	6.00±0.0
Final RPE (6-20), mean±SD	13	15.9±2.1	8	15.1±2.7	17	16.0±2.4	14	15.1±2.4
Resting VAS (0-10), mean±SD	13	1.3±1.4[bc]	8	1.1±1.0[e]				
Final VAS (0-10), mean±SD	13	3.5±1.9[bc]	8	3.4±1.4[de]				
Reported symptoms, participants may have reported more than one, n (%)	13		8					
• Nil		1 (7.7)		0 (0.0)				
• Dizziness		7 (53.9)		3 (37.5)				
• Headache		7 (53.9)		7 (87.5)				
• Light-headedness		5 (38.5)		5 (62.5)				
• Nausea		2 (15.4)		0 (0.0)				
• Fogginess		5 (38.5)		2 (25.0)				
• Changes to vision		1 (7.7)		2 (25.0)				
• Fatigue		1 (7.7)		1 (12.5)				
• Unsteady		2 (15.4)		0 (0.0)				
Resting systolic BP (mmHg), mean±SD	13	129.6±17.5	8	127.8±11.7	17	128.8±16.0	14	135.9±25.6

Post-BCTT systolic BP (mmHg), mean±SD	13	143.5±18.3	8	132.8±13.4	17	132.9±15.9	14	138.0±21.7
Resting diastolic BP (mmHg), mean±SD	13	80.1±12.3	8	82.8±7.3	17	76.1±7.7	14	83.3±11.7
Post-BCTT diastolic BP (mmHg), mean±SD	13	82.7±9.8	8	79.0±5.2	17	76.8±7.5	14	83.4±11.4
Resting blood lactate (mmol/L), mean±SD	13	1.7±0.6	6	1.6±0.8	15	2.0±0.6	10	1.8±0.5
Post-BCTT blood lactate (mmol/L), mean±SD	11	2.9±0.9[bc]	6	3.4±1.4	14	4.4±1.8	10	4.3±1.7

BCTT=Buffalo Concussion Treadmill Test
BPM=Beats per minute
BP=Blood pressure
HR=Heart rate
HRR=Heart rate recovery
RPE=Rating of Perceived Exertion
VAS=Visual Analogue Scale
a p<0.05 between active adults with mild TBI and sedentary people with mild TBI
b p<0.05 between active adults with mild TBI and healthy active adults
c p<0.05 between active adults with mild TBI and healthy sedentary adults
d p<0.05 between sedentary adults with mild TBI and healthy sedentary adults
e p<0.05 between sedentary adults with mild TBI and healthy active adults
f p<0.05 between healthy active adults and healthy sedentary adults

5.4 Discussion

This is the first study to explore underlying mechanisms impacting on BCTT performance in a general adult population with mild TBI, by comparing test performance in three groups: adults with a mild TBI, healthy active adults and healthy sedentary adults. We sought to understand if observed differences in physiological response are related to autonomic dysfunction or levels of physical activity in the past week. The test differentiated between those who can return to full levels of physical activity and those who experience autonomic dysfunction as a result of exercise stressing the physiological system. We have demonstrated that the BCTT is a true test of autonomic dysfunction irrespective of levels of physical activity in the past week. Study results suggest that threshold HR occurring before an individual reaches 90% of their age-predicted maximum HR was the best indicator of autonomic dysfunction. Test duration and post exercise recovery are both influenced by levels of physical activity in the past week and should not be solely used to determine autonomic dysfunction.

Thirty-three percent of the adults with mild TBI group were not able to reach 90% of their age-predicted HR, indicating exercise intolerance and physiological dysfunction. Physiological recovery is indicated when an individual with mild TBI can reach 85-90% of their age-predicted maximum HR on a graded exercise test such as the BCTT without exacerbation of symptoms (Leddy et al., 2010), thus the test can be used to monitor physiological recovery. This was further apparent in a post-hoc-analysis, comparing 13 active to eight sedentary adults with mild TBI, which indicated no significant difference between the two groups with regards to threshold HR. This demonstrates that under normal circumstances the autonomic nervous system (ANS) is capable of maintaining homeostasis within the body (Wehrwein et al., 2016) by regulating the sympathetic and parasympathetic nervous systems (Esterov & Greenwald, 2017). However, following a mild TBI, persistent alterations in neuronal depolarisation, cell membrane permeability, mitochondrial function, cellular metabolism and cerebral blood flow can cause physiological dysfunction (Ellis et al., 2015). Early termination on the BCTT due to exercise intolerance and symptom exacerbation is a marker of physiological dysfunction (Ellis et al., 2015). Shorter test duration and reduced threshold HR has previously been observed in people with mild TBI (Clausen et al., 2016; Kozlowski et al., 2013; Leddy, Haider, Ellis, et al., 2019). This may be attributed to the inability to effectively shift from a parasympathetic to sympathetic state during exercise, resulting in dampened sympathetic response (Hinds et al., 2016; Leddy et al., 2016). The findings of this study has demonstrated that physiological dysfunction can be elicited by a graded exercise test regardless of an individual’s level of physical activity. It has also highlighted the importance of considering test duration relative to level of physical activity in the past week.

Our study findings concur with previous work suggesting that early termination of exercise testing is a sign of incomplete recovery. It also expands on results of DeGroot et al. (2024), who found that the BCTT can be used to guide rehabilitation exercise post-mild TBI with the aim to return patients to their previous levels of activity. By comparing adults with mild TBI to active and sedentary healthy controls, our study has indicated that test results should be reviewed with respect to the individual's age-predicted maximum HR. Graded exercise testing can be used to identify the exercise intensity at which a symptomatic response is provoked, and subsequently to prescribe an intervention at subthreshold level. In our study, the BCTT elicited symptoms in 38.1% of adults with mild TBI. Repeating the tests over the course of a rehabilitation program allows for monitoring of progress (DeGroot et al., 2024). Further research investigating the utilisation of repeated graded exercise tests in mild TBI for monitoring recovery through exercise intervention is required.

Our study results indicate that slow post-exercise recovery may be an indicator of autonomic dysfunction, however these results should be interpreted with caution as they may be influenced by levels of physical activity in the past week. Initial analysis indicates that healthy adults had a better HRR than both the healthy sedentary and adults with mild TBI groups, however when adjusted for physical activity levels only the difference between healthy adults and those with mild TBI remained.

Sedentary individuals experience impaired ANS function and cerebral blood flow (Daniele et al., 2022), similar to those who experience physiological dysfunction following a mild TBI (Tan et al., 2014). Regular aerobic exercise shifts the ANS towards parasympathetic dominance due to increased vagal modulation and decreased sympathetic activity (Hautala et al., 2009), which may explain why healthy active adults in our study had the lowest resting HR and highest HRR post exercise. This difference may be more pronounced when comparing healthy active people to those with a mild TBI. However, physical activity levels do not appear to affect performance outcomes on the BCTT other than test duration. Adults with mild TBI and the healthy sedentary group demonstrated similar test durations. However, active adults with mild TBI had significantly longer test durations compared to their sedentary counterparts. This finding suggests that test duration alone is not a reliable indicator of exercise intolerance. Instead, it highlights the importance of using age-predicted maximum HR and symptom exacerbation as markers of physiological dysfunction when assessing exercise tolerance on the BCTT following a mild TBI. Instead of relying solely on test duration, we suggest that assessment should be individualised and involve HR monitoring, considering 90% of age-predicted maximum HR as the upper threshold.

We anticipated that RPE would vary across our study participants, however perceived exertion at test termination in our study was similar across all three groups, despite the fact that adults with mild TBI typically did not reach 90% of their age-predicted maximum HR. This is consistent with other studies that have reported consistently higher ratings of perceived exertion in individuals with mild TBI compared to healthy controls, relative to workload (Kochick et al., 2022; Merritta et al., 2010). It is important to continue monitoring age-predicted maximum HR in conjunction with subjective measures, such as the Borg RPE. This approach allows for assessment of any disconnect between perceived and actual work rate (Chen, 2013), which can also indicate autonomic dysfunction (Dawes et al., 2006; Hinds et al., 2016). In healthy individuals, the RPE is also closely related to blood lactate and HR, with higher values resulting in greater perceived exertion (Scherr et al., 2013). In our study, participants with mild TBI had a lower blood lactate level at exercise termination. This can likely be attributed to the fact that not all participants in this group exercised to 90% of their age-predicted HR maximum.

Baseline measures of depression, anxiety, and stress were significantly worse in adults with mild TBI than both healthy control groups when controlling for levels of physical activity in the post-hoc analysis. The average time since injury in our cohort was 36 days post-injury. Experiencing symptoms beyond the acute period may have contributed to poor mental health in the mild TBI group. The absence of differences in levels of depression, anxiety, and stress between the two healthy control groups suggests that these levels are likely related to the injury rather than physical activity levels. Physiological dysfunction of the ANS occurs in both mental health conditions and physiological dysfunction following a mild TBI, leading to overlapping symptoms (Baker et al., 2019; Purkayastha et al., 2019). Previous research has demonstrated that markers of physiological dysfunction, such as changes to HR, can persist beyond the acute phase (Antonellis et al., 2024; Kozlowski et al., 2013), potentially affecting exercise testing results. Although we screened for mental health in our study, it was not designed to differentiate between the effects of mental health and physiological dysfunction. It is possible one or both of these factors contributed to the early cessation of exercise in some of our participants. People who experience symptoms of anxiety or depression often suffer from fatigue and low motivation, leading to greater levels of perceived exertion (Meyer & Broocks, 2000; Vuu et al., 2023) and therefore may stop exercising earlier. Future studies should therefore consider controlling for levels of anxiety and depression in the design and analysis of results. Additionally, clinicians should consider screening for symptoms of depression and anxiety in people with mild TBI to better inform the multidisciplinary approach to intervention and care. Exercise has been shown to improve mental health outcomes (Kianian et al., 2018) suggesting that the combined effect of addressing mental health and increasing physical activity levels may result in a positive reinforcement for both outcomes. In our study, time since injury varied greatly. It is possible that the interaction between sedentary behaviour and mental health issues combined to effect the cessation of exercise in some individuals. Future studies should consider this effect in more detail.

Due to the BCTT protocol, some aspects of the results should be interpreted with caution. The absence of significant differences in BP between the three groups may be attributed to BP being measured in a seated position after the 2-minute cool down, and variations in the time taken to obtain BP measurements across participants. These factors may have allowed BP to return to baseline levels, as reflected in the results. HRR was obtained by subtracting the threshold HR from the HR at 1 minute and 5 minutes post exercise respectively, as it was not safe for participants to stop the test abruptly at their threshold HR. These HRR findings may reflect the physiological changes occurring during the 2-minute cool-down, when sympathetic activity gradually decreases and parasympathetic activity gradually increases to help restore the body to resting state. By 1 or 5 minutes post exercise, the parasympathetic nervous system may have become dominant. Additionally, the healthy active group likely did not reach volitional fatigue, as they were instructed to cease the test at 90% of their age-predicted maximum HR in accordance with the BCTT protocol. However, this is unlikely to have affected the results, as the BCTT is designed to assess physiological dysfunction rather than maximal exercise capacity.

This study has several strengths and limitations. This is the first study to investigate BCTT performance to identify autonomic dysfunction whilst taking into account levels of physical activity. Comparing active and sedentary healthy adults with individuals with a mild TBI highlighted performance indicators that were influenced by physical activity levels. One study limitation was that at the time of the study design, a power calculation was not undertaken as there was no previous work completed in this area to inform a power calculation. An attempt was made to recruit 25 participants in each group but due to the COVID-19 pandemic, there were difficulties with reaching 25 participants. Another limitation was the lack of instructions provided to participants regarding abstaining from caffeine or nicotine prior to the test, or screening for the use of any drugs that may affect HR, which may have affected HR levels during the BCTT. While we attempted to control for the variation in physical activity levels across the groups by including it as a covariate in a post-hoc analysis, we acknowledge that self-reporting of physical activity may not be accurate. An exploratory analysis was conducted to explore differences within the mild TBI group by dividing participants into active and sedentary subgroups. However, due to the small sample sizes in each subgroup and the fact that we did not specifically recruit participants with mild TBI based on activity levels, and physical activity was self-reported, these results should be interpreted with caution. Future studies should consider differences in physical activity levels in the general adult mild TBI population at the time of recruitment and utilise a validated outcome measure to measure physical activity levels.

5.5 Conclusion

This study demonstrated that for people with a mild TBI the inability to reach 90% of an individual’s age-predicted maximum HR is a better indicator of autonomic dysfunction than measures of test duration alone, as test duration can be influenced by physical activity levels. Perceived exertion should be monitored, but not used as an individual measure as there can be a disconnect between perceived and actual effort in people with physiological dysfunction. While HRR may be affected in those with a mild TBI, caution should be taken when attributing this solely to physiological dysfunction. Our findings suggest that physical activity levels appear to be an influencing factor for HRR in this population.

Preface

Individuals with a mild traumatic brain injury (TBI) often continue to experience persistent symptoms beyond expected timeframes. This suggests that various factors may influence the return to physical activity following a mild TBI. The findings from the systematic review of randomised controlled trials presented in Chapter 3 have demonstrated that aerobic exercise, when incorporated into a more comprehensive intervention, can improve persistent symptoms and support the return to physical activity. Chapters 4 and 5 reported results of a clinical audit and observational study, identifying that following a mild TBI individuals often experience poor mental health. Gaining a deeper understanding of these challenges is important to enhance goal setting and patient-centred care. The purpose of Chapter 6 was to *‘survey individuals with mild-to-moderate TBI symptoms lasting >10 days to understand the changes in physical activity levels, healthcare utilisation patterns, factors influencing return to physical activity and the impact of mental health*’.

CHAPTER 6: A SURVEY OF PHYSICAL ACTIVITY LEVELS AND FACTORS IMPACTING THE RETURN TO PHYSICAL ACTIVITY IN INDIVIDUALS WHO HAVE SUSTAINED A PAST MILD-TO-MODERATE TRAUMATIC BRAIN INJURY

6.1 Introduction

Each year an estimated 170,000 people in Australia suffer from a mild TBI (Thomas et al., 2020b). Approximately 10% suffer from chronic symptoms that do not resolve spontaneously within 10-14 days (Permenter et al., 2023), with 19% reporting three or more post-concussion symptoms (Ponsford et al., 2019). Factors that exacerbate these symptoms include older age, female gender (King, 2014b), and specific characteristics of the TBI such as prolonged loss of consciousness (LOC), post-traumatic amnesia (PTA), pre-existing mental health conditions (Ponsford et al., 2019), and delays seeking medical attention (Heyer et al., 2016).

The persistence of symptoms following a mild TBI can hinder individuals from returning to previous physical activities, including sports, work, and school (Büttner et al., 2020; Graff et al., 2021; Wildgoose et al., 2022). Often, individuals demonstrate increased sedentary behaviour post injury which can further exacerbate symptoms of mild TBI, such as headache, fatigue, and depression, leading to difficulties in meeting recommended levels of physical activity (Mercier et al., 2021). Persistent symptoms may decrease physical activity levels and quality of life (Ponsford et al., 2019).

The literature supports the use of aerobic exercise and other physical interventions to reduce ongoing symptoms and facilitate the return to physical activity (Alarie et al., 2021; Miutz et al., 2022; Thomas et al., 2017; Vuu et al., 2022). The latest Consensus Statement recommended that returning to physical activity should be gradual, and graded to a level so as to not exacerbate symptoms (Patricios et al., 2023). If symptoms do worsen, patients should be given reassurance, advice, modifications, and be provided with interventions specific to their symptoms by healthcare providers (DiFazio et al., 2016). There is further evidence that suggests physical activity interventions should be multimodal and provided by multiple disciplines to ensure targeted therapy (Moore et al., 2024; Schneider et al., 2023). Preliminary evidence indicates that mental health may influence the recovery of physical function (Schiehser et al., 2017; Silverberg et al., 2021). This highlights the importance of identifying factors that contribute to behavioural change, which should be incorporated into interventions aimed at enhancing the recovery of symptoms and increasing physical activity.

An array of behaviour change techniques have been used to increase physical activity, such as barrier identification, action planning, demonstration of the behaviour and self-monitoring (French et al., 2014; Gilchrist et al., 2024; J. M. Murray et al., 2017). However, these techniques have primarily been studied in non-clinical populations, limiting our understanding of their effectiveness in clinical contexts. A common method to utilised to frame the key factors for behaviour change is the Capability, Opportunity and Motivation-Behaviour (COM-B) model. This model provides a comprehensive theoretical framework that considers three essential components required for behaviour change (Michie et al., 2011). The model encompasses capability (physical and psychological capability), opportunity (physical and social opportunity) and motivation (automatic and reflective motivation) domains (Michie et al., 2011). Applying the COM-B model to clinical populations, such as those with mild-to-moderate TBI, can facilitate a deeper understanding of the processes and factors that contribute to behavioural change, particularly in relation to physical activity. By identifying the specific capabilities, opportunities, and motivations that influence physical activity in individuals with mild-to-moderate TBI, the COM-B model can inform the development of more targeted and effective interventions for this clinical population.

This survey study aims to quantify changes in physical activity levels, healthcare utilisation patterns, factors influencing return to physical activity, and mental health impacts among individuals with mild-to-moderate TBI symptoms lasting more than 10 days.

6.2 Methods

6.2.1 Study design

A cross-sectional survey was conducted to assess physical activity levels before and after a mild-to-moderate TBI, and to determine the factors influencing physical activity levels in individuals who had a past mild-to-moderate TBI and where the symptoms lasted longer than 10 days. The survey was administered online using Qualtrics (Qualtrics, 2024), between January 2022 and April 2024. Ethical approval was obtained from the Flinders University Human Research Ethics Committee (5142). The survey findings are described according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) (Eysenbach, 2004).

6.2.2 Recruitment and participants

Participants were recruited via multiple means, including advertisements on social media platforms such as X, LinkedIn and Facebook nationwide, as well as flyers distributed at universities, sports centres, and allied health centres in South Australia (see Appendices 8 and 9 for recruitment flyer and participant information sheet/consent form respectively). Participants were adults that had experienced a concussion, mild TBI or mild-to-moderate TBI, with symptoms lasting longer than 10 days and resided in Australia. Those with a moderate, severe, or moderate-to-severe TBI, those whose symptoms resolved within 10 days and those residing outside of Australia were excluded from study participation.

6.2.3 Survey

One author (SV) designed the online survey, which was then reviewed and refined by the research team until consensus was reached. Face validity was established by ensuring that questions addressed the study aim. The inclusion of the International Physical Activity Questionnaire (IPAQ), a valid and reliable self-report measure of physical activity (Booth, 2000), and use of the COM-B model, a framework of understanding factors influence behavioural change (Michie et al., 2011), further enhanced face validity. Wording was evaluated by the research team to ensure that it was suitable for respondents and easy to understand, resulting in minor revisions that enhanced conciseness. Usability was achieved by testing the survey on various electronic devices, including mobile phones, tablets, laptops and desktops, with adjustments made to the formatting of the questions to ensure usability across all platforms.

The survey consisted of closed questions designed to gain information pertaining to: (1) participant demographics, such as age and gender, as well as details related to the participant's TBI, including time since injury, cause of injury, LOC, PTA, brain scan results, TBI diagnosis, and symptoms experienced in the past seven days; (2) physical activity levels, including pre-TBI exercise modality, intensity and duration per week, as well as physical activity levels in the last seven days measured by the IPAQ (Booth, 2000); and (3) barriers and facilitators affecting the return to physical activity. A five-point Likert scale ranging from strongly disagree (1) to strongly agree (5) was utilised to rate the impact of factors affecting the ability to return to physical activity (see Appendix 10 for survey questions).

The IPAQ is a valid and reliable self-report measure of physical activity (Craig et al., 2003). This survey used the 9-item short form version, which assesses the types and intensity of physical activity to estimate the total physical activity levels in metabolic equivalent of task (MET) and the time spent sitting over the last seven days (Booth, 2000). The IPAQ categorises physical activity levels as high, moderate, or low, based on the METs reported by the participant (Booth, 2000).

Questions regarding factors potentially influencing the return to physical activity were framed using the COM-B model (Michie et al., 2011) with examples provided for each domain and a rating scale from 1 representing strongly disagree to 5 representing strongly agree. The interaction among the domains of physical and psychological capability, physical and social opportunity, and automatic and reflective motivation (Michie et al., 2011) contributes to altering an individual's ability to undertake physical activity.

6.2.4 Data analysis

All statistical analysis was performed using IBM SPSS Statistics 29. Data from the survey were analysed using descriptive statistics to characterise levels of physical, using mean (SD) for data that were normally distributed, median (IQR) for ordinal data and data that were not normally distributed and frequency (%) for categorical data. To explore the impact of mental health on factors affecting the return to physical activities, respondents were grouped based on the presence or absence of symptoms of anxiety and/or depression. A between-group comparison of participant demographics and factors pertaining to the TBI were compared using t-tests and chi squared tests, and Mann-Whitney U tests were conducted to compare responses related to the return to physical activity.

6.3 Results

6.3.1 Participant demographics

Thirty-nine individuals completed the survey. The mean age of participants was 38.8 ± 14.5 years and 22 (56.1%) were female. Thirty participants (76.9%) reported sustaining a mild TBI, while the remaining nine sustained a mild-to-moderate TBI, with 21 (53.8%) of these injuries being a sport-related injury. The average time since injury was 841.0 ± 1161.4 (median: 431, IQR: 10-5580) days (see Figure 6.1). Fourteen participants (39.5%) reported experiencing LOC, and 27 (71.1%) participants reported PTA, with the majority indicating no brain changes on imaging (n=28, 73.7%). Participants reported 16 different symptoms in the seven days prior to completing the survey, with headache, fatigue, noise sensitivity, light sensitivity and dizziness being the most common. Furthermore, 19 (48.7%) participants reported experiencing anxiety, depression, or a combination of both (see Table 6.1).

6.3.2 Physical activity

Prior to their TBI, participants reported varying levels of physical activity: nine (28.1%) engaged in low levels, ten (31.1%) in moderate levels, and 13 (40.6%) in high levels. Activities included walking, cycling or mountain biking, football, rugby, and gym workouts or classes. Following their TBI, in the seven days preceding completion of the survey, nine participants (31.0%) reported engaging in high levels of physical activity according to the IPAQ. The remaining participants reported engaging in moderate (n=8, 27.6%) or low (n=12, 41.4%) levels of physical activity. Participants reported an average of 447.5 ± 199.4 minutes spent sitting in the seven days prior to completing the survey (see Table 6.2).

6.3.3 Healthcare utilisation

Participants reported accessing a variety of healthcare services following their TBI, primarily physiotherapy (n=22, 84.6%) and general medicine (n=19, 73.1%) to facilitate their return to physical activity. Most commonly, care was provided in the outpatient setting (n=16, 61.6%), with participants receiving both education on physical activity and physical activity prescription (n=11, 45.8%) (see Table 6.2). Only two participants accessed psychological services to support their return to physical activity.

6.3.4 Factors influencing the return to physical activity

Results pertaining to factors influencing participants' return to physical activity is presented in Table 6.3. Overall, factors related to the domains of physical and psychological capability, as well as physical opportunity were perceived to have the most impact on return to physical activity. Specifically, 22 (71.0%) participants strongly agreed or agreed that factors related to the physical opportunity and physical capability domains influenced their return to physical activity. Additionally, 20 (64.5%) participants strongly agreed or agreed that their return to physical activity was affected by factors related to psychological capability.

6.3.5 The impact of mental health symptoms on the return to physical activity

Of the 39 participants who reported experiencing symptoms, 20 indicated suffering from anxiety and/or depression. Participants with self-reported mental health symptoms had a longer average time since injury (mean ± SD: 1142.9 ± 1516.9; median (IQR): 525 (22-5580) days) compared to those without these symptoms (mean ± SD: 574.6 ± 640.5 days; median (IQR): 602 (10-2009) days), though this was not statistically significant (p=0.08). Participants reporting mental health symptoms perceived factors related to all COM-B model domains as having a stronger influence on their physical activity levels, compared to those without mental health issues (see Figure 6.2). These observed differences between the two groups were statistically significant for the domains of psychological capability, physical opportunity, reflective motivation and automatic motivation.

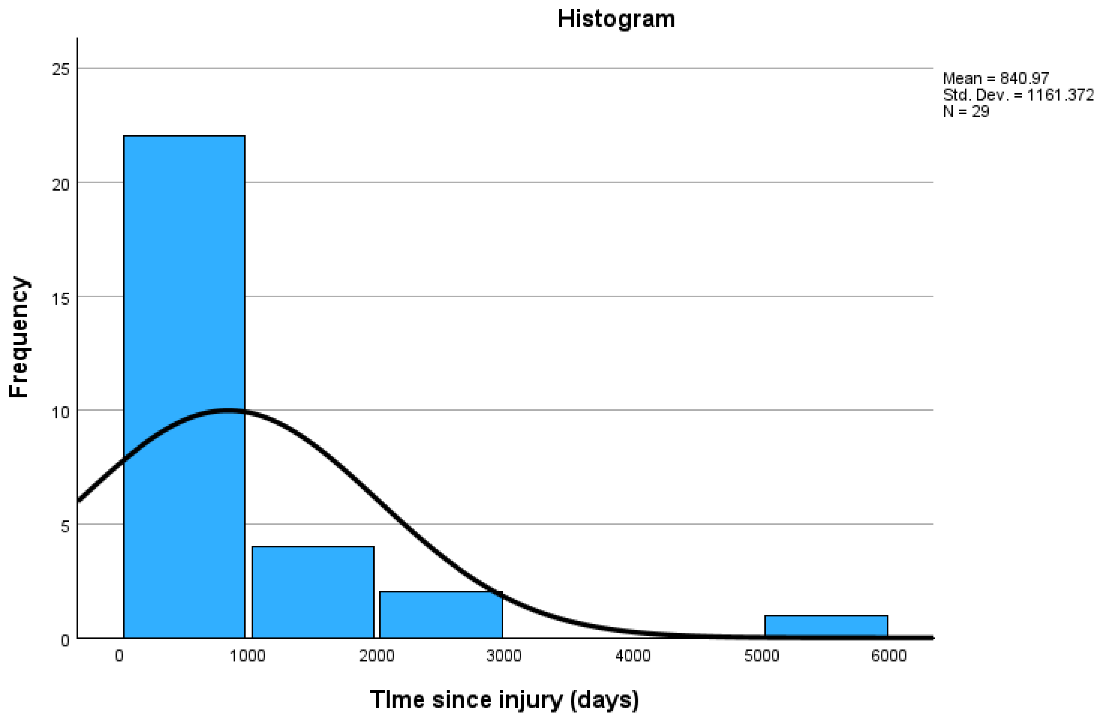

Figure 6.1 Spread of time since injury

Table 6.1 Survey responses for participant demographics

Participant demographics	Number	Results
Age (years), mean±SD (range)	39	38.8±14.5 (18-72)
Gender, n (%)	39	
• Male		17 (43.6%)
• Female		22 (56.4%)
Australian state, n (%)	30	
• South Australia		21 (70.0%)
• New South Wales		4 (13.3%)
• Victoria		4 (13.3%)
• Western Australia		1 (3.3%)
TBI classification, n (%)	39	
• Concussion/mild		30 (76.9%)
• Mild-to-moderate		9 (23.1%)
Cause of injury, n (%)	39	
• Cycling		5 (12.8%)
• Soccer		1 (2.6%)
• Rugby or football		6 (15.4%)
• Basketball		2 (5.1%)
• Climbing		2 (5.1%)
• Gym accident		1 (2.6%)
• Other sports		4 (10.3%)
• Work accident		5 (12.8%)
• Motor vehicle accident		5 (12.8%)
• Home accident		1 (2.6%)
• Assault		1 (2.6%)
• Fall		6 (15.4%)
Time since injury (days), mean±SD (range)	29	841.0±1161.4 (10-5580)
Loss of consciousness	38	
• Yes, ≤30 mins		5 (13.2%)
• Yes, >30 mins		1 (2.6%)
• Yes, but unknown duration		8 (20.1%)
• No		15 (39.5%)
• Unknown		9 (23.7%)
Post-traumatic amnesia	38	
• Yes, <24 hours		1 (2.6%)
• Yes, >1 day and <7 days		7 (18.4%)
• Yes, >7 days		10 (26.3%)

• No		7 (18.4%)
• Yes, but unknown duration		9 (23.7%)
• Unknown		4 (10.5%)
Brain scan changes	38	
• Yes		5 (13.2%)
• No		28 (73.7%)
• Unknown, as did not have a brain scan		5 (13.2%)
Symptoms, n (%), *participants may have reported more than one symptom*	38	
• Headache		29 (76.3%)
• Neck pain		19 (50.0%)
• Dizziness		20 (52.6%)
• Nausea		2 (5.3%)
• Light sensitivity		21 (55.3%)
• Noise sensitivity		24 (63.2%)
• Changes to vision		15 (39.5%)
• Balance problems		19 (50.0%)
• Fatigue		26 (68.4%)
• Sleeplessness		15 (39.5%)
• Restlessness		11 (29.0%)
• Anxiety		19 (50.0%)
• Irritability		19 (50.0%)
• Depression		17 (44.7%)
• Memory changes		3 (7.9%)
• Cognitive changes		4 (10.5%)

TBI=Traumatic brain injury

Table 6.2 Survey responses to physical activity questions

Physical activity levels	**Number**	**Results**
Pre-TBI type of physical activity, n (%), *participants may have reported more than one type of physical activity*	31	
• Nil		3 (9.7%)
• Walking		20 (64.5%)
• Hiking		4 (12.9%)
• Running		4 (12.9%)
• Cycling or mountain biking		9 (29.0%)
• Swimming		3 (9.7%)
• Dancing		2 (6.5%)
• Soccer		1 (3.2%)
		8 (25.8%)

• Rugby or football		3 (9.7%)
• Netball		4 (12.9%)
• Basketball		1 (3.2%)
• Cricket		4 (12.9%)
• Climbing		10 (32.3%)
• Gym and gym classes		
Pre-TBI physical activity category (estimation) using the IPAQ, n (%)	32	
• Low		9 (28.1%)
• Moderate		10 (31.3%)
• High		13 (40.6%)
IPAQ		
• Physical activity category in the last 7 days, n (%)	29	
○ Low		12 (41.4%)
○ Moderate		8 (27.6%)
○ High		9 (31.0%)
• Sitting minutes in the last 7 days, mean±SD	24	447.5±199.4 (180-960)
Healthcare services accessed for return to physical activity, n (%), *participants may have reported more than one service*	26	
• General medicine		19 (73.1%)
• Neurologist		8 (30.8%)
• Orthopaedic surgeon		1 (3.9%)
• Ophthalmology or optometry		7 (26.9%)
• Physiotherapy		22 (84.6%)
• Occupational therapy		10 (38.5%)
• Exercise physiology		8 (30.8%)
• Exercise trainer/personal trainer		6 (23.1%)
• Psychology		2 (7.7%)
Settings, n (%), *participants may have reported more than one setting*	26	
• Acute/inpatient service		13 (50.0%)
• Subacute rehabilitation unit or TBI service		13 (50.0%)
• Outpatient/community-based service		16 (61.5%)
Interventions received, n (%)	24	
• Education regarding physical activity		10 (41.7%)
• Physical activity prescription		3 (12.5%)
• Both education regarding physical activity and physical activity prescription		11 (45.8%)

IPAQ=International Physical Activity Questionnaire
TBI=Traumatic brain injury

Table 6.3 Factors on the COM-B model influencing the return to physical activity

COM-B model domains	All participants, median (IQR), n=39	n=19 with self-reported mental health symptoms, median (IQR)	n=20 without self-reported mental health symptoms, mean (IQR)	Significance level
	1=strongly disagree; 2=disagree; 3=neutral; 4=agree; 5=strongly agree			
Physical capability	4 (1-5)	5 (3-5)	4 (1-5)	0.154
Psychological capability	4 (1-5)	4 (3-5)	3.5 (1-5)	0.006*
Physical opportunity	4 (1-5)	4 (3-5)	4 (1-5)	0.043*
Social opportunity	4 (1-5)	4 (2-5)	3 (1-5)	0.052
Reflective motivation	4 (1-5)	5 (2-5)	2.5 (1-5)	0.003*
Automatic motivation	3 (1-5)	4 (2-5)	3 (1-5)	0.012*

COM-B=Capability, Behaviour and Motivation-Behaviour
*$p<0.05$

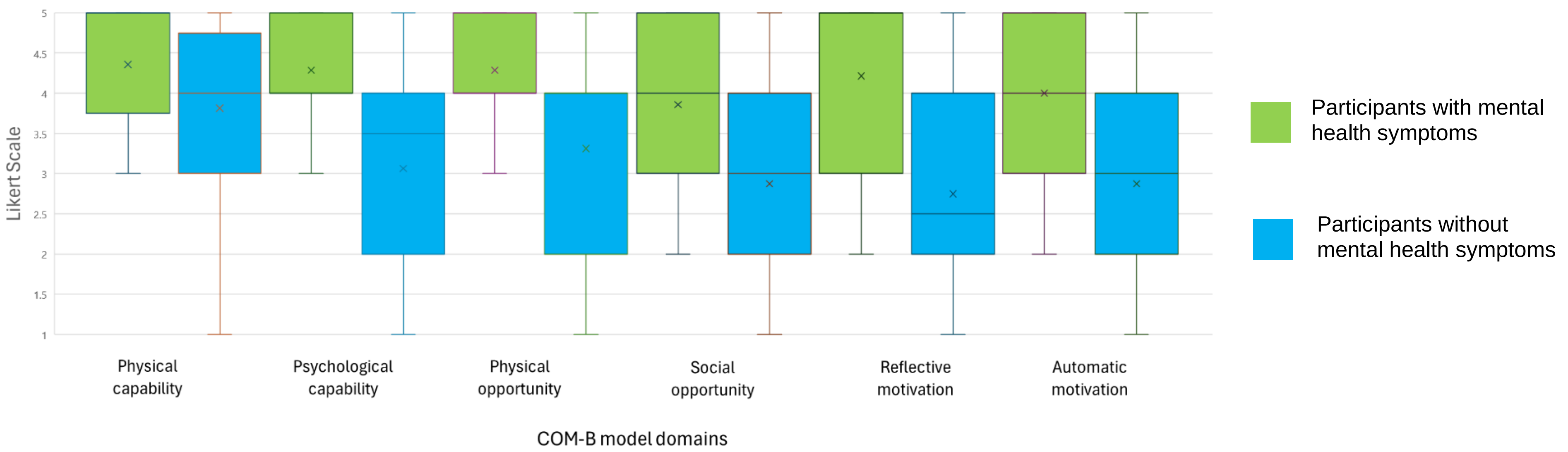

Figure 6.2 Factors influencing the return to physical activity comparing participants with and without mental health symptoms

6.4 Discussion

This study aimed to assess changes in physical activity levels in individuals with mild-to-moderate TBI experiencing symptoms for more than 10 days. The majority of participants reported a decrease in physical activity levels following their TBI compared to pre-injury levels. Most respondents reported the use of outpatient medical and physiotherapy services to support their return to activity, with these services typically providing education and physical activity prescription. Survey results indicated that, across the sample, factors related to capability including both physical and psychological capability, as well as physical opportunity were perceived as the most significantly influencing the return to physical activity. Notably, a subgroup analysis of participants reporting anxiety or depression suggested that factors across all domains of the COM-B model had a more pronounced impact on their ability to resume physical activity compared to the overall cohort. These results underscore the complex nature of returning to physical activity post mild-to-moderate TBI and highlight the need for tailored interventions, particularly for individuals experiencing mental health challenges following their injury.

Previous evidence indicates that symptom experience (i.e., number, type and intensity of symptoms) influences the ability to return to physical activities following TBI (Gilworth et al., 2008; McMahon et al., 2014; O'Brien et al., 2017). Prior to their TBI, 40.6% of participants reported undertaking high levels of physical activity, whereas following their TBI, only 31.0% reported high levels of physical activity in the past seven days, as measured by the IPAQ. Respondents identified headache and fatigue as the most common symptoms. Previous research suggests that these symptoms can significantly limit the return to physical activity (Lucas et al., 2014; Mercier et al., 2021; Norrie et al., 2010; van Markus-Doornbosch, Peeters, van der Pas, et al., 2019). Although the precise mechanism warrants further investigation, survey findings suggest that symptoms may be a contributing factor to reduced levels of physical activity.

Patients with TBI typically present to emergency departments for evaluation (Koval et al., 2020; Mitchell et al., 2021). However, the majority of patients with mild TBI are discharged from hospital after initial assessment and receive follow-up care in outpatient settings, if any at all (de Koning et al., 2017), meaning that the individual will likely have to pay out of pocket to access healthcare services. This may affect their ability to receive interventions to address their symptoms, potentially leading to chronic issues, as seeking early intervention is associated with improved symptom outcomes (Grool et al., 2016; Ponsford et al., 2001). In our study the mean time since injury was longer than two years, indicating that a failure to resolve symptoms in the subacute phase can lead to long-term conditions. Our results indicate that participants accessed a variety of healthcare services following their mild-to-moderate TBI. Physiotherapy was reported most frequently, while psychological services were the least utilised. This pattern of healthcare utilisation may reflect the study focus on recovery of physical activity, as physiotherapists play a key role in providing rehabilitation strategies for physical function (Brown & Camarinos, 2019; Patricios et al., 2023; Quatman-Yates et al., 2015).

The findings of the current study align with recent literature suggesting that mild TBI management requires an individualised approach to care, involving expertise from various disciplines to address different symptoms and physical activity goals (Moore et al., 2024). A systematic review of multidisciplinary care for patients with persistent symptoms following a mild TBI found that neuropsychologists, occupational therapists, physicians and physiotherapist were the most commonly reported healthcare providers to aid in the recovery of persistent symptoms (Moore et al., 2024). Our survey results, focusing specifically on services utilised for the recovery of physical activity, highlight the prominent role of physiotherapy in this aspect of post mild-to-moderate TBI care.

Despite research into effective interventions for individuals following a mild-to-moderate TBI, various factors may influence access, uptake and compliance with these interventions. Our survey results highlight some of these unique challenges. Participants indicated that factors related to physical and psychological capability, as well as physical opportunity, significantly influenced their return to physical activity. In the context of the COM-B model, capability refers to the physical and psychological skills, strength, or stamina required to perform the physical activity (Michie et al., 2011). Our findings suggest that symptoms such as depression and anxiety may impact a persons' capability to return to a range of physical activities. Physical opportunity refers to the environment, including aspects such as time, finances, resources, and location (Michie et al., 2011). Our survey results revealed that following a TBI, physical activity including work-related activities, is often reduced. This reduction can have a significant impact on an individual's finances and access to resources required for facilitating the recovery of physical activity levels (Boake et al., 2005; Theadom et al., 2017; Tuominen et al., 2012).

Our results indicate that participants who reported having mental health issues (anxiety, depression, or both) perceived all factors within the COM-B model as influencing their return to physical activity to a greater extent. This finding aligns with existing literature that has found that individuals with a higher number of mental health symptoms following a mild TBI experienced a greater severity, duration, and number of symptoms (Ettenhofer & Abeles, 2009; Lange et al., 2011; Losoi et al., 2016). This relationship may be attributed to the overlapping mechanisms and symptoms of mild TBI and mental health conditions (Barlow, 2016).

The results identified depression and anxiety among the most common symptoms following a mild-to-moderate TBI. A subgroup analysis of survey results was conducted between those who did and those who did not report experiencing symptoms of depression and anxiety. While irritability was also reported by many participants, it was not considered a mental health symptom in our subgroup analysis. This decision was based on the understanding that irritability is a behaviour or emotion occurring with minimum provocation or at a reduced threshold (Barata et al., 2016), rather than a distinct mental health condition. These findings underscore the importance of integrating psychological interventions in mild-to-moderate TBI management. In addition, previous research has shown that psychological interventions, such as cognitive behavioural therapy, counselling, psychoeducation, and education/reassurance, can improve persistent symptoms following a mild TBI (Sullivan et al., 2020). Such interventions may help prevent maladaptive behaviours and psychological mechanisms, worsening of symptoms, and chronicity of symptoms (Mott et al., 2012; van der Horn et al., 2020).

Participants in the survey reported a wide range of time since injury, with an average of 2.3 years post-injury. While acute TBI can lead to symptom onset and persistence, the literature suggests that as more time passes since injury, additional factors may contribute to the continuation or mimicry of post-concussion symptoms. A pre-existing mental health or chronic pain condition, a history of TBI or maladaptive behaviours (Eisenberg et al., 2013; Snell et al., 2023; Snell et al., 2018) are known risk factors for persistent symptoms and can impact the ability to engage in physical activity. A limitation of this study was that co-morbidities were not collected as part of the patient demographic data, and as a result, preventing analysis of their influence on symptom presentation and return to physical activity. Furthermore, due to the broad range of time since injury, other life factors, such as changes to personal and social relationships, employment and physical activity routines, may also have contributed to reduced levels of physical activity.

A primary limitation of this study was the small sample size, which may affect the generalisability of the findings. Furthermore, the wide range of time since injury reported by participants, and the absence of an upper limit, may have introduced recall bias, potentially resulting in skewed or unreliable data. Although a valid and reliable outcome measure was used to measure physical activity levels, test-retest reliability was not assessed prior to the survey, which may have additionally influenced the reliability and validity of the results. Participants in the survey reported changes to vision years following their TBI, which was not accounted for during the design of the survey to consider other survey formats (i.e. paper-based; vision friendly formats).

6.5 Conclusion

Despite limitations such as a broad range of time since injury and the small sample size, this research provides valuable insights into the experiences of adults with mild-to-moderate TBI as they attempt to return to physical activity. The findings indicate that most respondents experienced a decrease in physical activity levels following mild-to-moderate TBI as a result of their symptoms, as well as other factors that were not explored in this study. Participants primarily accessed physiotherapy and medical services in outpatient settings to facilitate their return to physical activity, suggesting a need for specialised and accessible services. Factors related to physical and psychological capability, as well as physical opportunity were identified as influencing participants' return to physical activity. This underscores the multifaceted nature of recovery from mild-to-moderate TBI and the necessity for comprehensive interventions that address various aspects of capability and opportunity. Additionally, the survey revealed a relationship between mental health symptoms and perceived barriers to physical activity. In participants with self-reported mental health symptoms, factors across all domains of the COM-B model appeared to influence return to physical activity to a greater extent, suggesting that mental health plays a crucial role in the recovery process. These findings contribute to our understanding of the complex interplay between physical recovery, mental health, and return to activity following mild-to-moderate TBI. However, they also emphasise the need for further research to explore in greater depth the experiences of adults with mild-to-moderate TBI as they work to return to their pre-injury physical activities, investigate the specific mechanisms by which mental health symptoms influence this process, and develop targeted interventions that address both mental health symptoms and other mild-to-moderate TBI symptoms.

Preface

This chapter builds upon the survey study (Chapter 6), which identified that following a mild-to-moderate traumatic brain injury (TBI), physical activity levels are reduced. Using the Capability, Opportunity and Motivation-Behaviour (COM-B) model, factors related to physical and psychological capability, and physical opportunity were identified as influencing participants' return to physical activity. In addition, participants who reported to have depression or anxiety tended to perceive all domains of the COM-B model as negatively impacting their return to physical activity. Furthermore, aerobic exercise was found to improve persistent symptoms following a mild TBI in Chapter 3, and in Chapters 4 (clinical audit) and 5 (observational study), individuals following a mild TBI experienced higher levels of depression, anxiety and stress. More research is required to understand the experiences of adults with mild TBI as they attempt to return to their physical activities, as well as the interplay of mental health symptoms to enhance interventions, and recovery of symptoms and physical activity. This chapter sought to identify and expand on these factors by *'exploring the barriers and facilitators to physical activity in adults following a mild TBI with symptoms lasting greater than 10 days'*, is under review with Neuropsychological Rehabilitation journal.

Publication

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CHAPTER 7: EXPLORING THE BARRIERS AND FACILITATORS THAT ADULTS WITH MILD TRAUMATIC BRAIN INJURY AND PERSISTENT SYMPTOMS EXPERIENCE AS THEY RETURN TO PHYSICAL ACTIVITY

7.1 Introduction

The majority of people with mild TBI or concussion recover spontaneously from injury, however, approximately 30% continue to experience symptoms up to three months post-injury (Shenton et al., 2012). Recovery of individuals with a moderate-to-severe TBI focuses predominantly on physical impairment and recovery of mobility and self-care (Tate et al., 2005). The recovery of individuals with mild TBI typically focusses on the management of physical, cognitive and behavioural symptoms (Heslot et al., 2022; Ryan & Warden, 2003). As symptoms improve, the focus shifts towards returning to previous activities such as sport, work or school (Patricios et al., 2023; Putukian et al., 2023).

Caspersen et al. (1985) defines physical activity as “any bodily movement produced by skeletal muscles that requires energy expenditure”. This refers to all movement during times of leisure such as sports, play and active recreation, transport, work-related activities and household activities. Individuals with mild TBI who experience persistent symptoms following their injury are commonly limited by their symptoms and demonstrate reduced levels of physical activity (Mercier et al., 2021; Vuu et al., 2022). Reduced levels of physical activity increases the risk of anxiety, depression (Junn et al., 2015), illnesses such as cardiovascular disease, and worsen symptoms (Broshek et al., 2015; Hanna-Pladdy et al., 2001), which further impacts on life satisfaction and quality of life (Jacobsson et al., 2010).

A myriad of factors play a role in the return to physical activity following a mild TBI, including but not limited to environmental factors, personal factors, motivation to participate in physical activity, and knowledge of physical activity (Driver et al., 2012; Hamilton et al., 2016; Pham et al., 2022). Barriers and facilitators to physical activity have been explored in athletes, children and adolescents with TBI returning to sport or school (Chrisman et al., 2013; Walshe & Ryan, 2023; Wildgoose et al., 2022). However, it is unknown what factors influence the return to physical activity in non-athletic adult population with mild TBI. This study will explore the barriers and facilitators to return to physical activity in non-athletic adults with mild TBI experiencing prolonged symptoms. Having an awareness and understanding of these factors can support individuals with mild TBI, and health professionals working with patients with mild TBI, with recognising and overcoming barriers to facilitate their return to physical activity through greater levels of self-efficacy (Driver & Woolsey, 2016). Self-efficacy underpins behaviour change to promote positive health behaviours (Holloway & Watson, 2002).

7.2 Methods

7.2.1 Study design

A qualitative study was conducted, using a semi-structured interview approach to explore barriers and facilitators to physical activity. Ethical approval was obtained from the Flinders University Human Research Ethics Committee (5142). This study was completed and reported in accordance with the Consolidated Criteria for Reporting Qualitative Research (COREQ) (Tong et al., 2007).

The study design was informed by the Theoretical Domains Framework (TDF) (Atkins et al., 2017) and COM-B model (Michie et al., 2011). The TDF contains 14 domains to provide a theoretical lens to observe cognitive, affective, social, and environmental influences on behaviour, and is used to understand patient behaviour (Atkins et al., 2017). The COM-B model includes three essential conditions for behaviour change (Michie et al., 2011).The TDF domains were linked to the COM-B model counterparts. These models can be used together to facilitate the understanding of barriers and facilitators to returning to prior physical activities and factors that contribute to strategies or interventions that support behavioural change.

7.2.2 Interview structure

Interviews were conducted and audio recorded via Microsoft Teams, at a suitable time for both the participant and researcher, to overcome geographical barriers. One author (SV) conducted the interviews and transcribed the interviews. This author was a female senior physiotherapist with a Graduate Certificate in Clinical Rehabilitation and Bachelor of Physiotherapy. She possessed five years of research experience, this includes undertaking focus groups, thematic analysis and dissemination of mixed method research. She also possessed 10 years of clinical experience at the time of the interviews with much of her research and clinical experience focussing on the neurological population. She did not have professional or personal relationships with the participants prior to study commencement.

The interview began with an introduction to the study and provided an opportunity for participants to ask any questions. Socio-demographic information was gathered, such as professional background, occupational status and physical activity goals. Interview questions pertaining to types and patterns of both structured and incidental physical activity were asked to gain insight into underlying COM-B model factors enabling or hindering return to physical activity (see Appendix 11 for interview guide). Participants were asked if they wanted a copy of the transcript at the end of the interview.

7.2.3 Participants

Fourteen non-athletic adults who had experienced a mild TBI with symptoms lasting >10 days and self-reported reduced physical activity levels were recruited to this study between August 2022 and January 2024.

Participants were recruited in a national online survey study as reported in chapter 6 (see Appendices 8 and 9 for recruitment flyer and participant information sheet/consent form respectively), with optional participation in a follow up interview. Demographic and TBI related information (age, gender, time since injury, cause of injury, symptoms experienced in the past seven days and state) were collected through the survey. Participants were recruited until data saturation was reached, which was defined as no new themes for three consecutive interviews.

7.2.4 Rigour

Lincoln and Guba (2004) criteria for establishing rigor in qualitative research were employed to ensure trustworthiness of the study. To establish credibility, the interview protocol was tested in the first two interviews, transcribed verbatim then discussed with all authors to ensure the interview guide generated valuable information to address the research aim. The data from these two interviews were found to effectively address the study aim and were therefore included in the analysis. During the interview, points made by the participant were summarised by the interviewer to confirm what the participant said was understood correctly. Upon conclusion of the interview, participants were provided the opportunity to discuss any other experiences when attempting to return to physical activity. Participants were asked if they wished to receive a copy of the transcript to confirm accuracy of data. The interviewer debriefed with the research team to confirm validity of data. Transferability was achieved by ensuring the interview guide was followed and by keeping records (audio recording and transcriptions) of the interviews to justify the findings. Dependability was maintained through note taking, observation and noting of non-verbal data, recording and transcription and minimising personal bias by following structured processes (i.e., multiple rounds of the study protocol and interview guide were drafted). All interviews were undertaken, transcribed verbatim and entered in NVivo for analysis by one author, further strengthening dependability. No interviews were excluded from data analysis based on content. Two authors analysed data for reoccurring factors. Any discrepancies in coding were discussed until consensus was reached. Confirmability was achieved by having a second independent coder, ensuring research findings were a true reflection of the participant's voices and opinions. A discussion was then undertaken to ensure that factors were agreed upon by all authors.

7.2.5 Data analysis

Audio recordings of the online interviews were transcribed verbatim and de-identified. To ensure confidentiality of all personal data, each interview was coded with a study number to prevent identification and results were stored securely. Using an inductive and deductive approach to content analysis (Alhasani et al., 2021; Christie et al., 2023; Creswell, 2007; Keetley et al., 2024; Levy et al., 2022), two authors coded the transcriptions using NVivo data management software (version 12) (Limivero, 2022). For the first stage of coding, the authors familiarised themselves with the data by repeatedly reading four transcripts to document the initial factors identified. The process of the first stage of coding was to keep the factors as broad as possible to avoid untimely conclusion on interpretation. During the second stage of coding, the authors expanded broad factors into specific domains. During both stages, inductive content analysis was performed to identify barriers and facilitators that met the aim of the study, disagreements were resolved by discussion and consensus, and if not, a third reviewer was consulted. The factors were then deductively mapped to the TDF (Atkins et al., 2017) and COM-B model (Michie et al., 2011) and reviewed by the entire research team. Participants chose not to provide feedback on the findings.

7.3 Results

Fourteen adults with mild TBI who experienced symptoms and physical activity limitations lasting >10 days were interviewed. Interview duration ranged from 20 to 90 minutes. The mean age of participants was 38.8±12.5 years, 57.1% were male, time since injury was an average of 647.8±620.7 days and the majority (57.1%) sustained a sport-related injury. The majority of participants (n=11, 78.6%) reported reduced working capacity or not working at all and their physical activity goal as returning to sport. Participants' characteristics are presented in Table 7.1.

Initial inductive data analysis identified six barriers to physical activity, including environmental factors, fatigue, mental health, sensory overload, symptoms, and social expectations. In addition, the data revealed six facilitators supporting the return to physical activity, including current physical activities, assistive items, the environment, health professional support, mental health, and social support. These barriers and facilitators were mapped deductively to all the TDF and COM-B model, specifically to the domains of physical and psychological capability, physical and social opportunity, and reflective and automatic motivation, and are summarised in Table 7.2 and Figure 7.1.

Table 7.1 Participant characteristics

Participant number	Age, year	Gender	Time since injury, days	Cause of injury	Symptoms in the past 7 days	Occupational category	Occupational status	Physical activity goals	State
1	39	Male	48	Cycling accident	Headache Dizziness Noise sensitivity Balance problems Sleeplessness	Professional and business	Reduced working capacity	Return to sport Return to work	South Australia
2	19	Female	Missing	Football	Headache Neck pain Dizziness Light sensitivity Noise sensitivity Changes to vision Balance problems Fatigue Sleeplessness Restlessness Anxiety Irritability Depression	Student	Reduced working capacity	Return to sport Return to learn	South Australia
3	19	Female	19	Fall	Headache Dizziness Light sensitivity Noise sensitivity Changes to vision Fatigue Sleeplessness Restlessness	Student	Reduced working capacity	Return to sport Return to learn	South Australia
4	56	Male	1364	Work accident	Headache Neck pain Dizziness Noise sensitivity Balance problems Fatigue Anxiety Depression Irritability Vertigo	Retail	Not currently working	Return to activities of daily living	South Australia

5	29	Male	Missing	Basketball	Headache Light sensitivity Fatigue Brain fog	Healthcare	Full working capacity	Return to sport	South Australia
6	49	Female	1904	Cycling accident	Light sensitivity Noise sensitivity Fatigue Cognitive problems	Professional and business	Full working capacity	Return to sport	Victoria
7	31	Female	1220	Work accident	Headache Neck pain Light sensitivity Noise sensitivity Fatigue Anxiety	Healthcare	Reduced working capacity	Return to sport Return to work	South Australia
8	52	Female	612	Work accident	Headache Neck pain Changes to vision Fatigue Irritability	Education	Reduced working capacity	Return to work	South Australia
9	52	Female	239	Cycling accident	Headache Neck pain Dizziness Light sensitivity Noise sensitivity Balance problems Fatigue Irritability	Finance and insurance	Reduced working capacity	Return to sport Return to work	South Australia
10	35	Male	980	Home accident	Headache Neck pain Dizziness Light sensitivity Noise sensitivity Balance problems Fatigue Sleeplessness Restlessness Anxiety Nausea	Education	Not currently working	Return to activities of daily living	Victoria
11	44	Male	431	Soccer	Headache Light sensitivity Noise sensitivity	Professional and business	Reduced working capacity	Return to sport Return to work	Western Australia

					Changes to vision Balance problems Fatigue Sleeplessness Anxiety Irritability Depression				
12	30	Male	22	Soccer	Headache Dizziness Light sensitivity Noise sensitivity Changes to vision Balance problems Fatigue Sleeplessness Restlessness Anxiety Irritability Depression	Computer and technology	Not currently working	Return to sport Return to work	South Australia
13	53	Male	92	Motor vehicle accident	Headache Neck pain Dizziness Light sensitivity Noise sensitivity Changes to vision Balance problems Fatigue Sleeplessness Restlessness Irritability	Transportation	Reduced working capacity	Return to sport Return to work	South Australia
14	35	Male	842	Rugby	Light sensitivity Noise sensitivity Changes to vision Balance problems Fatigue Irritability Cognitive problems	Education	Full working capacity	Return to sport	South Australia

Figure 7.1 Factors influencing physical activity deductively mapped to the COM-B model domains

7.3.1 Capability

Fatigue, physical activity, and mental health

All participants reported on their reduced ability to undertake sport, work, social activities, and household chores following their injury. Fatigue was reported as one of the main barriers preventing participants from returning to their previous activities, described as extreme tiredness preventing activities that required mental and physical exertion, therefore restricting their capacity to undertake physical activity. Participants referred to both mental and physical feelings of fatigue limiting their physical capabilities. They described mental fatigue as the brain getting tired, affecting their ability to think and focus, *'That mental fatigue, I could only do activities quite briefly, couldn't sustain any cognitive concentration'* (Participant 5, 29-year-old male). Physical fatigue limited physical activities and was described as difficulty with moving the body, *'When you're not exercising, it becomes a physical fatigue'* (Participant 6, 49-year-old female). Participants explained that they had a limited amount of physical and mental energy to expend per day, so they prioritised activities that involved maintaining aspects of their livelihood such as work or family activities over sports, social interaction, and housework, *'I got a brain energy bucket and it's leaky. I don't have the brain energy resilience that I used to. It's been five years since my injury and I will recurrently sleep all day on a Saturday to just support my life, which also kills my life because I don't get chores done'* (Participant 6, 49-year-old female). Participants associated fatigue with poorer mental health, as they either had difficulty or were unable to complete basic activities, *'Washing the floors, cooking, cleaning, vacuuming, the basics, you just do it with no mental thought but now it takes so much mental strain and that's what affects your mental health because you lack the energy to do it'* (Participant 9, 52-year-old female). Other participants found it difficult to differentiate between symptoms of fatigue and their declining mental health, *'It's hard to draw the line, the symptoms of depression and the symptoms of concussion, especially with tiredness and mood, they definitely do blur a lot'* (Participant 2, 19-year-old female).

Mental health was identified as a barrier to engaging in physical activity, due to feelings of anger, frustration, anxiety, depression, fear and apprehension, reduced confidence, reduced motivation, and stress. Most participants referred to feeling several negative emotions, which decreased their motivation to engage in physical activity, *'The anxiety, despair, frustration, anger, are at levels when things spike, can be cyclic. The anxiety will lead to and can really limit you, hold you back from engaging in physical activity'* (Participant 11, 44-year-old male). Other participants described the fear and apprehension surrounding the risk of sustaining a second concussion and exacerbation of post-concussion symptoms as preventing the return to physical activity, *'I wouldn't ever play football again. I'm not confident. I'm apprehensive about doing that, AFL, contact sport, or anything that can hit my head. Just concerned about having a second concussion and exacerbating all those symptoms again'* (Participant 14, 35-year-old male).

Whilst some participants found it difficult to return to their previous levels of activity, others reported undertaking therapeutic physical activity facilitated their recovery and improved their function, *'The bike rides I do with the kids, the cruising doesn't do much in the way of cardio, it's probably more about balancing and control'* (Participant 11, 44-year-old male). Participants described how increasing physical activities in turn promoted their capability to increase other physical exercises. One participant discussed how embedding their structured therapeutic exercises into their daily routine further facilitated their recovery due to increased dose of therapeutic exercise, '*I go to the gym a couple times a week. The rehab program I was doing for physio, I'm able to translate that to the gym. I find it very beneficial to control weight and improve cardio'* (Participant 10, 35-year-old male). Participants expressed that physical activity improved their post-concussion symptoms such as fatigue and reduced cognition, *'I associate physical activity and exercise as improving my energy levels and combatting fatigue rather than the other way around. If I'm feeling fatigue and brain fog in the afternoon, I just walk for 10 minutes'* (Participant 1, 39-year-old male). Undertaking physical activity was also associated with improvement in mental health, as exercising with others increased both physical and social engagement, '*Physical activity, it's confidence boosting, it's a good endorphins thrive. It pushes you to break your hermit bubble because it's very easy to become self-isolated'* (Participant 8, a 52-year-old female). Participants further explained that the long-term benefits of engaging in physical activity, such as improvements in post-concussion symptoms and mental health, outweighed the short-term symptom exacerbation experienced, '*I made a commitment to do my exercises everyday. While I'm a bit bombed out after, overall, I'm feeling better, my body feels better, it helps me to deal with the mental health aspects because of the endorphins. I think it's contributing to neurological maintenance and repair'* (Participant 11, 44-year-old male).

The capacity to take on more physical activity was associated with improved mental health, as this prompted the sense of returning to normalcy (i.e., baseline levels of physical activity prior to their concussion/mild TBI). Participants reported improved confidence with being able to resume prior physical activities, as this gave them confidence that they were on the road to recovery, '*Exercise has always been a big portion of my life so if I can resume that, it gives me confidence the rest will fall into place*' (Participant 9, 52-year-old female). Other participants recognised that they would never recover to their previous levels of physical function and were accepting of this by adapting their lifestyle to meet their functional limitations, *'You can get back to 90% or whatever function I am but you have to make accommodations and accept that you're where you at now. Work with what you've got instead of trying to be what you think normal is'* (Participant 6, 49-year-old female). These adaptations were demonstrated by participants seeking less demanding occupational roles and playing sports with no or less contact. Participants also associated increased physical activity levels with an improvement in fatigue levels and post-concussion symptoms, which in turn improved mental health, '*My mood was pretty bad to start with the concussion but overtime, definitely improved, with more activities, I'm doing more activities now and my psychology, symptoms, all that has improved'* (Participant 2, 19-year-old female).

7.3.2 Opportunity

Environment, sensory overload, and assistive items

Participants reported their environment as impacting their ability to undertake physical activity. They stated that their community environment was unsafe for walking or commuting, leading to an apprehension with partaking in physical activity, '*I've got a set walking lap and it follows the edge of a golf course. I'm kind of weary of the golfers because they are pinging golf balls over the fence and I don't want to get hit by one'* (Participant 13, 53-year-old male). Participants further explained their physical environment, for example, the cold, rainy or even hot weather could reduce their motivation to exercise, especially since their symptoms already dissuaded them. *'When it's raining and cold, the last thing I want to do is go out in the rain and cold knowing that when you get back you've got to shower and change clothes'* (Participant 13, 53-year-old male).

Busy or demanding environments were believed to cause sensory overload, which was acknowledged as a barrier to physical activity. Sensory overload was described as multiple sensory inputs overloading the brain, exacerbating participants' post-concussion symptoms, and diminishing their ability to undertake physical activities, *'The light and noise, when exposed for too long, I get overstimulated and get kind of foggy and sick feeling in my head, then the fatigue kicks in and brain feels slow, body feels slow and it physically feels hard to put one foot in front of the other'* (Participant 7, 31-year-old female). Sensory overload was further explained as the prolonged exposure to, and accumulation of, sensory inputs through the day (i.e., light and noise inputs) preventing their ability to complete physical activities in a timely manner due to having to pace themselves to manage their post-concussion symptoms, *'I have a lot of stimulation through bike riding in the light of day. When I get into the office, I have to get changed and showered and dressed. By the end of it, I'm completely bombed, I'm wobbly, I have brain pressure and sore eyes. I need to sit still and breathe for a bit and let the body catch up. And then I'll go off to work'* (Participant 11, 44-year-old male). There were some interviewees that found their experience of sensory overload too overwhelming in their environment. This meant that they could not tolerate any further physical activities, '*A lot of it is that environmental, like light and noise, just not being able to avoid those things. That's in the workplace. Then you just get too overstimulated at work. And then, gym or social things, or whatever else after work is too hard because work has been too much'* (Participant 7, 31-year-old-female).

There were two specific techniques that participants implemented to address these issues of sensory overload within their environment through undertaking their physical activity in a less stimulating environment and using assistive items to reduce the impact of sensory inputs. Interviewees reported they would alter their environment to minimise light and noise sensitivity by doing their exercises at home, *'I'm home and at home, exercises is good because it's quiet, I can control my environment. It's a space for recovery and doing some exercise stuff at my own pace'* (Participant 7, 31-year-old female). Those who wanted to complete physical activity in the community chose a time when their environment was less busy, *'When I go to the gym because of how loud and really busy, my brain gets overwhelmed very quickly. The only time I can stand to go to the gym is after 11pm because that way, there's fewer people and lessons'* (Participant 10, 35-year-old male). Other participants reported affordable assistive items as a facilitator to their recovery. The use of earplugs, headphones, and sunglasses lessened the light and noise inputs, and therefore prevented sensory overload, *'If I go to the shops or for a walk, I wear sunglasses and earplugs because of the light and noise sensitivity'* (Participant 10, 35-year-old male). Mobile phone applications and calendars were identified as facilitating their adherence to their rehabilitation program and recovery, '*I set reminders in my calendar to do the exercises and I'm able to remember to do those balance exercises, it's supposed to be up to five times a day'* (Participant 1, 48-year-old male).

Social expectations and social support

Although all interview questions were framed in the context of returning to physical activity, many participants spoke about this in the context of returning to their workplace, and completing physical activities as part of their household duties. The working environment and social expectations of the workplace were considered a barrier to returning to work. Participants reported a social expectation from their workplace to return to work at full working capacity while they were still recovering from their post-concussion symptoms, *'I'm supposed to have reduced workload, hasn't worked out that way. I'm doing a minimum of 10 hours a day'* (Participant 1, 39-year-old male). The workplace's lack of understanding of the significance of post-concussion symptoms and the implications made participants feel unsupported and misunderstood, causing their mental health to decline, *'When I went back to work, I had someone say that I needed to have someone with me all the time, which I didn't. It felt very degrading. I haven't lost my brain, just a bit slower than I was'* (Participant 9, 52-year-old female). Therefore, some participants felt as though they were no longer capable of fulfilling their previous work role, *'I'm aware that I'm not at the capacity before concussion. I'm having thoughts about whether I fit in the work environment I'm in now. It might be that in the not too distant future they might make you resign and find a job that's less taxing'* (Participant 13, 53-year-old male).

Receiving social support from their workplace was a facilitator to returning to work. Social support was demonstrated through the workplace providing supports to facilitate with building their work capacity or not returning to work until their post-concussion symptoms had resolved, *'Work is very understanding. They say people are priority one so take as much time as you need, don't push myself or do half days. I'm not feeling pressure to do anything at all'* (Participant 12, 30-year-old male). This also occurred in the sporting environment, whereby participants reported their team supporting their gradual return to sport, *'It's mixed basketball. I, they understand the idea of coming back when I'm ready'* (Participant 5, 29-year-old male). Having social support in all environments (i.e., work, sport, social) was instrumental in facilitating recovery. The support and accommodation from others allowed participants to focus on their recovery or work within their functional limitations, allowing them a graded approach to resuming prior physical activities, *'Social support in terms of my husband, family, workplace. They've all been supportive. I've been able to drop hours and pick it back up at work. Family, we'll catch-up at the house or they're quite mindful to pick somewhere quieter. It's all helpful'* (Participant 7, 31-year-old female).

7.3.3 Motivation

Symptoms and health professional support

Support from healthcare professionals was associated with motivation, beliefs, and goals about undertaking physical activity. All participants referred to symptoms as a barrier to physical activity. Symptoms were categorised as cardiovascular and physical function, cognitive symptoms, headaches and migraines, post-TBI related outcomes and vestibular symptoms. The majority of participants reported several symptoms significantly impacting them both physically and mentally, '*I would put post-concussion syndrome up there(…) It just doesn't affect the brain, it affects the entire body, it's both a mental and physical disorder'* (Participant 10, 35-year-old male). Symptoms physically limited participants from undertaking physical activity, or the fear of exacerbation of symptoms prevented them from undertaking physical activity, '*There's always nausea. The last thing I want to do is stay home but I mean, even trying to undertake a simple task, I quickly realise my limitations. I have a fear of falling over, moving around so then I don't* (Participant 10, 35-year-old male).

Health professional support involving medical and allied health professionals was reported by eleven participants as increasing their motivation to participate in physical activity through education, advice, and reassurance that exercise would not aggravate their symptoms and was required as part of their rehabilitation, *'The fear of repercussions by that point was huge. It took my GP pushing me. GP said no, you need to increase gently, push your heart rate a little further and go ride a little bit longer* (Participant 6, 49-year-old female). Participants also identified allied health professionals as facilitating their return to physical activity, *'I've had speech pathology with memory, word finding and cognition for studying. Exercise physiologist and psychologist for returning to AFL, I'm not really sure yet, nervous about that but I'm focusing on returning to the gym. Every time I ran, it felt like those horror movies that went up and down but that's settled with my neurophysio'* (Participant 2, 19-year-old female). This individualised, multidisciplinary approach to care targeted at symptoms appeared to be the key factor for treating post-concussion symptoms that participants could resume their prior physical activities, as they were no longer limited by their symptoms.

Table 7.2 Barriers and facilitators to physical activity following concussion/mild TBI mapped to the TDF and COM-B

TDF	COM-B	Key barriers and facilitators	Example quotes
Physical skills	**Capability – physical** Physical skills, strength or stamina to perform the behaviour	**(B) Fatigue** Mental fatigue Physical fatigue	P2: *I was more tired too, which affects ability to be able to participate in sport and stuff. I think it has affected my mood, which affects ability to participate in sport* P10: *I find myself losing a lot of energy and becoming very nauseated with simple tasks. Prior to my concussion, I could easily do 45 minutes on an exercise bike, now I can do 10 minutes*
		(F) Physical activity	P6: *I was determined not to lose the exercise. I think somebody who wasn't as dedicated would've lost the exercise entirely. I was not going to let that injury take it away from me. I committed to doing a little bit, doing it everyday, increasing little by little* P11: *If I'm having a day where I'm really worried about things, where it's giving me too much anxiety, again, that physical exercise really helps to tone that down*
Knowledge **Cognitive and interpersonal skills** **Memory, attention and decision processes** **Behavioural regulation**	**Capability – psychological** Knowledge, psychological skills or stamina to perform the behaviour	**(B) Mental health** Anger and frustration Anxiety Depression Fear and apprehension Reduced confidence Reduced motivation Stress	P5: *I'm sometimes a bit weary because this injury occurred in basketball, getting knocked over. I incurred a blow to the back of the head and then a few months later, I was playing basketball. I didn't incur any direct hit to the head but I did feel the same sort of symptoms that had occurred. I felt slow and then extreme light sensitivity to a point that it felt like a concussion, I couldn't look at my phone, extreme fatigue, and whatnot* P10: *I have a fear of falling over moving around. When I get severe nausea, it brings it on. I'm on antidepressants and that brings me slight feelings of depression knowing that I used to be well, I used to be okay. Now when I get severe nausea, I get depression because I get so sick of the experience*
		(F) Mental health Increased confidence Positive outlook	P6: *I think that physical activity is flushing out my brain, positive effects on your mental health. Even in the limited, I'm rebuilding, I can see I'm improving overtime* P9: *Some days, I would just go two or five minutes on the bike but I'd say, I'm here, I've showed up. 100% it does make me feel better and I'm always so glad I came*
Environmental context and resources	**Opportunity – physical** Environment in terms of time, triggers, resources, locations, and physical barriers	**(B) Environment**	P1: *City council keeps closing off roads and access points making it harder to cycle safely* P13: *My loungeroom floor is laminated so it's slippery. If I get down there, I'm not getting back up again. I'm not doing the exercises where I'm required to get down on the ground because I'll be spending half a day lying on the floor or struggling to get up and risk hurting myself trying to get up*

		(B) Sensory overload	P7: *The overstimulation, the light and noise and all that kind of stuff, physically like I feel exhausted just trying to walk in a straight line* P10: *The only thing I can do that's a basic task is I'm able to walk. If I'm standing on a busy street, and there's a lot of busy traffic around me, just taking into the sights and sounds, and the movement is enough to give me severe nausea*
		(F) Environment	P3: *I'll go out even if it's dark to walk, it's safe and well lit roads* P9: *We live on 20 acres so I walk up to the sheds and down to the sheds, and we've got animals, so I'm going there a couple of times a day. And then I've done half an hour walk, just like incidental walking through the day*
		(F) Assistive items	P4: *When I'm using the walker to walk, I'm very safe because I've got brakes so you can hold on, lean into it or sit down* P11: *I've got treatment through the types of glasses that I wear to help manage the changes to visual acuity but also an overactive peripheral vision*
Social influences	**Opportunity – social** Social in terms of interpersonal influences, social cues and cultural norms	**(B)Social expectations**	P1: *There's an unspoken but obligation around working at full capacity and you've got to be available* P2: *I definitely felt the pressure to return straightaway back to everything and I used to work a lot too, not recognising that I couldn't work as much*
		(F) Social support	P4: *I've got exercises that I do at home at night and one of my boys helps me with it. I have my workers that help me do that as well. On the weekend, we go to a big park and go for a walk with the dogs. My wife, she works full time and gets tired but she's always looking out for me* P12: *My partner, she did everything for me, cooking, cleaning. Now I'm feeling a bit better, I can help more with supper*
Intentions **Beliefs about capabilities** **Optimism** **Intentions** **Goals** **Beliefs about consequences**	**Motivation – reflective** Reflective in terms of self-conscious planning and evaluations about beliefs	**(B) Symptoms** Cardiovascular and physical function Cognitive symptoms Headaches and migraines Post-TBI related outcomes Vestibular symptoms	P5: *I did feel there was some brain fog, I did feel a bit slower, my cognitive processing, I wasn't able to play sport or anything like that, coordination was off* P14: *With my perception sort of issues, my vision is a bit off putting sometimes when you're running along, things don't look as they did before. I suppose, just all the symptoms dampens your enthusiasm*
Reinforcement **Emotion**	**Motivation – automatic** Automatic in terms of processes involving wants,	**(F) Health professional support**	P7: *I had overloaded in terms of number of appointments and that was actually a barrier, having to travel to different appointments so we worked with the team to cut that down*

	needs, desires, impulses and reflex responses		P8: *When I've had the injections, I have more neck movements. My ability to actually reposition my head has improved. I can do the physio associated balance exercises, that's improved. You feel like you're not walking around in massive amount of pain, which is good for you, your mental attitude*

(B) Barrier
(F) Facilitator
P Participant

7.4 Discussion

This study aimed to gain an enhanced understanding of barriers and facilitators to returning to physical activity following a mild TBI in adults with symptoms lasting >10 days post-injury. Study participants reported on an array of symptoms preventing their ability to return to prior physical activities, including work, sport, exercise, and domestic activities. Four key barriers (fatigue, sensory overload, symptoms, social expectations) and four key facilitators (physical activity, assistive items, social support, health professional support) were identified. Two factors (mental health, environment) were identified as both a barrier and facilitator to physical activity. Study findings highlighted that an interplay of factors, including experienced symptoms, the environment, and the use of assistive items, influence physical activity levels.

The vestibular system works with the visual and somatosensory system to maintain physical function (Akin et al., 2017). In our study, participants reported vestibular symptoms as the most physically debilitating symptom, as this impacted their ability to stand and walk. Some study participants attributed vestibular symptoms as exacerbating their cognitive symptoms, which affected their ability to undertake complex and cognitively challenging tasks, such as work and school. This is supported by a retrospective case series by Alsalaheen et al. (2016), involving adolescents with concussion. Study participants reported vestibular and cognitive symptoms were exacerbated by multiple sensory inputs, which they referred to as sensory overload. This occurred within their complex environments (i.e., in their sporting and work environments), and affected their ability to engage in social roles. Recent studies have highlighted the importance of sensory sensitivities as markers of TBI recovery. In two longitudinal studies, noise sensitivity was found to be a dominant predictor of persistent symptoms (Dischinger et al., 2009; Shepherd et al., 2020). Participants in our study identified removing themselves from the stimulating environment as a strategy for reducing sensory overload. When participants could not remove themselves, they used assistive items to minimise the effects of light and noise to maximise the day-to-day activities they could undertake.

Participants reported that both fatigue and mental health reduced their capability to undertake physical activities. All study participants reported fatigue as a barrier to returning to prior physical activities. In individuals with TBI, cognitive and physical fatigue have been associated with psychiatric symptoms (Schiehser et al., 2017), which may explain why several participants reported they could not differentiate between symptoms of fatigue and poor mental health. Evidence suggests that both symptoms of fatigue and mental health can result from physiological dysfunction, and therefore are exacerbated by physical or cognitive exertion (Ellis et al., 2015), as well as stressors (Hanna-Pladdy et al., 2001). Fatigue can prevent individuals with mild TBI from undertaking social activities and roles that provide them with purpose, meaning and identity (Landau & Hissett, 2008). Participants indicated that avoidance of certain environments is a common strategy to limit symptoms. Removal of an individual from their daily activities and environments can induce anxiety, depression, low motivation (Schiehser et al., 2017) and loss of identity, which are exacerbated by poor perception and stigma from others (Norrie et al., 2010; Todd et al., 2018). Study participants reported an improvement in mental health with increased physical activity. The ability to increase physical activity is an indication of recovery as reflected in other studies reporting the ability to return to prior physical activities (i.e., work and sport), improved fatigue, mental health and physical function (Alarie et al., 2021; Vuu et al., 2022). The link between physical activity and mental health is bidirectional, and it is unclear what cause and effect exists for the participants in this study.

Many participants spoke about the return to physical activity in the context of returning to work, sport, exercise, and domestic activities. This is in line with the definition of physical activity by Caspersen et al. (1985). Findings from the interview data suggest that social expectations, social support, and health professional support interact, influencing physical activity levels. Study participants explained that social expectations involved behaviours anticipated by their social circle, such as returning to their role as an employee, student or teammate. The lack of support and understanding from those around them was felt to negatively impact their mental health. This is consistent with previous research that has demonstrated that individuals with mild TBI face significant challenges in maintaining their social relationships due to a reduction in community participation, causing distress and reduced life satisfaction (Stålnacke, 2007). This is further exacerbated by the social pressures, personal feelings of letting people down, and fear of repercussions of not being able to contribute adequately to society (Kroshus et al., 2015; McLeod et al., 2017). In contrast, participants in our study expressed that social support also facilitated their return to physical activity, as they were given assistance and time to gradually increase their ability to participate in activities to return to their previous physical activity levels, which aligns with previous studies that have reported social support to be a facilitator for returning to work, school or sports (Graff et al., 2021; McLeod et al., 2017; Register-Mihalik et al., 2021; Wildgoose et al., 2022). Interdisciplinary and multidisciplinary approaches to manage persistent post-concussion symptoms have found to be effective in reducing symptoms, and improving mood and quality of life (Jennings & Islam, 2023; Moore et al., 2024). This is consistent with the reports from our study participants, whereby individuals described health professionals working together to achieve their physical activity goal as facilitating their recovery of physical activity.

Our interviewees reported a multitude of symptoms that contributed to limiting their physical activity levels, suggesting that multimodal or multidisciplinary intervention may be required to address these limitations. However, to date, most studies have focused on the impact of specific symptoms, limiting specific physical activities. Kapadia et al. (2019) reported that overall, successful management of post-concussion syndrome requires a multidisciplinary and individualised approach to care. These multidisciplinary interventions should be symptom-based and graded, involve education and counselling, while ensuring consistent collaboration and communication between the disciplines regarding return to physical activities (Al Sayegh et al., 2010; Condor & Conder, 2015; Eliyahu et al., 2016; Mallory et al., 2022; Pundlik et al., 2020; Ramsay & Dahinten, 2020). The integration of multiple healthcare services enhances symptom improvement and the return to physical activities. This multidisciplinary approach allows for addressing a multitude of symptoms concurrently, which is particularly beneficial as mental health symptoms may exacerbate other symptoms and prolong recovery (Cuff et al., 2022; Doroszkiewicz et al., 2021; Lange et al., 2011).

Using the TDF (Atkins et al., 2017) and COM-B (Michie et al., 2011) model to guide the development of the interview and data analysis have enabled the identification of key factors impacting physical activity across all contexts (e.g. social, recreational and occupational). The study findings may inform a more holistic approach to returning to physical activities for adults with mild TBI and prolonged symptoms lasting greater than 10 days. A limitation of the study was that individuals unable to communicate in English were excluded from participation. Individuals unable to look at screens were also excluded, as all interviews were conducted online. These exclusions may have reduced the research team's capacity to report on the potential impact of language barriers or visual inputs as factors influencing the returning to prior physical activities. Another limitation is that despite recruiting nationally, most interview participants were from South Australia, which limits external validity.

7.5 Conclusion

Adults in the general population with prolonged symptoms for greater than 10 days post-mild TBI report that a combination of symptoms, including fatigue and sensory overload, impact their ability to return to physical activity. The environment, social support structures, and access to health professional support are key factors impacting on an individual's return to physical activities. Symptoms can limit physical activities, conversely increased physical activity can improve symptoms. Further research is required with larger sample sizes to determine how key facilitators to physical activity can be incorporated within an intervention for individuals with persistent symptoms following a mild TBI to enhance the recovery of symptoms and physical activity.

Preface

In this thesis five different research designs were employed including a systematic review, clinical audit, observational study, survey study, and qualitative study. This chapter will discuss the key findings from the research presented in Chapters 3 to 7 relating to exercise and physical activity in individuals with persistent symptoms following a mild traumatic brain injury (TBI), whilst answering the three key research objectives of the thesis. Subsequently, it will discuss the implications of mental health, an incidental and significant finding throughout Chapters 4 to 7. The chapter also provides the implications for clinical practice, strengths and limitations of the included studies, and a conclusion and recommendations for future research.

CHAPTER 8: DISCUSSION

Most adults with mild TBI make a full recovery within 10 days, however, up to 31% continue to experience persistent symptoms three to six months post-injury (Makdissi et al., 2013). The findings of Chapters 6 and 7 indicate that some people following a mild-to-moderate TBI can experience symptoms and physical activity limitations up to 15.3 years post-injury. Traditionally, it was considered that "rest is best", however, more recent research suggests that for individuals with persistent symptoms, prolonged rest can lead to deconditioning and secondary complications, and reinforce the persistence of symptoms (Schneider et al., 2013; Silverberg & Iverson, 2013). Therefore, this thesis aims to assess and guide the return to physical activity in people with persistent symptoms following a mild TBI.

8.1 Overall thesis aims and key findings

The subtle nature of persistent symptoms can result in underdiagnosis and inadequate management of long-term effects. Although mild TBI is the most common form of TBI, it has been referred to as a 'silent pandemic' (Thomas et al., 2020a). This term is used because symptoms of mild TBI often resolve spontaneously without intervention, leading to many cases going unrecognized and untreated. With greater recognition that some mild TBI symptoms do not resolve without intervention and that rest is no longer recommended as a pathway to full recovery, especially for individuals with persistent symptoms, more recent research advocates for active rehabilitation. However, much of the evidence that focusses on active rehabilitation for people with mild TBI focusses on the acute, young and athletic population for return-to-sport purposes, which cannot be generalised to those who fall outside of this population. Three key objectives for this thesis aim were identified:

1. **To examine the impact of physical exercise interventions on persistent symptoms.**

The systematic review (Chapter 3) found that the most prevalent interventions were aerobic exercise to treat 'persistent symptoms', whereas vestibular exercises were prescribed to treat migraine, dizziness and headache symptoms specifically. A meta-analysis confirmed that aerobic exercise improved persistent symptoms compared to usual care. A trend was observed of greater exercise intensity (i.e., 80% of the symptom-limited threshold heart rate (HR) achieved on graded exercise testing) and longer exercise duration (i.e., ≥6 weeks) resulting in greater improvement of persistent symptoms following a mild TBI. Only one of the three included randomized controlled trials (RCTs) prescribing vestibular exercise reported an improvement in persistent symptoms when compared to a sham intervention.

Vestibular exercise interventions included a combination of canalith repositioning manoeuvres, and habituation, gaze stabilisation and balance exercises. Furthermore, seven studies included different types of interventions such as education, advice, visualisation and manual therapy alongside an exercise intervention. Three studies utilised a multidisciplinary approach to care. This demonstrates that addressing a diverse range of symptoms requires a multidisciplinary approach, incorporating various treatment modalities for a more comprehensive intervention. The findings reported in Chapters 6 and 7 support this conclusion. Survey respondents reported accessing a variety of healthcare services, while interviewees indicated that a multimodal intervention delivered by a multidisciplinary team enhanced the recovery of persistent symptoms and facilitated the return to physical activity.

2. **To investigate the use of graded exercise testing in the general adult population to assess physiological dysfunction and guide subsymptom threshold exercise interventions.**

The clinical audit and observational study reported in Chapters 4 and 5 found that the inability to reach 90% of an individual's age-predicted HR on the Buffalo Concussion Treadmill Test (BCTT) or Buffalo Concussion Bike Test (BCBT), due to symptom exacerbation, was an indication of physiological dysfunction following mild-to-moderate TBI. Therefore, how close an individual's threshold HR was to 90% of their age-predicted maximum HR provided an indication of how close an individual was to physiological recovery. Other commonly used outcome measures such as the rating of perceived exertion (RPE), test duration and HR recovery (HRR) were less reliable as a true indicator of physiological dysfunction, as they can be affected by other factors including having a history of a psychological condition, experiencing higher levels of mental symptoms at the time of the test, and levels of physical activity in the past week. Generally, the threshold HR forms the basis of the aerobic exercise intensity. As supported by the systematic review in Chapter 3, an aerobic exercise program at 80% of the symptom-limited threshold HR can improve persistent symptoms compared to usual care. The BCTT and BCBT were safe to use in a chronic and mild-to-moderate TBI population, as no adverse events occurred.

3. **To explore factors that impact return to physical activity in the general adult population.**

Chapters 6 and 7 explored the factors that impact upon the return to physical activity in individuals with mild-to-moderate TBI symptoms lasting >10 days, utilising the Capability, Opportunity and Motivation-Behaviour (COM-B) model, a behaviour change model as a framework. Survey participants reported a reduction of physical activity levels post-TBI (up to 15.3 years post-injury) compared to pre-TBI and identified that factors related to physical and psychological capabilities, and physical opportunities influenced their return to physical activity (Chapter 6). It emerged that participants who reported experiencing mental health symptoms (i.e., depression and/or anxiety), perceived a greater impact of factors relating to psychological capability, physical opportunity, and reflective and automatic motivation on their ability to return to prior levels of physical activity. In

Chapter 7, adults post-mild TBI (up to 5.2 years post-injury) shared how a combination of symptoms negatively influenced their motivation to return to physical activity, resulting in fatigue and sensory overload, affecting their physical capability and opportunity to return to physical activity. Poor mental health and restrictive environmental factors contributed to the barriers to physical activity, but conversely environments that were supportive, and did not cause sensory overload, facilitated improved levels of physical activity and in turn improved mental health. Increasing physical activity was further facilitated by the positive input from health professionals and social support, and the use of assistive items to decrease sensory overload.

8.2 Use of the Buffalo Concussion Treadmill Test and Buffalo Concussion Bike Test for assessment and re-assessment

8.2.1 Using the Buffalo Concussion Treadmill Test and Buffalo Concussion Bike Test to identify physiological dysfunction

To investigate the use of the BCTT and BCBT for the identification of physiological dysfunction and exercise prescription following a mild-to-moderate TBI, a clinical audit and observational study were undertaken (Chapters 4 and 5). Following a mild TBI, individuals may experience persistent symptoms and exercise intolerance, which is referred to as physiological dysfunction of the autonomic nervous system (ANS) (Ellis et al., 2015; Kozlowski et al., 2013). Although there is no gold standard for assessing physiological dysfunction, graded exercise tests have an advantage over other tests given that they provide objective information and reduce reliance on subjective symptom reporting, which may be unreliable or underreported (Kerr et al., 2015; Meier et al., 2015).

The most recent consensus statement on concussion states that, *“Healthcare professionals with access to exercise testing can prescribe subsymptom threshold aerobic exercise within 2-10 days after sport-related concussion, based on the individual’s HR threshold that does not elicit more than mild symptom exacerbation during the exercise test”* (Patricios et al., 2023, p. 701). The use of the BCTT for diagnosing physiological dysfunction and monitoring physiological recovery are supported by the referenced studies within the consensus statement (Leddy, Haider, Ellis, et al., 2019; Leddy et al., 2021) and two systematic reviews (Haider et al., 2023; Quatman-Yates et al., 2018). However, most of the literature investigating the BCTT have been in acute, young or athletic populations for return-to-sport purposes (Chizuk et al., 2021; Haider, Leddy, et al., 2019; Leddy, Haider, Ellis, et al., 2019; Leddy et al., 2021; Quatman-Yates et al., 2018). This limits generalisability to people with mild TBI in the general population. Like most existing literature, the research included in this thesis focussed on the BCTT rather than BCBT, as the BCTT is the more commonly used version of the two. This may be due to the fact that the treadmill version stimulates functional movement (i.e., walking), whereas the bike version is more so used for people with significant vestibular or orthopaedic issues that prevent them from standing to undertake a treadmill test safely (American College of Sports Medicine, 2021).

The research presented in this thesis explored the use of the BCTT for adults with mild-to-moderate TBI who on average experienced chronic symptoms. Participants were not excluded based on the cause of injury, prior medical history, or athletic status, which are known to be factors that complicate recovery (Déry et al., 2023; Tator et al., 2024). No adverse events were reported in the findings of Chapters 4 and 5, suggesting that the BCTT was safe to use in a complex, chronic general population with mild-to-moderate TBI. This may have been due to the graded approach and symptom-limited nature of the BCTT protocol, allowing individuals to terminate the test at any point for any reason. This ensures that participants can safely explore their symptom-limited threshold within the constraints of their ANS, thereby minimising the risk of symptom exacerbation.

The results suggest that the inability to reach 90% of an individual's age-predicted maximum HR due to symptom exacerbation indicates physiological dysfunction (Chapters 4 and 5). The threshold HR (i.e., the HR achieved at test termination relative to their individualised age-predicted maximum heart rate) emerged as the best indicator of physiological dysfunction, as it can be measured independently of levels of physical activity in the past week, mental health symptoms, or a history of a psychological condition. These findings align with published work investigating the use of the BCTT in a young and athletic mild TBI population (Cordingley et al., 2016; Hinds et al., 2016; Leddy et al., 2018; Rutschmann et al., 2021). As reported in Chapters 4 and 5, participants with physiological dysfunction following a mild-to-moderate TBI experienced symptom exacerbation as the intensity of the exercise increased, resulting in an earlier test termination. Similar results have been reported previously when comparing individuals in the chronic stage of mild TBI to uninjured controls (Kozlowski et al., 2013) or symptomatic individuals in either the acute or chronic stage of their TBI to those who have recovered (i.e., no longer symptomatic) (Hinds et al., 2016; Leddy et al., 2010). The results of Chapters 4 and 5 support these findings that irrespective of time since injury or athletic background, the test may be robust enough to be used to monitor for physiological recovery. The proximity of an individual's threshold HR to 90% of their age-predicted maximum HR can indicate how close they are to physiological recovery when the test is repeated (Baker et al., 2012; Leddy, Haider, Ellis, et al., 2019; Leddy et al., 2018; Leddy et al., 2021; Leddy & Willer, 2013).

8.2.2 Factors influencing the performance outcome of the Buffalo Concussion Treadmill Test

A key factor to consider when using the BCTT to assess for physiological dysfunction is the potential impact of mental health on performance and the interaction between mental health and physical activity levels. In Chapter 4 it was observed that patients who had a history of a psychological condition, or reported higher depression scores on the DASS prior to the test, experienced greater symptom severity both before and after testing. Previous studies have found that reporting depression and anxiety as symptoms, or having a history of these conditions, is associated with reports of more severe symptoms. This may be due to mental health predisposition, poor psychological resilience or as a result of sustaining a mild TBI (Doroszkiewicz et al., 2021; Durkis et al., 2019; Weber et al., 2018). The primary criterion for terminating the test was experiencing symptom exacerbation, defined as a 3-point increase in symptom severity on the Visual Analogue Scale (VAS) for those who rated ≤5/10 for baseline VAS, or a 1-point increase for those who rated >5/10 at baseline. Consequently, participants with a history of a psychological conditions or experiencing higher levels of depression at the time of the test are likely to terminate the test earlier due to symptom exacerbation.

Another factor to consider when using the BCTT is the level of perceived exertion at termination of the graded exercise test. Following a mild TBI, patients often report a higher RPE than the associated workload when compared to healthy controls (Chapter 5). Conversely, in people with a mild TBI who terminate a graded exercise test due to symptom exacerbation, they often report a RPE lower than the workload reached at test termination. Taken together, these findings indicate that people with a mild TBI demonstrate a disconnect between the perceived effort and actual workload. This in in agreement with previous studies in which people with mild TBI reported altered levels of perceived exertion relative to workload compared to healthy controls and those who have had a mild TBI but had not yet achieved a complete recovery (Hinds et al., 2016; Kozlowski et al., 2013). The findings of Chapters 4 and 5, and previous literature indicates that RPE is a not a reliable indicator of physiological dysfunction with patients reporting altered levels of perceived exertion relative to workload. This may have implications for the utilisation of the test, as one criterion for terminating the test is the patient reporting ≥19/20 on the Borg RPE. Patients who rate their RPE too high relative to workload may therefore terminate the test too early, resulting in a lower intensity to guide aerobic exercise intervention. Patients who rate their RPE as too low relative to workload may exceed their threshold HR and consequently experience an exacerbation of their symptoms.

Test duration was shorter for individuals with mild TBI when compared to healthy controls (Chapter 5), and among individuals with mild-to-moderate TBI, those who experienced symptom exacerbation had the shortest test duration (Chapter 4). However, Chapter 5 determined that test duration was an unreliable measure of physiological dysfunction. When the 21 adults with mild TBI were sub-grouped to active (n=13) and sedentary (n=8), active adults with mild TBI lasted significantly longer on the BCTT compared to sedentary adults with mild TBI. In these studies, shorter test durations were observed in patients with higher levels of depression and lower levels of physical activity in the past week. From these results, it appears that factors such as levels of physical activity and mental health status can impact test duration on a graded exercise test. Consequently, test duration alone cannot be used to identify or assess physiological dysfunction.

HRR was also influenced by levels of physical activity in the past week. The observational study (Chapter 5) revealed that HRR was lowest in healthy active adults compared to healthy sedentary adults. These findings may be explained by the fact that aerobically fit individuals tend to perform better on exercise tests for measures involving HR and test duration. This superior performance is due to greater parasympathetic activation and sympathetic withdrawal within the ANS during exercise in fit individuals compared to their sedentary counterparts (Borresen & Lambert, 2008; Gibbons et al., 1997).

In summary, despite the availability of a battery of measures in a graded exercise test, most are not reliable for determining the presence of physiological dysfunction. Symptom scoring on the VAS was affected by mental health status. Performance outcomes such as RPE, test duration and HRR were not reliable indicators of physiological dysfunction. This was the result of patients' inability to accurately perceive exertion, and the influence of physical activity levels in the past week on test duration and HRR. The most effective method for identifying physiological dysfunction on the BCTT was the inability to reach 90% of an individual's age-predicted maximum HR due to symptom exacerbation.

8.3 Symptom experience and differential diagnosis

8.3.1 Recognising symptom manifestations

The literature indicates that the chronicity of symptoms following a mild TBI may be related to the amount of force sustained in the TBI (Sterr et al., 2006). Other factors that may play a role are related to the demographics of the individual such as older age (King, 2014a), having a history of a mental health condition (Karr et al., 2021; King & Kirwilliam, 2011) and having a history of a prior TBI (Mooney et al., 2022). In Chapters 4 and 5, participants reported mild-to-moderate levels of depression, anxiety and stress, nearly one third of those included in each study reported a history of a psychological condition, and at least one quarter reported a history of a prior TBI. This may partially explain why participants in Chapters 4 to 7 reported the persistence of symptoms months to years following their initial TBI.

Participants reported an array of physical, cognitive, behavioural and mental health symptoms (Chapters 4 to 7). In order to better manage the range of symptoms experienced following a mild-to-moderate TBI, researchers have attempted to cluster these symptoms broadly into physiologic, vestibulo-ocular and cervicogenic post-concussion disorders (PCDs), and to a lesser extent migraine headaches, which may occur together or separately (Ellis, Leddy, et al., 2016; Ellis et al., 2015). Clustering symptoms facilitates the assessment and management of these diverse symptoms. Physiological dysfunction or physiological PCD is a collection of symptoms that are exacerbated by physical or cognitive exertion. These symptoms commonly include, but are not limited to, headache, nausea, vomiting, light sensitivity, noise sensitivity, dizziness, fatigue and difficulty concentrating (Ellis, Leddy, et al., 2016; Ellis et al., 2015). As supported by Chapters 4 and 5, exercise tests such as the BCTT and BCBT can assess and diagnose physiological dysfunction, whereby an inability to reach 90% of an individual's age-predicted maximum HR due to symptom exacerbation was an indication of physiological dysfunction.

8.3.2 Using the Buffalo Concussion Treadmill Test and Buffalo Concussion Bike Test for differential diagnosis

Symptom exacerbation during the BCTT or BCBT implies that complete recovery has not yet occurred, due to the presence of symptoms that indicate a physiologic PCD (Ellis et al., 2015). However, these symptoms fall under more than one PCD. For example, physiological PCD includes symptoms such as headache, nausea and light sensitivity; vestibulo-ocular PCD includes dizziness, nausea, and light sensitivity; and cervicogenic PCD includes headache (Ellis et al., 2015). Therefore, it is recommended that once symptoms are identified on the BCTT or BCBT, further testing specific to the symptoms are conducted to determine which PCD and system dysfunction is dominant. Balance/postural control, vestibulo-ocular reflex and ocular motor assessments are recommended for vestibulo-ocular PCDs (Quintana et al., 2021) and cervical injury assessments for cervicogenic PCDs (Cheever et al., 2016). These specific tests can direct the most appropriate interventions to treat the system dysfunction of the PCD. The findings of the systematic review presented in Chapter 3 confirmed this approach in some cases, finding that subthreshold aerobic exercise was used to treat a variety of 'post-concussion symptoms', whereas vestibular exercise was more so used to specifically treat symptoms of dizziness, migraine and headache.

The BCBT was adapted from the BCTT to allow people with significant vestibular dysfunction to undertake the test safely, as cycling does not stimulate the vestibular system as much as running due to a seated position for exercise testing (Haider, Johnson, et al., 2019). In the presented work, the treating therapist permitted patients with significant vestibular issues to undertake the BCBT rather than BCTT to minimise the exacerbation of vestibulo-ocular symptoms during standing in the clinical audit (Chapter 4). The patients with mild TBI in Chapters 4 and 5 may therefore have been experiencing both symptoms of vestibulo-ocular and physiological dysfunction, whereas the cohort of patients undertaking the BCBT in Chapter 4 may have only experienced physiological symptoms due to minimising the stimulation of the vestibulo-ocular system in sitting. Therefore, the BCTT may be able to differentiate symptoms from a vestibular or physiological origin, and both the BCTT and BCBT can be used to identify symptoms of a physiological origin.

In the clinical audit (Chapter 4) comparing the BCTT to BCBT, a statistically significant greater threshold HR was achieved on the BCTT compared to the BCBT. This should be interpreted with caution given that the study was not adequately powered to assess such a difference (i.e., 42 participants completed the BCTT versus 7 participants completing the BCBT). More rigorous studies specifically comparing the BCTT and BCBT have found that both tests demonstrate similar threshold HRs and test durations (Graham et al., 2021; Haider, Johnson, et al., 2019), indicating that the BCBT does not compromise the effectiveness of the test for identifying physiological dysfunction and exercise intolerance. This means that if a patient is unable to undertake the BCTT due to vestibulo-ocular symptoms, they can still undertake the BCBT to identify physiological dysfunction.

8.3.3 The application of the Buffalo Concussion Treadmill Test and Buffalo Concussion Bike Test for people with persistent symptoms

Emerging research suggests that exercise intolerance (i.e., the inability to exercise to an individual's age-predicted maximum HR due to symptom exacerbation) is prevalent in all types of PCDs (Antonellis et al., 2024), although the underlying mechanism remains unclear. Both the survey and qualitative chapters revealed a wide range of time since injury among participants. Survey respondents recounted an array of symptoms and indicated, on average, high levels of physical activity before their TBI, but low levels of physical activity following their TBI, with an average of seven hours of sitting per day. All participants interviewed in the study presented in Chapter 7 reported that their symptoms, including fatigue, sensory overload and mental health were a barrier to physical activity. This reduction in physical activity levels aligns with previous findings in people experiencing persistent symptoms following a mild TBI (Mercier et al., 2021; Pellerine et al., 2024).

In Chapter 5, healthy adults and adults with mild TBI who had lower levels of physical activity were observed to have shorter test durations due to reaching 90% of their age-predicted maximum HR faster. Extended periods of rest and reduced cardiovascular fitness can lead to physical deconditioning or further physiological dysregulation. This can manifest as decreased cerebral blood flow, parasympathetic dominance rather than sympathetic dominance, and reduced neuroplasticity, which are observed following a mild TBI and in those with sedentary behaviours (Chin et al., 2015; Goldstein et al., 1998; Mossberg et al., 2007; Tan et al., 2014). Previous research has demonstrated a relationship between lower physical activity levels and poorer mental health (De Moor et al., 2006; Kim et al., 2012). Aerobic exercise has been shown to support improvement in mental health (Schuch et al., 2016; Silveira et al., 2013), cardiovascular fitness (Chin et al., 2015; Hassett et al., 2017), persistent symptoms and return to physical activity (Lal et al., 2018; Langevin et al., 2020; McIntyre et al., 2020; Powell et al., 2020), all of which were symptoms reported by individuals following a mild-to-moderate TBI (Chapters 4 to 7). Therefore, all individuals following a mild-to-moderate TBI should be recommended to undertake a validated and reliable graded exercise test such as the BCTT or BCBT, and aerobic exercise as guided by the individual's age-predicted maximum HR achieved on exercise testing. This approach would facilitate the prevention of deconditioning and address physiological dysfunction, as individuals with mild TBI can exercise within their body's autoregulatory capabilities to restore their ANS without symptom exacerbation (Ellis, Leddy, et al., 2016; Leddy & Willer, 2013).

8.4 Incorporating exercise as a more comprehensive, multidisciplinary intervention

8.4.1 Aerobic and vestibular exercise for improving persistent symptoms

The systematic review's meta-analysis confirmed that aerobic exercise improves persistent symptoms compared to usual care. Aerobic exercise programs reporting greater improvement in persistent symptoms were generally of greater intensity (i.e., ≥80% of the symptom threshold HR) and longer duration (i.e., ≥6 weeks) (Chapter 3). The intensity of aerobic exercise appears to be the primary driver of improvement in persistent symptoms, as three studies in the systematic review found that subthreshold aerobic exercise was more beneficial than light exercise for improving persistent symptoms (Bailey et al., 2019; Kurowski et al., 2017; Leddy, Haider, Ellis, et al., 2019). These findings have been corroborated by other systematic reviews, which also support the prescription of aerobic exercise at 80% of the symptom threshold HR for 20 minutes, 5 to 6 days per week for 6 to 8 weeks (Howell et al., 2019; McIntyre et al., 2020). These aerobic exercise interventions were found to be safe to implement in the acute and chronic stage of a mild TBI (Cordingley & Cornish, 2023; Powell et al., 2020), as individuals exercised below the point of symptom exacerbation.

The systematic review revealed limited evidence for the use of vestibular exercise in improving persistent symptoms, with only three studies meeting the inclusion criteria. All vestibular exercise interventions commenced at least 10 days post-injury, with only one study reporting a significant improvement in persistent symptoms, after 4 weeks, for participants with migraine symptoms when compared to a sham intervention (Reneker et al., 2017). Other systematic reviews that did not limit study type to RCTs included more studies and found that vestibular exercise improved vestibulo-ocular symptoms such as headache, dizziness, nausea, fogginess and reduced balance in people with mild TBI (Aljabri et al., 2024; Kinne et al., 2018; D. A. Murray et al., 2017). However, the optimal dosage could not be ascertained due to the heterogeneity of the interventions (Aljabri et al., 2024; Kinne et al., 2018; D. A. Murray et al., 2017). The most recent consensus statement concurs with the findings of the systematic review of Chapter 3, recommending that subsymptom threshold aerobic exercise can be commenced within 2 to 10 days post-injury, and cervicovestibular rehabilitation for symptoms of dizziness, headache and neck pain symptoms persisting for greater than 10 days (Patricios et al., 2023).

8.4.2 Multidisciplinary and multimodal approach to care

Due to the array of symptoms experienced following a mild-to-moderate TBI, a multidisciplinary approach to care is imperative for specialised input. In the systematic review (Chapter 3), three of the studies utilised a multidisciplinary approach to care (Chan et al., 2018; Kleffelgaard et al., 2019; Rytter et al., 2019), all of which found improvements in persistent symptoms when compared to usual care or another physical intervention. A multidisciplinary approach to care was further supported by interviewees in Chapter 7, who specified health professional support as a key facilitator for the recovery of symptoms and physical activity. The interviewees described how different health professionals were responsible for addressing various symptoms, allowing for specialised care for the array of symptoms that were experienced following a mild TBI. A systematic review of multidisciplinary care for people with persistent symptoms following a mild TBI found this approach more beneficial compared to usual care for reducing persistent symptoms (Moore et al., 2024). The review identified physicians, neuropsychologists, occupational therapists and physiotherapists as the most commonly reported healthcare providers (Moore et al., 2024). Different disciplines have distinct roles in the management of individuals with persistent symptoms, but when multiple disciplines collaborate to address the experienced symptoms, patients have the best chance of a full recovery (Makdissi et al., 2017; Schneider et al., 2023; Schneider et al., 2017). The primary role of physiotherapists is to provide rehabilitative interventions and strategies that aid in the recovery of physical function (Brown & Camarinos, 2019). This may explain why participants in the survey (Chapter 6) reported physiotherapy service as the most commonly accessed healthcare service for returning to physical activity.

Identifying and grouping the symptoms into PCDs is important for targeted and specialised healthcare delivery (Ellis, Ritchie, et al., 2016; Jennings & Islam, 2023; Moore et al., 2024; Winkler & Taylor, 2015). A medical professional is usually involved in the initial assessment and subsequently facilitates the referral process to other disciplines depending on assessment findings and symptoms experienced (Ellis, Ritchie, et al., 2016; Nguyen et al., 2024; Zasler et al., 2019). The literature recommends that for patients with more severe or chronic symptoms following a TBI, having a case manager can enhance the coordination, monitoring, and review of healthcare services provided to the patient (Lannin et al., 2014; Moore et al., 2024). A case manager would be beneficial to the patient cohort included in this thesis. All participants presented with symptoms that did not resolve within 10 days and on average were in the chronic stage of their TBI. Furthermore, Chapters 4 and 5 included patients with mild-to-moderate TBI, and Chapters 6 and 7 found that participants were accessing a variety of healthcare services.

The systematic review included seven studies that incorporated multiple components in addition to an exercise intervention, such as education, advice, visualisation and manual therapy. Some studies recommend that aerobic exercise should be combined with cognitive behavioural therapy, and vestibular exercise should include cervical therapy (Makdissi et al., 2017; Reid et al., 2022). However in these multi-component studies it is difficult to isolate the specific effects of the exercise intervention (Thomas et al., 2017). Exercise should be considered as part of a broader rehabilitation program (Lyons et al., 2022; McIntyre et al., 2020; Reid et al., 2022; Schneider et al., 2023; Schneider et al., 2017).

Participants reported several factors impacting their return to physical activity following a mild-to-moderate TBI. Framed within the COM-B behaviour change model (Michie et al., 2011), participants in Chapter 6 reported factors within the domains of physical and psychological capability, and physical opportunity as influencing the return to physical activity. In Chapter 7, four of the six barriers for returning to physical activity were related to symptoms following a mild TBI. The adverse effects of persistent symptoms following a mild TBI on an individual's participation in social, leisure, domestic and vocational activities have previously been reported (Cooksley et al., 2018; Graff et al., 2021; Mercier et al., 2021). Currently, there are established guidelines for returning to school and sport (Patricios et al., 2023), and to a lesser extent for returning to work (Cancelliere et al., 2014; Marshall et al., 2015). The variability in work-related guidelines may be due to the diverse range of occupations requiring different levels of mental and cognitive activity. In the case of returning to sport, a symptom exacerbation threshold HR is recommended to guide the individual through the stages of returning (Patricios et al., 2023). In contrast, returning to school and work is guided by the ability to complete mental activities (Cancelliere et al., 2014; Marshall et al., 2015; Patricios et al., 2023). These specific return to sport, school or work guidelines require a graduated stepwise approach to physical activity, starting with basic, less physically and cognitively stimulating activities, and progressing through stages to more stimulating activities as tolerated by the individual (i.e., no more than mild symptom exacerbation) (Cancelliere et al., 2014; Marshall et al., 2015; Patricios et al., 2023). An individualised or targeted approach to care based on symptom presentation and physical activity goals has been shown to enhance the recovery of persistent symptoms following a mild TBI (Kapadia et al., 2019; Marwaa et al., 2023; Reid et al., 2022; Schneider et al., 2023; Thomas et al., 2017). This further highlights the importance of using a multidisciplinary and multimodal approach to address individual symptoms, as symptoms are a driver of behavioural change and therefore recovery of physical activity.

8.5 Mental health implications following a mild traumatic brain injury

8.5.1 The implications of mental health symptoms

Patients in Chapters 4 and 5 reported mild-to-moderate levels of depression, anxiety and stress. While exploring the impact of mental health on recovery was not identified as a key thesis objective and individual studies were not designed to specifically measure or investigate mental health, it had notable implications on assessments and interventions throughout the research. Poor mental health is common across patient cohorts with all TBI severities, and can arise from multiple aetiologies such as genetic predisposition, psychosocial factors, neurobiological consequences of the TBI or may co-exist alongside other conditions (American Psychiatric American Psychiatric Association, 2022; Brent & Max, 2017; Doroszkiewicz et al., 2021; Lange et al., 2011; van der Horn et al., 2020). Mental health issues may be influenced by symptoms impacting a person's ability to participate in their usual activities (DiFazio et al., 2016). Although it may be not always be possible to pinpoint the aetiology, poor mental health is associated with increased symptom reporting (Ho et al., 2020; Lange et al., 2011) and chronicity of symptoms (Doroszkiewicz et al., 2021).

In Chapter 4, presenting the clinical audit study, patients who reported a history of a psychological conditions experienced higher symptom severity before the test. Additionally, a higher level of depression post-TBI at the time of testing was associated with higher symptom reporting at test termination. The literature has shown that mental health affects symptom reporting (Ho et al., 2020; Lange et al., 2011). These findings have implications for the tests, as patients with a history of a psychological condition or experiencing depressive symptoms following their mild TBI may be more likely to experience more severe symptoms at baseline. Consequently, they may terminate the test earlier (i.e., due to ≥3-points on the VAS or a 1-point increase for those who rated >5 on the VAS prior to test commencement). Further research needs to be undertaken to investigate the link between mental health status and symptom reporting on the VAS, as well as other measures of post-mild TBI symptomatology such as the Post-Concussion Symptom Scale (Lovell & Collins, 1998) and Rivermead Post-Concussion Symptoms Questionnaire (King et al., 1995), which were reported on in Chapters 3 and 4. The impact of mental health issues may influence the level of exercise that patients can achieve, and reduced levels of physical activity can exacerbate mental health issues. This potential cycle could result in longer recovery times, highlighting the importance of a multidisciplinary and multimodal approach to care to ensure that mental health symptoms are sufficiently addressed. To further investigate interventions that support mental health, future research should consider intervention studies that incorporate psychological services within a multidisciplinary team approach to determine whether this improves both mental health symptoms and symptoms associated with mild TBI.

In Chapter 6, participants who reported mental health symptoms agreed that factors related to psychological capability, physical opportunity, and reflective and automatic motivation influenced their return to physical activity. Participants indicated that good mental health can facilitate physical activity, while poor mental health can be a barrier, highlighting the importance of addressing mental health (Chapter 7). Previous research reports that persistent symptoms decreased physical functioning (i.e., physical activity) and prevented individuals from participating in meaningful activities which in turn reduced their quality of life (Landau & Hissett, 2008; Scholten et al., 2015; Voormolen, Polinder, et al., 2019). This may be impacted by motivation, as identified by participants in the survey (Chapter 6), where reflective and automatic motivation were significantly worse in those with mental health symptoms. All interviewees reported symptoms as a motivational barrier. Within the COM-B model domains, reflective motivation refers to reflective processes (i.e., planning and evaluations), while automatic motivation refers to automatic processes (i.e., desires, impulses and reflex responses) (Michie et al., 2011). As expressed by interviewees in Chapter 7, the persistence and impact of symptoms decreases their motivation to engage in physical activity.

Some individuals highlighting that they could not distinguish between the symptoms of poor mental health and symptoms of mild TBI, particularly for symptoms such as low motivation and fatigue.

8.5.2 Addressing mental health symptoms

Physiological dysfunction of the ANS occurs both in mental health conditions, and following a mild TBI, resulting in overlapping symptoms (Baker et al., 2019; Purkayastha et al., 2019). For example, fatigue, cognitive issues, low motivation and irritability are common symptoms in mental health conditions and symptoms of physiological dysfunction following a mild TBI (American Psychiatric American Psychiatric Association, 2022; Ellis et al., 2015). Aerobic exercise can improve symptoms of mental health conditions and mild TBI through similar mechanisms, such as enhancing neurotrophic factors, cognitive functioning, neurogenesis and neuroplasticity (Deslandes et al., 2009), as well as social engagement (Schuch et al., 2016; Tate et al., 2015). The systematic review in Chapter 3 identified that aerobic exercise improves physiological symptoms, but its impact on psychological outcomes was less clear. One study compared aerobic exercise to usual care and found no significant difference in depression measures between the two groups after 6 weeks (Chan et al., 2018). However, another study that included aerobic exercise, psychoeducation, and sessions with a neuropsychologist reported a significant improvements in depression at a 6 month follow-up (Rytter et al., 2019). This discrepancy may highlight that more time is required to observe improvements in depression outcomes and may be attributed to additional intervention components (i.e., psychoeducation) and involvement of a multidisciplinary team (i.e., neuropsychologist) tailored to address mental health symptoms. Psychological interventions have been shown to improve psychological outcomes and persistent symptoms following a mild TBI (Al Sayegh et al., 2010; Sullivan et al., 2020; Teo et al., 2020). When psychological interventions (i.e., cognitive behavioural therapy) and health professionals (i.e., psychologist, psychiatrist) are added to an aerobic exercise intervention, this has shown to further enhance recovery (Makdissi et al., 2017; McCarthy et al., 2016; McCarthy et al., 2021). Additionally, motivational interviewing, a directive, client-centred counselling approach to elicit behaviour change, can be utilised to help clients explore their goals and resolve ambivalence, thereby supporting engagement in rehabilitation and therapy (Medley & Powell, 2010).

Despite Chapters 4 to 7 identifying the prevalence of mental health issues among individuals following a mild-to-moderate TBI, only two respondents in the survey reported utilising psychological services (Chapter 6). This is consistent with evidence that patients following a mild TBI tend not to seek support from mental health services (Agnihotri et al., 2021) unless they have a pre-existing mental health condition (Jimenez et al., 2017) or it is incorporated into a specific concussion or TBI clinic (Baker et al., 2019; Vargo et al., 2016). Healthcare professionals specialising in mental health play a crucial role in recognising and integrating interventions for cognitive and psychological symptoms with exercise interventions and other forms of allied health interventions (Baker et al., 2019). In Chapter 7, some participants expressed that they had difficulty differentiating between mental health symptoms and symptoms of a mild TBI such as low mood and motivation. Others described how symptoms of fatigue, low motivation and sensory overload prevented them from actively seeking healthcare services including psychological support. Health professionals across all disciplines should aim to recognise when a patient is experiencing poor mental health and advocate for early psychological interventions. This approach can help prevent the chronicity of symptoms and further mental health deterioration (Agnihotri et al., 2021; Baker et al., 2019; Leddy et al., 2023; Leddy, Haider, Ellis, et al., 2019; Leddy et al., 2021; Rytter et al., 2019; Schneider et al., 2017). This is particularly relevant to the cohorts within the thesis, as most individuals were in the chronic stage of their TBI, and physical activity was negatively affected by their mental health symptoms.

8.6 Implications for clinical practice

The findings within the thesis have demonstrated that following a mild-to-moderate TBI, individuals experienced symptoms lasting for months to years. As shown in Chapters 6 and 7, these symptoms decreased physical activity levels and influenced the return to physical activity. Clinicians utilising graded exercise tests can determine physiological dysfunction through the inability of an individual in reaching 90% of their age-predicted maximum HR due to symptom exacerbation (Chapters 4 and 5). These tests can be used for reassessments, whereby the proximity to 90% of the age-predicted maximum HR could determine how close an individual is to physiological recovery. The HR achieved at test termination forms the symptom threshold HR used to guide aerobic exercise intensity prescription. The systematic review (Chapter 3) supports the intensity of 80% of the symptom threshold HR achieved at test termination for improving persistent symptoms following a mild TBI. Other outcomes on the BCTT or BCBT such as perceived exertion, test duration and HRR should be interpreted with caution. These outcomes were affected by factors including pre-existing psychological conditions, higher levels of post-TBI depression, and physical activity levels in the past week. Overall, the results presented in Chapters 4 and 5 demonstrated that the tests were safe to use in a chronic, non-athletic, mild-to-moderate TBI population, as no adverse events occurred.

An incidental finding in this body of research was that many participants with ongoing symptoms following mild-to-moderate TBI reported mental health symptoms. These mental health symptoms negatively affected symptom reporting and the return to physical activity. Despite this, participants in Chapter 6 reported psychological services as the least accessed healthcare service. However, interviewees in Chapter 7 indicated that when mental health is addressed through professional support, it facilitates the recovery of physical activity. Interviewees also indicated that increasing physical activity and adopting a multidisciplinary approach to care, tailored to individual symptoms and goals for returning to physical activity, can enhance symptom recovery and improve physical activity levels. Therefore, physical exercise interventions can be enhanced through the inclusion of multiple disciplines and components to address both symptoms of mild-to-moderate TBI and mental health symptoms.

Based on the findings of the thesis, healthcare providers should consider implementing the following into clinical practice when involved in the care of individuals with a mild-to-moderate TBI:

- Routinely using the BCTT or BCBT in conjunction with other assessments to identify and monitor physiological dysfunction. The inability to reach 90% of an individual's age-predicted maximum HR due to symptom exacerbation provides an indication of physiological dysfunction. The proximity of the threshold HR to 90% of the individual's age-predicted maximum HR provides an indication of how close the individual is to physiological recovery.

- Prescribing aerobic exercise at 80% of the symptom threshold HR achieved on the BCTT or BCBT to improve persistent symptoms, whilst incorporating multiple intervention components and disciplines to target an array of symptoms.

- Physical exercise intervention integrated within a multidisciplinary approach to care, based on the specific symptoms experienced by each individual and their physical activity goal.

- Healthcare professionals should remain attentive to the psychological challenges that individuals with mild-to-moderate TBI may experience. They should consider screening for psychological issues, identifying those in need, and referring patients to psychological services if indicated or when it falls outside their scope of practice.

8.7 Strengths and limitations

The body of evidence presented in this thesis significantly contributes to current knowledge, by enhancing the understanding of assessment and management of people with persistent symptoms following a mild-to-moderate TBI. This research focused on a more complex population than much of the existing literature, as participants were, on average, older and in the chronic stage of their mild-to-moderate TBI, thus expanding the population scope. The findings highlighted the implications of mental health on assessments and symptom recovery, as well as the experiences of people with persistent symptoms in their efforts to regain physical activity. This knowledge equips healthcare professionals to better support the recovery in individuals who experience symptoms beyond 10 days post-injury, supporting the return to their physical activities and enhancing their quality of life.

The strength of the individual studies within the thesis are multifaceted and contribute to the robustness of the research. For the clinical audit and observational study, recruitment and clinical insights were supported by clinicians specialising in TBI from a mild TBI service. This collaboration enhanced the clinical relevance and applicability of the findings. The systematic review employed a comprehensive and rigorous approach to evaluating the quality and reliability of included studies. The use of established tools such as the Critical Appraisal Skills Programme (CASP), Template for Intervention Description and Replication (TIDieR) and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) allowed for well-found recommendations for interventions. While individual RCTs had small samples and effect sizes, this limitation was addressed through a meta-analysis examining the effect of aerobic exercise compared to usual care on persistent symptoms. The observational study was the first to investigate the use of the BCTT to identify physiological dysfunction whilst considering levels of physical activity. The comparison between healthy active and sedentary adults with age and gender matched individuals with a mild TBI highlighted performance indicators influenced by physical activity levels. Another strength was that the survey and qualitative study drew from the same cohort, which allowed for greater exploration and analysis of findings. Both these studies were also informed by the COM-B model (Michie et al., 2011), which facilitated the understanding of factors contributing to behavioural change. All studies adhered to appropriate reporting guidelines, ensuring a systematic approach to dissemination of findings. These included the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for the systematic review, Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for the observational study, Checklist for Reporting Results of Internet E-Surveys (CHERRIES) for the survey and Consolidated Criteria for Reporting Qualitative Research (COREQ) for the qualitative study.

The limitations of the studies within this thesis are acknowledged and provide important context for interpreting the results. A limitation of this thesis was the lack of standardisation in the terminology of concussion and mild TBI, and the symptoms following. Terms varied regarding the type of symptoms, the duration of symptoms, and the outcome measures applied following TBI, complicating comparisons both between chapters of this thesis and with published literature. Future research should prioritise the standardisation of terminology for concussion or mild TBI, post-TBI symptoms, and the outcome measures used to assess individuals following mild TBI. Since the clinical audit was retrospective, missing data meant that not all patients seen in the service were included in the study. The observational study faced several limitations. Due to the COVID-19 pandemic lockdowns, there were difficulties with recruitment leading to unequal group sizes. The healthy sedentary adults had the smallest number of participants due to difficulties in engaging this population within the age and gender matching constraints. Contact restrictions prevented core temperature measurements, a physiological measure of ANS function. It would have been beneficial to confirm an expected reduction in the ability to maintain internal body temperature in the presence of increasing exercise workload in individuals following a mild TBI compared to healthy controls. In Chapters 6 and 7, time since injury ranged from >10 days post-injury to 15.3 years post-injury. At the time of study design, the 5th Consensus Statement on

Concussion defined 'persistent symptoms' as symptoms lasting >10 days (McCrory, Meeuwisse, et al., 2017). With such a broad time since injury, the results of Chapters 6 and 7 may have been influenced by other factors such as changes to lifestyle or the presence comorbidities. The survey had a reduced number of participants than anticipated. One potentially contributing reason was potential participants reporting screen-related symptom aggravation. Although the sample size was small, statistical analysis was still feasible. Lastly, the qualitative study in Chapter 7 was limited to English speaking participants, potentially missing insights on language barriers influencing the return to physical activity.

Despite these limitations, the overall quality of the research is evident; Chapters 3 to 5 and 7 have either been published or are under review in high quality journals. This adherence to rigorous reporting standards and peer review processes underscores the high quality of research contained within this thesis employed to address the thesis aims and objectives.

8.8 Conclusion and recommendations for future research

This existing research supports the use of exercise testing for identifying physiological dysfunction and aerobic exercise at a symptom-limited threshold HR for improving persistent symptoms of a physiological nature. However, previous studies have primarily focused on acute, young and athletic populations for return-to-sport purposes, limiting generalisability to broader populations. The research within this thesis provides clinical guidance to individuals who were mostly in the chronic stage of their TBI and had other factors impacting recovery, such as poor mental health.

The findings have demonstrated that individuals experience a range of symptoms months to years following their initial TBI, and that these symptoms negatively impact physical activity levels. A meta-analysis confirmed that aerobic exercise improves persistent symptoms compared to usual care, with trends favouring higher exercise intensities (i.e., 80% of the symptom threshold HR) and longer durations (i.e., ≥6 weeks) for improving persistent symptoms. The effects of vestibular exercise on persistent symptoms were less clear. The systematic review additionally highlighted the potential benefits of a multidisciplinary approach to care for improving persistent symptoms. Health professional support was identified as a key facilitator in the recovery of physical activity. Given that the evidence supporting a multidisciplinary approach to care, it is essential to conduct an intervention study that incorporates aerobic exercise intervention as part of a more comprehensive treatment plan delivered by a multidisciplinary team. This study should aim to determine the effectiveness of this approach in improving persistent symptoms compared to aerobic exercise intervention alone.

This research demonstrated the inability to reach 90% of age-predicted maximum HR due to symptom exacerbation on the BCTT or BCBT indicates physiological dysfunction of the ANS following a mild TBI. The tests could be used for re-assessment to provide an indication of how close an individual is to physiological recovery by determining the proximity of the threshold HR to 90% of the age-predicted maximum HR. Other outcome measures such as perceived exertion, test duration and HRR were found to be impacted by a history of a psychological conditions, higher levels of depression post-TBI and levels of physical activity in the past week. Overall, the tests were found safe to use in a mild-to-moderate TBI population that were older and in the chronic stage of their TBI. Future research could explore the potential of these tests for differential diagnosis between physiological and vestibulo-ocular symptoms. In addition, to confirm the results of the observational study, an adequately powered observational study is warranted, designed with four groups; active and sedentary individuals with mild TBI, as well as active and sedentary healthy controls.

The work presented in this thesis also revealed that mental health significantly influences the return to physical activity, yet psychological services were underutilised. This highlights the need for further investigation into mental health interventions in mild-to-moderate TBI populations, potentially combining psychological and subthreshold aerobic exercise interventions to enhance the improvement of persistent symptoms, mental health, and return to physical activity.

APPENDICES

Appendix 1 Systematic review publication in NeuroRehabilitation

Location of Physical exercise for people with mild traumatic brain injury: A systematic review of randomized controlled trials: https://doi.org/10.3233/NRE-220044

Appendix 2 Systematic review PROSPERO registration

Location of PROSPERO registration for Physical exercise for people with mild traumatic brain injury: A systematic review of randomized controlled trials:
https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=131703

Appendix 3 Clinical audit publication in the Journal of Head Trauma Rehabilitation

Location of The Buffalo Concussion Treadmill and Bike Tests in people with mild-to-moderate traumatic brain injury: An exploratory clinical audit:

https://doi.org/10.1097/HTR.0000000000000879

Appendix 4 Observational study participant information sheet/consent form

Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Flinders University

Title	Physiological Response to the Buffalo Concussion Treadmill Test: A Comparison Between People with Mild-to-Moderate Traumatic Brain Injury, Healthy Active Adults and Healthy Sedentary Adults
Chief Investigator	Dr Maayken van den Berg
Co-ordinating Principal Investigator	Associate Professor Chris Barr
	Dr Maggie Killington
Investigators	Ms Sally Vuu
Senior Physiotherapist	Ms Joanne Howie
Location	Repatriation General Hospital Flinders University Sturt gym

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project: Physiological Response to the Buffalo Concussion Test: A Comparison Between People with Mild-to-Moderate Traumatic Brain Injury, Healthy Active and Healthy Sedentary Adults. This is because you either have suffered a mild-to-moderate traumatic brain injury (TBI) or identify yourself as healthy and 'active' or healthy and 'sedentary'. The research project is investigating the physiological response using the Buffalo Concussion Treadmill Test (BCTT).

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
• Understand what you have read
• Consent to take part in the research project
• Consent to have the tests and treatments that are described
• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information Sheet and Consent Form to keep.

2 What is the purpose of this research?

The aim of this study is to compare the body's response to the treadmill test during and after the test between adults with mild-to-moderate TBI, healthy active adults and healthy sedentary adults. The treadmill test will be a physical exertion test and the study is designed to enhance our understanding of how exercise may improve symptoms after brain injury.

The results of this study will assist the student, Sally Vuu, towards achieving her Doctorate of Philosophy at Flinders University.

3 What does participation in this research involve?

You will be asked to attend one session to complete a treadmill test. While you are completing this test the physiological response of your body will be monitored, such as heart rate, blood pressure and body temperature. The treadmill test will take up to 30 minutes, however you may stop at any time point. The whole session should last up to 2-3 hours.

4 What do I have to do?

If you agree to participate in this study, you will be asked to sign a consent form at the beginning of the session. You will then be asked to walk on a treadmill. The test will commence at a comfortable brisk walking speed, with no incline. Following, the treadmill will slowly incline up to a maximum of 15 degrees. Next, the walking speed will slowly increase. The test will end whenever you feel you are unable to continue, or your level of effort or heart rate approach the maximum we would expect you to manage. For adults with TBI, the test will also be terminated if there is a significant increase in current symptoms or new symptoms are being experienced. During the completion of the test we will closely monitor your bodily responses. We will record:

Pre-test:

- mental health using the Depression Anxiety Stress Scale (DASS)
- thinking ability using the Montreal Cognitive Assessment (MoCA) and Trail Making Test (a short subset of the MoCA)

We are interested in the DASS and MoCA, as mental health and thinking issues may arise because of a TBI and are known to affect physical performance.

During the test:

- heart rate using a portable machine
- blood pressure using a portable machine
- blood oxygen levels using a portable machine
- blood lactate levels using a finger prick lactate analyser
- core body temperature using a telemetric pill, which you will be asked to take 3-8 hours before the session, and receiver
- perceived exertion, by asking you
- post-concussion symptoms, for adults with mild-to-moderate TBI, by asking you
- test duration.

Portable machine

Lactate analyser

Telemetric pill and receiver

5 Other relevant information about the research project

This project will be conducted at the Repatriation General Hospital or Flinders University Sturt gym. We intend to recruit up to 25 participants in each group.

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign, and you will be given a copy to keep.

Your decision whether to take part, or not to take part and then withdraw, will not affect your treatment or relationship with the Repatriation General Hospital or Flinders University.

7 What are the alternatives to participation?

Participation is entirely voluntary, and you can choose not to take part in this study. If you have a mild-to-moderate TBI, you do not have to take part in this research project to receive treatment at this hospital. If you choose not to participate, your treatment will not be affected. For people without TBI, you can withdraw without any consequences.

8 What are the possible benefits of taking part?

There are no benefits to you in taking part in this research. The results will help us understand the physiological response to exercise for people with a TBI. Participants will not receive payment for taking part in this study.

9 What are the possible risks and disadvantages of taking part?

The treadmill test that we ask you to complete is conducted routinely as part of usual clinical care of people with mild-to-moderate TBI in the Mild to Moderate TBI Clinic. You may feel signs and symptoms associated with aerobic exercise exertion during the test and potentially some muscle soreness after the test, which will generally resolve within a week. To measure blood lactate a finger prick is required from which a drop of blood will be collected. You may experience mild local tenderness in the area of the prick which should resolve within a few minutes. To measure core body temperature, we ask you to take a telemetric pill 3-8 hours before the test. There are no known side-effects to taking the pill and it will be expelled through your bowel movements.

As part of this study we will closely monitor heart rate, blood pressure, blood oxygen levels and any signs of distress, limiting any risks involved in the completion of the test. You can end the test at any point in time and the researcher will terminate the test as soon as distress becomes evident.

10 What if I withdraw from this research project?

Participation in this project is voluntary. You are free to withdraw from the project at any stage. If you do withdraw your consent during the project, the researchers will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. If you decide to withdraw from the project, please notify a member of the research team. A withdrawal from the study form is not required, as participants can withdraw at any time with no follow-up required.

11 What happens when the research project ends?

This project only involves one session. People with TBI will continue their rehabilitation as per normal. However, if participants display significant concerns on the DASS or MoCA, the researchers sit down and discuss with the participants their results. Participants in the TBI group will be referred to the EMMBIRS' social worker or psychologist as part of their multidisciplinary care. Participants in the healthy active and healthy sedentary groups will be advised to seek a follow-up appointment with their general practitioner.

Part 2 How is the research project being conducted?

12 What will happen to information about me?
By signing the consent form, you consent to relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. We will keep information in locked cabinets or password protected computers at Flinders University, which will be accessible to the research team only. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law. All information from this research project will be retained by Flinders University for 5 years and then securely destroyed.

It is anticipated the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

In accordance with relevant Australian and/or South Australian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You will also be given the right to request any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

13 Complaints and compensation
If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

14 Who is organising and funding the research?
This research project is being conducted through Flinders University. No member of the research team will receive personal or financial benefit from your involvement in the research project.

19 Who has reviewed the research project?
All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the Southern Adelaide Clinical Human Research Ethics Committee (SAC HREC).

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact
The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal researcher on 72218437 or any of the following people:

Clinical contact person

Name	Ms Joanne Howie
Position	Senior Physiotherapist
Telephone	08 711 75125
Email	Joanne.howie@sa.gov.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	Dr Maggie Killington
Position	Co-ordinating Principal Investigator
Telephone	0400 061 204
Email	Maggie.killington@sa.gov.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	*Southern Adelaide Clinical*
HREC Executive Officer	*Executive Officer*
Telephone	*8204 6453*
Email	*Health.SALNOfficerforResearch@sa.gov.au*

Local HREC Office contact (Single Site -Research Governance Officer)

Name	*Southern Adelaide Local Health Network*
Position	*Research Governance Officer*
Telephone	*8204 6453*
Email	*Health.SALHNOfficerforResearch@sa.gov.au*

Consent Form - *Adult providing own consent*

Title	Physiological Response to the Buffalo Concussion Treadmill Test: A Comparison Between People with Mild-to-Moderate Traumatic Brain Injury, Healthy Active Adults and Healthy Sedentary Adults
Chief Investigator	Dr Maayken van den Berg
Co-ordinating Principal Investigator	Associate Professor Chris Barr
	Dr Maggie Killington
Investigators	Ms Sally Vuu
Senior Physiotherapist	Ms Joanne Howie
Location	Repatriation General Hospital Flinders University Sturt gym

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

For people with mild-to-moderate TBI only, I give permission for my physiotherapist to release information to Flinders University concerning my medical data about my brain injury for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) ______________________________

Signature ______________________ Date ______________________

interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Senior Researcher†

I have given a verbal explanation of the research project; its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) ______________________________

Signature ______________________ Date ______________________

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

Appendix 5 Observational study recruitment flyer for healthy active and sedentary adults

Flinders UNIVERSITY
College of Nursing & Health Sciences

INSPIRING ACHIEVEMENT

Participants wanted!!

Flinders University (Clinical Rehabilitation) and Brain Injury Rehabilitation Services are conducting a study to find out how people with traumatic brain injury respond to exercise and how exercise can assist with recovery.

We are looking to recruit adults that do not have a current traumatic brain injury who are willing to complete a one-off data collection session – approx. 45mins to 1 hr at the Flinders Sturt gym.

Participation involves:

- Being on the treadmill at walking speed up to 15 mins
- Sitting for up to 10 mins
- Undertaking a quick mood and cognition test
- Having physiological measurements taken such as blood pressure and heart rate

The session should take about 45 mins to 1 hr and is held at the Flinders Sturt gym.

To be eligible to participate in this study you must:

Age	Gender	Physical activity level
22-31	Male	Sedentary
42-55	Male	Sedentary
57-63	Male	Sedentary
30-36	Male	Active
42-61	Male	Active
18-22	Female	Sedentary

flinders.edu.au

Age	Gender	Physical activity level
31-37	Female	Sedentary
63-69	Female	Sedentary
18-22	Female	Active
63-69	Female	Active

For more information contact:

Sally Vuu
Sally.vuu@flinders.edu.au

This study has received approval from the Southern Adelaide Clinical Human Research Ethics Committee – HREC/19/SAC/286.

Appendix 6 Buffalo Concussion Treadmill Test protocol for adults with mild traumatic brain injury

BCTT Protocol for People with Mild-to-Moderate TBI

People with mild-to-moderate TBI will undergo the BCTT as part of their clinical care. The treating clinician (senior physiotherapist) at the hospital will be administering the test. The assessor will only be recording the results and will have no active participation in administering the test.

Safety Considerations for Participants:

- Participants must be dressed for exercise (comfortable clothing/sportswear, running shoes), wearing any vision or hearing aids, and should be well hydrated and rested
- One clinician and one assessor must be present at the session at all time to ensure safety of the participant
- The clinician will have Cardiopulmonary Resuscitation training and a working Automated External Defibrillator present during the test. The clinician will have the training and experience to deal with adverse events in people with mild-to-moderate TBI
- The clinician will engage in conversation with the participant during the exercise test to assess changes in cognitive and communicative functioning. As the exercise intensifies, the clinician will note if the participant has difficulty communicating, looks suddenly pale or withdrawn, or otherwise appears to be masking serious discomfort.

Equipment Requirements:

- Treadmill with the capacity to reach 15 degrees of elevation

- Sphygmomanometer measuring heart rate, blood pressure and oxygen saturation

Version 1 25/09/2020

- Blood lactate analyser

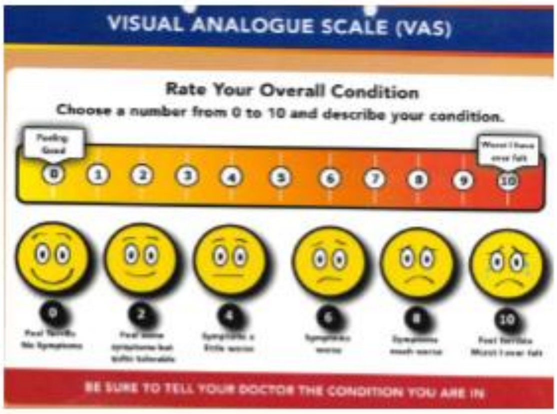
- Core body temperature using the telemetric pill and receiver

- Stopwatch
- Borg Rating of Perceived Exertion Scale

Borg's Rating of Perceived Exertion (RPE) Scale

Perceived Exertion Rating	Description of Exertion
6	No exertion. Sitting & resting
7	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

- Concussion Symptom Severity on the Visual Analogue Scale



- Chair, water and towel for participant recovery after the test

Setup:

- All devices will be setup according to the manufacturer's instructions
- The Borg Rating of Perceived Exertion and Concussion Symptom Severity Scale on the Visual Analogue Scale will be placed in front of the participant within comfortable viewing distance without having to turn their head.

<u>Test Protocol (Completed by the Treating Clinician as Part of Clinical Practice):</u>

1. Inform the participant about test procedures and what to expect during the BCTT.
2. Explain and demonstrate the Borg Rating of Perceived Exertion Scale and Concussion Severity Scale on the Visual Analogue Scale.
   The Borg Perceived Exertion is a measure of perceived physical exertion and can be explained to participants as a measure of "how hard you feel like your body is working". The scale's numbers are 6-20.
   The Concussion Symptom Severity on the Visual Analogue Scale is a measure of symptom severity ("how good/bad your symptoms are making you feel right now"). The scale's numbers are 0-10.
3. The participant is asked to rate their perceived exertion and symptom severity before the test.
4. The participant should begin by standing on the ends of the treadmill while the treadmill is turned on. The clinician will set the treadmill at a speed of **5.8km/h** for participants over 165cm and **5.1km/h** for those 165cm and under. Starting incline is **0 degrees**. Speed can be adjusted depending on athletic status or overall comfort of treadmill speed (participants should be moving at a brisk walking pace).
5. After 1 minute at this pace, treadmill incline is increased to 1 degree. The participant is asked to rate perceived exertion and symptom severity every minute. The treadmill is increasing in incline at a rate of 1 degree/minute.
6. Once the treadmill reaches maximum incline (15 degrees), speed is increased by **0.6km/h** each minute in lieu of increased incline.
7. Once the test is terminated (see below), speed is reduced to **4.0km/h** and incline reduced safety back to 0 for a 2 minute cool-down (if participant is safe to continue).
8. The participant will then sit to rest for 30 minutes after the 2 minute cool-down. The participant will be monitored each minute during the test and for 30 minutes after cool-down. This includes being asked to rate perceived exertion and concussion severity every minute.

Terminating the Test:
Test continues until:

- Maximum exertion (RPE score of 19.5) is reported or
- Test is terminated by the clinician due to a symptom exacerbation that causes significant increase in pain or symptom severity (an increase of more than three points from resting score, addition of several new symptoms, or marked increase in the severity of symptoms resulting in difficulty continuing the test) or
- Clinician notes a rapid progression of complaints (e.g. headache to searing focal pain) between symptom reports, participant appears faint or unsteady, or determines that continuing the test constitutes a significant health risk for the participant, or
- Participant reaches >90% of age-predicted heart rate, or
- Participant wishes to stop.

Measurement Protocol (Completed by the Assessor Observing the Test):

1. Obtain all baseline measures – heart rate, blood pressure, oxygen saturation, blood lactate, core temperature, perceived exertion, concussion symptoms, Depression Anxiety Stress Scales, Montreal Cognitive Test and general observations.
   Care will be taken to ensure that symptoms reflect either a new symptom or if the symptom is an exacerbation of current symptoms.
2. Heart rate, blood pressure, oxygen saturation, core temperature, perceived exertion, concussion symptoms and general observations are recorded every minute during the test, cool-down period and 30-minute rest period. Blood lactate is recorded immediately after termination of test.
3. Duration of the test will be measured by a stopwatch by starting the stopwatch at the commencement of the test and stopping the stopwatch at termination of the test.

Outcome Measures:

- Heart rate – Measured with the sphygmomanometer. Maximal heart rate is commonly used in clinical practice for determining maximal aerobic capacity, prescribing exercise intensity and terminating exercise testing, and estimated using the age-predicted equation of 220-age [1-3].
- Blood pressure - Measured with the sphygmomanometer. Post-exercise hypotension can occur with aerobic exercise, as it is attributed to an increase in cardiac output and/or systematic vascular resistance [4, 5].
- Oxygen saturation – Measured with the sphygmomanometer. Reduced oxygen saturation may change the supply of intramuscular oxygen, producing a more acidic and anabolic environment, which could affect the participant's perceived exertion [6, 7].
- Blood lactate – Measured with the blood lactate analyser (AccuTrend) and involves a finger prick sample from participants. Blood lactate concentration can be measured during exercise testing and during performance, as the lactate threshold is a better predictor of performance than VO_{2max} and better indicator of exercise intensity than heart rate, thus can be used to determine the individual's maximum aerobic capacity and cardiovascular fitness [8].
- Core body temperature – Measured using the telemetric pill and receiver. It is proposed that the telemetric pill should be ingested approximately 6 hours before data collection to avoid temperature fluctuations in the upper gastrointestinal tract and sensor expulsion before data collection [9]. However, ingestion 3-8 hours before data collection also allows sufficient time for the pill to travel into the small and large intestines [10, 11]. The oxidation of substrates during muscle contractions during exercise impacts our thermoregulatory system, as only 20% is used for muscle power, whilst the 80% is released as heat [12-14]. Therefore, the elevated metabolic heat production during exercise typically exceeds the heat dissipation capacity,

resulting in an increased core body temperature [15, 16]. If the temperature rises above the hypothalamic set point [17], there may be reduced exercise performance, which may eventually lead to the development of heat-related disorders [18].

- Borg Rating of Perceived Exertion – Affordable, practical, valid and reliable psycho-physical tool used to assess and monitor subjective perception of effort during exercise, and strongly correlated with heart rate and blood lactate, and not influenced by gender, age, physical activity status and exercise testing modality [19, 20].
- Concussion Symptom Severity – Measured on the Visual Analogue Scale. The subscales for the measure will be dependent on the participant's self-reported symptoms at baseline and during the test.
- Duration of test – Measured by a stopwatch. By measuring duration of test, we hope to ascertain the reason for stopping.
- Depression Anxiety Stress Scales (DASS) – We will use the DASS-21 version, which consists of half the items of the DASS-42 and comprises of 3 scales – depression, anxiety and stress, each with 7 items [21]. The DASS-21 has good reliability and validity in the clinical and non-clinical populations [22, 23] and only takes 10-15 minutes to administer [24].
- Montreal Cognitive Test (MoCA) – The MoCA is a valid, reliable and sensitive screening tool for many disorders, with major cognitive domains including executive function, short-term memory, language abilities and visuospatial processing [25], and only takes 10 minutes to administer [26].

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Appendix 7 Buffalo Concussion Treadmill Test protocol for healthy active and sedentary adults

<u>BCTT Protocol for Healthy Sedentary and Healthy Active Adults</u>

The healthy sedentary and healthy active adults will be recruited for the purpose of the research. One researcher with clinical experience will administer the test, while the other researcher will record the results.

Safety Considerations for Participants:

- Participants must be dressed for exercise (comfortable clothing/sportswear, running shoes), wearing any vision or hearing aids, and should be well hydrated and rested
- Two researchers must be present at the session at all time to ensure safety of the participant
- At least one researcher will have Cardiopulmonary Resuscitation training and a working Automated External Defibrillator present during the test
- The researcher administering the test will talk to the participant during the exercise test to assess changes in cognitive and communicative functioning. As the exercise intensifies, the researcher will note if the participant has difficulty communicating, looks suddenly pale or withdrawn, or otherwise appears to be masking serious discomfort.

Equipment Requirements for Participants:

- Treadmill with the capacity to reach 15 degrees of elevation

- Sphygmomanometer measuring heart rate, blood pressure and oxygen saturation

Version 2 11/09/2020

- Lactate analyser

- Core body temperature using the telemetric pill and receiver

- Stopwatch
- Borg Rating of Perceived Exertion Scale

Borg's Rating of Perceived Exertion (RPE) Scale

Perceived Exertion Rating	Description of Exertion
6	No exertion. Sitting & resting
7	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

- Chair, water and towel for participant recovery after the test

Setup:

- All devices will be setup according to the manufacturer's instructions
- The Borg Rating of Perceived Exertion will be placed in front of the participant within comfortable viewing distance without having to turn their head

Test Protocol (Completed by a Researcher with Clinical Experience):

1. Inform the participant about test procedures and what to expect during the BCTT.
2. Explain and demonstrate the Borg Rating of Perceived Exertion Scale.
   The Borg Perceived Exertion is a measure of perceived physical exertion and can be explained to participants as a measure of "how hard you feel like your body is working". The scale's numbers are 6-20.
3. The participant is asked to rate their perceived exertion before the test.
4. The participant should begin by standing on the ends of the treadmill while the treadmill is turned on. The researcher will set the treadmill at a speed of **5.8km/h** for participants over 165cm and **5.1km/h** for those 165cm and under. Starting incline is **0 degrees**. Speed can be adjusted depending on athletic status or overall comfort of treadmill speed (participants should be moving at a brisk walking pace).
5. After 1 minute at this pace, treadmill incline is increased to 1 degree. The participant is asked to rate perceived exertion every minute. The treadmill is increasing in incline at a rate of 1 degree/minute.
6. Once the treadmill reaches maximum incline (15 degrees), speed is increased by **0.6km/h** each minute in lieu of increased incline.
7. Once the test is terminated (see below), speed is reduced to **4.0km/h** and incline reduced safely back to 0 for a 2 minute cool-down (if participant is safe to continue).
8. The participant will then sit to rest for 30 minutes after the 2 minute cool-down. The participant will be monitored each minute during the test and for 30 minutes after cool-down. This includes being asked to rate perceived exertion every minute.

Terminating the Test:

Test continues until:

- Maximum exertion (RPE score of 19.5) is reported or
- Participant appears faint or unsteady, or determines that continuing the test constitutes a significant health risk for the participant, or
- Participant reaches >90% of age-predicted heart rate, or
- Participant wishes to stop.

Measurement Protocol (Completed by a Researcher):

1. Obtain all baseline measures – heart rate, blood pressure, oxygen saturation, blood lactate, core temperature, perceived exertion, Depression Anxiety Stress Scales, Montreal Cognitive Test and general observations.
2. Heart rate, blood pressure, oxygen saturation, core temperature, perceived exertion and general observations are recorded every minute during the test, cool-down and 30-minute rest period. Blood lactate is recorded again immediately after termination of the test.
3. Duration of the test will be measured by a stopwatch by starting the stopwatch at the commencement of the test and stopping the stopwatch at termination of the test.

Outcome Measures:

- Heart rate – Measured with the sphygmomanometer. Maximal heart rate is commonly used in clinical practice for determining maximal aerobic capacity, prescribing exercise intensity and terminating exercise testing, and estimated using the age-predicted equation of 220-age [1-3].
- Blood pressure - Measured with the sphygmomanometer. Post-exercise hypotension can occur with aerobic exercise, as it is attributed to an increase in cardiac output and/or systematic vascular resistance [4, 5].
- Oxygen saturation – Measured with the sphygmomanometer. Reduced oxygen saturation may change the supply of intramuscular oxygen, producing a more acidic and anabolic environment, which could affect the participant's perceived exertion [6, 7].
- Blood lactate – Measured with the blood lactate analyser (AccuTrend) and involves a finger prick sample from the participant. Blood lactate concentration can be measured during exercise testing and during performance, as the lactate threshold is a better predictor of performance than VO_{2max} and better indicator of exercise intensity than heart rate, thus can be used to determine the individual's maximum aerobic capacity and cardiovascular fitness [8].
- Core body temperature – Measured using the telemetric pill and receiver. It is proposed that the telemetric pill should be ingested approximately 6 hours before data collection to avoid temperature fluctuations in the upper gastrointestinal tract and sensor expulsion before data collection [9]. However, ingestion 3-8 hours before data collection also allows sufficient time for the pill to travel into the small and large intestines [10, 11]. The oxidation of substrates during muscle contractions during exercise impacts our thermoregulatory system, as only 20% is used for muscle power, whilst the 80% is released as heat [12-14]. Therefore, the elevated metabolic heat production during exercise typically exceeds the heat dissipation capacity, resulting in an increased core body temperature [15, 16]. If the temperature rises above the hypothalamic set point [17], there may be reduced exercise performance, which may eventually lead to the development of heat-related disorders [18].
- Borg Rating of Perceived Exertion – Affordable, practical, valid and reliable psycho-physical tool used to assess and monitor subjective perception of effort during exercise, and strongly correlated with heart rate and blood lactate, and not influenced by gender, age, physical activity status and exercise testing modality [19, 20].
- Duration of test – Measured by a stopwatch. By measuring duration of test, we hope to ascertain the reason for stopping.
- Depression Anxiety Stress Scales (DASS) – We will use the DASS-21 version, which consists of half the items of the DASS-42 and comprises of 3 scales – depression, anxiety and stress, each with 7 items [21]. The DASS-21 has good reliability and validity in the clinical and non-clinical populations [22, 23] and only takes 10-15 minutes to administer [24].
- Montreal Cognitive Test (MoCA) – The MoCA is a valid, reliable and sensitive screening tool for many disorders, with major cognitive domains including executive function, short-term memory, language abilities and visuospatial processing [25], and only takes 10 minutes to administer [26].

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Appendix 8 Survey and interview recruitment flyer

Flinders UNIVERSITY
College of Nursing & Health Sciences

INSPIRING ACHIEVEMENT

Have you had a concussion / mild traumatic brain injury?

We would love to hear from you!

Flinders University is conducting a study that aims to:

- Gain insight into how concussion affects people's ability to undertake physical activity
- Increase the understanding of barriers and facilitators to physical activity

Are you >18 years old and have you experienced a concussion with symptoms lasting more >10 days?

We invite you to take part in this study!

Please visit: https://qualtrics.flinders.edu.au/jfe/form/SV_cHcDoRExxv6cjWu

or scan QR code to continue.

For more information, contact: Sally Vuu at sally.vuu@flinders.edu.au

This study has been approved by Flinders University [ethics code: 5142].

Appendix 9 Survey and interview participant information sheet and consent form

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Title: Barriers and Facilitators to Physical Activity Following a Concussion/Mild Traumatic Brain Injury

Chief Investigator
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Supervisor
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Description of the study
You are invited to take part in this research project: Barriers and Facilitators to Physical Activity Following a Concussion/Mild Traumatic Brain Injury (mTBI). This is because you have s sustained a concussion/mTBI and have experienced symptoms for >10 days. To understand the impact of a concussion/mTBI on physical activity levels, this research project aims to gather data on how active people are following a concussion/mTBI, as well as perceived barriers and facilitators to physical exercise following a concussion/mTBI.
This project is supported by Flinders University, College of Nursing and Health Sciences.

Purpose of the study
The purpose of this study is to investigate the impact of concussion/mTBI on physical activity levels in people who have experienced symptoms for >10 days, which is beyond the expected timeframe of recovery through gathering self-reported and objective physical activity levels, and exploring barriers and facilitators to physical activity.

Benefits of the study
The sharing of your experiences will help us to better understand how physical activity levels are impacted in people following a concussion/mild TBI so we can assist people with returning to their usual physical activities including daily, social, and recreational activities.

inspiring achievement

Participant involvement and potential risks

If you agree to participate in the research study, you will be asked to:

- Undertake an online survey that will take up to 30mins to complete
- Optional: wear an accelerometer during waking hours over 7-days
- Optional: attend a one-on-one interview with a researcher via Microsoft Teams that will take up to 1 hour to complete. In this interview, the researcher will ask you things such as factors that affect your capability, opportunity, and motivation to undertake physical activity. This interview will be audio recorded for transcript purposes, and participants will have the opportunity to review and edit their interview transcript.

The researchers do not expect the questions to cause any harm or discomfort to you. However, if you experience feelings of distress as a result of participation in this study, please let the research team know immediately. You can also contact the following services for support:

- Lifeline – 13 11 14, www.lifeline.org.au
- Beyond Blue – 1300 22 4636, www.beyondblue.org.au

Withdrawal Rights

You may, without any penalty, decline to take part in this research study. If you decide to take part and later change your mind, you may, without any penalty, withdraw at any time without providing an explanation. To withdraw, please contact the Chief Investigator or you may just refuse to answer any questions / close the internet browser / leave the online survey or online interview and return the accelerometer via the postage paid parcel. Any data collected up to the point of your withdrawal will be securely destroyed.

Confidentiality and Privacy

Only researchers listed on this form have access to the individual information provided by you. Privacy and confidentiality will be assured at all times. The research outcomes may be presented at conferences, written up for publication or used for other research purposes as described in this information form. However, the privacy and confidentiality of individuals will be protected at all times. You will not be named, and your individual information will not be identifiable in any research products without your explicit consent.

No data, including identifiable, non-identifiable and de-identified datasets, will be shared or used in future research projects without your explicit consent.

Data Storage

The information collected may be stored securely on a password protected computer and/or Flinders University server throughout the study. Any identifiable data will be de-identified for data storage purposes unless indicated otherwise. All data will be securely transferred to and stored at Flinders University for no more than 5 years after publication of the results. Following the required data storage period, all data will be securely destroyed according to university protocols.

How will I receive feedback?

Participants will have no feedback to receive.

Ethics Committee Approval

The project has been approved by Flinders University's Human Research Ethics Committee (5142).

Queries and Concerns

Queries or concerns regarding the research can be directed to the research team. If you have any complaints or reservations about the ethical conduct of this study, you may contact the Flinders

University's Research Ethics & Compliance Office team via telephone 08 8201 2543 or email human.researchethics@flinders.edu.au.

Thank you for taking the time to read this information sheet which is yours to keep. If you accept our invitation to be involved, please sign the enclosed Consent Form.

CONSENT FORM

Consent Statement

☐ I have read and understood the information about the research, and I understand I am being asked to provide informed consent to participate in this research study. I understand that I can contact the research team if I have further questions about this research study.

☐ I am not aware of any condition that would prevent my participation, and I agree to participate in this project.

☐ I understand that I am free to withdraw at any time during the study.

☐ I understand that I can contact Flinders University's Research Ethics & Compliance Office if I have any complaints or reservations about the ethical conduct of this study.

☐ I understand that my involvement is confidential, and that the information collected may be published. I understand that I will not be identified in any research products.

I further consent to:

☐ completing an online survey
☐ optional: wearing an accelerometer over 7 consecutive waking days
☐ optional: participating in an online interview and having my information audio recorded for transcript purposes
☐ my data and information being used in this project for an extended period of time (no more than 5 years after publication of the data)

Signed:

Name:

Date:

Appendix 10 Survey questions

<u>Have you had a concussion / mild traumatic brain injury? We would love to hear from you!</u>

<u>Flinders University is conducting a study that aims to gain insight into how concussion affects people's ability to undertake physical activity.</u>

<u>If you are interested in participating, please click and read the attached Participant Information Sheet/Consent Form prior to continuing with the survey.</u>

The following questions will confirm eligibility for study participation.

Are you ≥18 years old?

- ☐ Yes
- ☐ No

Have you been experiencing symptoms following a concussion / mild traumatic brain injury, that have lasted for more than 10 days?

- ☐ Yes
- ☐ No

Do you consent to participating in a one-off interview (30-60 min duration) about barriers and facilitators to physical activity?

- ☐ Yes
- ☐ No

Please select your preferred way of being contacted with further details about the online interview.

- ☐ Phone, please leave your contact number:
- ☐ Email, please leave your email:
- ☐ Other, please specify:

The following questions will gather information about you and your concussion / mild traumatic brain injury.

1. How old are you (years)?
2. What is your gender?

☐ Male

☐ Female

☐ Transgender

- ☐ Non-binary
- ☐ Other

3. When did you sustain your concussion (dd/mm/yyyy if known)?
4. How did you sustain your concussion?
    - ☐ Sport, which sport?
    - ☐ Motor vehicle
    - ☐ Motor bike
    - ☐ Push bike
    - ☐ Fall, how?
    - ☐ Other, specify:
5. Did you experience loss of consciousness?
    - ☐ Yes, how long? Please indicate how many minutes, hours or days:
    - ☐ Yes, but unknown
    - ☐ No
    - ☐ I am unsure
6. Did you experience post-traumatic amnesia (i.e., feeling confused or disorientated)?
    - ☐ Yes, how long? Please indicate how many minutes, hours or days:
    - ☐ Yes, but unknown duration
    - ☐ No
    - ☐ I am unsure
7. Did you have a brain scan?
    - ☐ Yes, normal scan
    - ☐ Yes, abnormal scan
    - ☐ Yes, unknown
    - ☐ No
8. Did you know how your brain injury was classified?
    - ☐ Mild traumatic brain injury
    - ☐ Moderate traumatic brain injury

- ☐ Mild-to-moderate traumatic brain injury
- ☐ I am unsure

9. What symptoms have you been experiencing in the last 7 days? Tick as relevant?

- ☐ Headache
- ☐ Neck pain
- ☐ Dizziness
- ☐ Light sensitive
- ☐ Noise sensitivity
- ☐ Changes to vision
- ☐ Balance problems
- ☐ Fatigue
- ☐ Sleeplessness
- ☐ Restlessness
- ☐ Anxiety
- ☐ Irritability
- ☐ Depression
- ☐ Other, please specify:

10. Please indicate below if you have received any of the health service listed below, for how long, and in which setting?

	Acute hospital services (numbers of days per week)	Subacute rehab unit or brain injury services (number of days per week)	Outpatient or community-based services (number of days per week)
General medicine			
Physiotherapy			
Exercise physiology			
Exercise training			
Occupational therapy			
Medical specialist, which specialists?			
Other services, which			

services?			

11. Please indicate below (by ticking the relevant box) if the received health services included any education on, and or prescription of physical exercise or activity in the intervention program.

	Acute hospital services		Subacute rehab or brain injury services		Outpatient or community-based services	
	Education on physical exercise/activity	Prescription of exercise/activity	Education on physical exercise/activity	Prescription of exercise/activity	Education on physical exercise/activity	Prescription of exercise/activity
General medicine	☐	☐	☐	☐	☐	☐
Physiotherapy	☐	☐	☐	☐	☐	☐
Exercise physiology	☐	☐	☐	☐	☐	☐
Exercise training	☐	☐	☐	☐	☐	☐
Occupational therapy	☐	☐	☐	☐	☐	☐
Medical specialist, which specialists?	☐	☐	☐	☐	☐	☐
Other services, which services?	☐	☐	☐	☐	☐	☐

The following questions are related to physical activity prior to your concussion.

1. Prior to your concussion, were you undertaking regular physical activities?

   ☐ Yes

   ☐ No

2. Prior to your concussion, what physical activities were you undertaking per week?

   ☐ Football

   ☐ Soccer

   ☐ Bask

- ☐ Netball
- ☐ Volleyball
- ☐ Cricket
- ☐ Cycling
- ☐ Running
- ☐ Hiking
- ☐ Walking
- ☐ Individual gym
- ☐ Gym classes
- ☐ Dance
- ☐ Climbing
- ☐ Other, please specify:

3. Prior to your concussion, on average, how many days per week were you undertaking physical activity (days per week)?

4. Please detail the duration and intensity of each physical activity that you undertook per week.

	Duration (mins) per day	Days per week	Intensity (light, moderate, vigorous or combination)
State physical activity 1:			
State physical activity 2:			
State physical activity 3:			
State physical activity 4:			

International Physical Activity Questionnaire – This questionnaire helps to understand your current physical activity level.

Think of all the vigorous activities that you did in the last 7 days. Vigorous physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

1. During the last 7 days, on how many days did you do vigorous activities like heavy lifting, digging, aerobics, or fast bicycling?

    - Days per week:
    - No vigorous physical activities

2. How much time did you usually spend doing vigorous physical activities on one of those days?

    - Hours per day:
    - Minutes per day:
    - Don't know/not sure

Think about all the moderate activities that you did in the last 7 days. Moderate activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the last 7 days, on average, how many days did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

    - Days per week:
    - No moderate activities

4. How much time did you usually spend doing moderate physical activities on one of those days?

    - Hours per day:
    - Minutes per day:
    - Don't know/not sure

Think about the time you spent walking in the last 7 days. This includes at work anda t home, walking to travel from place to place, and any other walking that you have done solely for recreation, sport, exercise, or leisure.

5. During the last 7 days, on how many days did you walk for at least 10 minutes at a time.

    - Days per week:
    - No walking

6. How much time did you usually spend walking on one of those days?

    - Hours per day:
    - Minutes per day:
    - Don't know/not sure

The last question is about the time you spent sitting on weekdays during the last 7 days. Include time spent at work, at home, whilst doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the last 7 days, how much time did you spend sitting on a week day?

    - ☐ Hours per day:
    - ☐ Minutes per day:
    - ☐ Don't know/not sure.

We would like to gain insight into what factors may potentially have impacted on your physical activity levels following your brain injury. To what extent do you agree or disagree with the following statements? I find the following factors limiting my ability to undertake physical activity:

	Strong agree	Agree	Neutral	Disagree	Strongly disagree
Physical capability (i.e., skills, strength, stamina)	☐	☐	☐	☐	☐
Psychological capability (i.e., knowledge, skills, strength, stamina)	☐	☐	☐	☐	☐
Physical opportunity (i.e., time, triggers, resources, locations, physical barriers)	☐	☐	☐	☐	☐
Social opportunity (i.e., personal, social, cultural influences)	☐	☐	☐	☐	☐
Reflective motivation (i.e., self-conscious planning, evaluations, beliefs)	☐	☐	☐	☐	☐
Automatic motivation (i.e., wants, desires, needs, impulses, reflex responses)	☐	☐	☐	☐	☐

We thank you for your time spent taking this survey. Your response has been recorded.

Appendix 11 Qualitative study interview guide

Background for semi-structured interview guide

TDF and COM-B adapted from Michie, van Stralen & West (2011)	
TDF	**COM-B model**
Capability: There must be the 'capability' to do it: the person or people concerned must have the physical strength, knowledge, skills, stamina etc. to perform the behaviour	
Skills	**Physical capability:** Having the physical skills, strength, or stamina to perform the behaviour
Knowledge **Behaviour regulation** **Memory** **Attention** **Decision making**	**Psychological capability: H**aving the knowledge, psychological skills, strength or stamina to perform the behaviour
Opportunity: There must be the 'opportunity' for the behaviour to occur in terms of a conducive physical and social environment: e.g., it must be physically accessible, affordable, socially acceptable and there must be sufficient time	
Environmental context **Resources**	**Physical opportunity:** What the environment allows or facilitates in terms of time, triggers, resources, locations, physical barriers, etc
Social influences	**Social opportunity:** Including interpersonal influences, social cues and cultural norms
Motivation: There must be sufficient strong 'motivation': i.e., they must be more highly motivated to do the behaviour at the relevant time than not to do the behaviour, or to engage in a competing behaviour	
Intentions **Goals** **Social/professional role & identity** **Belief about capabilities** **Optimism**	**Reflective motivation:** Involving self-conscious planning and evaluations (beliefs about what is good or bad)
Reinforcement **Emotion**	**Automatic motivation:** processes involving wants and needs, desires, impulses, and reflex responses

Introduction to interview:

Hello, my name is Sally Vuu and I am conducting a research project that aims to investigate the impact of concussion or mild traumatic brain injury on physical activity levels. Many thanks for agreeing to participate in an interview about your experiences concerning physical activity following concussion/mild traumatic brain injury.

There are no right or wrong answers, as we are trying to learn from your experiences and perceptions.

The interview will take up to an hour. We can skip any questions that you don't feel comfortable answering and stop the interview at any point without incurring any consequences.

Do you give me permission to audio record this interview for transcript purposes?

If participant answers "No": No worries, we will take notes instead.

Do you have any questions before we proceed with the interview?

1. **Could you tell me a little about your physical activity patterns before you experienced your brain injury?**

- Did you participate in any sports?
- Did you walk or cycle to work?
- Did you walk any pets?
- Were you active around the house?

2. **Could you tell me about your current physical activity patterns?**

- Do you participate in any sports?
- Do you walk or cycle to work?
- Do you walk any pets?
- Are you active around the house?

3. **Have you noticed a change in your physical ability to participate in physical activity since you have sustained your brain injury?**

- Yes/No.
- If yes, prompt for changes in skills, strength, and stamina.

4. **Have you noticed a change in your psychological ability to participate in physical activity since you have sustained your brain injury?**

- Yes/No.
- If yes, prompt for changes in mental skills, strength and stamina.

5. **How confident are you about undertaking physical activity?**

- Prompt for social and cultural influences.

6. **Do you currently have any physical activity goals?**

7. **Are these different from your goals prior to your brain injury?**

8. **Did something trigger you to alter your physical activity levels following your brain injury?**

- Prompt for Yes/No.
- If yes, prompt for explanations of triggers.

9. **What do you understand about undertaking physical activity after a brain injury?**

- Prompt for knowledge about importance of physical activity.
- Prompt for knowledge about an appropriate type and amount of physical activity.

10. **How do you feel about physical activity after your brain injury?**

- Prompt for positive and negative associations.

11. **Have you received education about physical activity since you have sustained your concussion?**

- Yes/No.
- If yes, prompt for what the education was about.

12. **Has physical activity (e.g., physical or walking exercises) been embedded in any therapy or intervention you have received since you have sustained your brain injury?**

- Yes/No.
- If yes, prompt for what physical activity training they have received.

13. **How does your home environment (e.g., your living space) influence your physical activity following your brain injury?**

- Prompt for increase or decreased of physical activity.

- Prompt for time, resources, and physical barriers.

14. **How does your community environment (e.g., your neighbourhood, local park, and gym) influence your physical activity following your brain injury?**

- Prompt for increase or decrease of physical activity.
- Prompt for time, resources, location, and physical barriers.

15. To what extent does your family or friends assist you with participating in physical activity following your brain injury?

- Prompt for family and friends.
- Prompt for other relationships.

16. Do you feel you have a responsibility to return to your pre-exercise activity levels?

- Yes/No.
- Prompt for further explanation.

That's all the questions I have for you.

Has anything occurred to you about this topic that we haven't spoken about?

Do you have any questions for us?

Thank you for your time. Have a good day.

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