INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Protocol: Potential Benefits of Daily-Life Physical Activity During Recovery from Mild Traumatic Brain Injury: A Systematic Review

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Review question / Objective: **Is daily-life physical activity beneficial to recovery from mild traumatic brain injury?**
Eligibility criteria: **Human subjects, acute mTBI injury, daily life physical activity (e.g. jogging, walking, running, swimming, etc) as opposed to a structured programme instructed by a clinician or a research group, language is in english, the study is not a pilot, preliminary study, meta-analysis or review, the outcome being studied is symptomatic recovery from mTBI.**
Main outcome(s): **(1) Looking at whether daily-life physical activity impacts recovery from mTBI. Specifically, does it improve recovery (i.e. less symptoms, sooner) or make recovery worse (e.g. more symptoms or lasting longer) (2) Is there a particular intensity, timing, duration of physical activity that is most beneficial for recovery from mTBI (e.g. moderate activity, within the first 72 hours, for example).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 November 2022 and was last updated on 23 November 2022 (registration number INPLASY2022110113).

INTRODUCTION

Review question / Objective: **Is daily-life physical activity beneficial to recovery from mild traumatic brain injury?**

Rationale: **Research now points to the possibility that physical activity (PA) may constitute an effective component of recovery for mTBI. However, several questions remain unanswered about what type, timing, duration, and intensity of PA impact recovery trajectory. This systematic review aims to look at the current evidence provided by human-subject studies about the impact of PA on recovery from mTBI. This review will focus specifically on daily-life PA that is carried out in the**

participants' own time, without using a structured rehabilitation programme. There are two principal reasons for concentrating only on daily-life PA, as opposed to prescribed PA programmes. Firstly, there is substantial evidence already suggesting that structured aerobic exercise programmes have a beneficial impact on recovery from mTBI (e.g. Gagnon et al., 2016; Kurowski et al., 2017; Leddy et al., 2019; Micay et al., 2018; Powell et al., 2020; Prince et al., 2020; Shen et al., 2021). However, the evidence is less evident in regards to the efficacy of the PA that patients might engage in of their own accord on an everyday basis. Secondly, there may be significant under-reporting of mTBIs (due to the apparent low severity of the injury or fear of missing sporting events, for example) that subsequently are not under ongoing medical surveillance (e.g. at a concussion clinic) (Cusimano et al., 2017; Delaney et al., 2015; Hon et al., 2019; Theadom et al., 2016). Therefore, it is essential to understand the impact of activities patients might engage in of their own volition separate from clinic-prescribed programmes. If we can better understand the effect daily-life PA has on recovery from mTBI, healthcare professionals can further individualise their suggestions and treatment plans about incorporating PA. While numerous reviews have been conducted looking at the link between PA and mTBI recovery, there are several key reasons why the current review is necessary. Firstly, many of the existing reviews on the connection between PA and mTBI recovery are not systematic (e.g. Dech et al., 2019; Haider et al., 2021; Howell et al., 2019; Leddy et al., 2018) and selection bias risk of relevant studies may not have been included, or conversely, some may have been included that were not directly applicable. Existing reviews, whether systematic or not, contained a small number of studies (e.g. Henke et al., 2022 with three, Prince et al., 2020 with four and Lempke et al., 2019 and Powell et al. 2020 with five studies each). With limited samples, it isn't easy to comprehensively understand the link between PA and mTBI recovery. Furthermore, many reviews focused solely on aerobic exercise (e.g. De Wandel et al., 2019; Henke et al., 2022; Howell et al., 2019; Kulpa et al., 2020; McIntyre et al., 2020; Powell et al., 2020; Ritter et al., 2019) and/or structured exercise programmes (e.g. Carter et al., 2021; Prince et al., 2020; Quatman-Yates et al., 2016; Reid et al., 2022; Shen et al., 2021). While these are important, it is also essential to discover how daily-life PA impacts recovery and further review is warranted in this area. Lastly, when surveying the existing literature, the results are incredibly mixed when it comes to answering the question of whether PA enhances recovery or not. Therefore, systematic analysis of the latest evidence would be beneficial.

Condition being studied: Mild traumatic brain injury (mTBI), also often known as "concussion", is one of the most common and disabling brain conditions (McInnes et al., 2017; Verboon et al., 2021). mTBI is the most common form of TBI, and between 70% and 90% of TBIs are considered mild (Kozlowski et al., 2013; Markovic et al., 2021; Verboon et al., 2021). Approximately 35,000 New Zealanders suffer from a TBI yearly, and 95% of these are mild brain injuries. Common symptoms of mTBI include headaches, difficulty concentrating, a foggy feeling, loss of consciousness, disturbed balance, confusion, slowed reaction times, slurred speech, nausea, changes in vision, sensitivity to light, loss of smell or taste and irritability (Markovic et al., 2021; Verboon et al., 2021). A mTBI occurs when a person experiences a strong force on the head that causes the brain to move within the skull, which can lead to bruising and bleeding (Willer et al., 2019; Verboon et al., 2021). The predominant mechanism of injury is thought to be a sudden impact, rotational force or rapid deceleration or acceleration of the brain without causing a gross structural lesion (Alam et al., 2020; Willer et al., 2019; Verboon et al., 2021). The primary injury from mTBI is the immediate mechanical damage to the brain that can include lacerations and contusions, and can damage blood vessels, axons, nerve cells and glia (Alam et al., 2020). Following this primary injury, a cascade of secondary

injuries can occur, including metabolic disturbances, glutamate toxicity, cellular membrane disruption, blood-brain barrier disruption and neuroinflammation (Alam et al., 2020; Majerske et al., 2008; Soltani et al., 2020).

METHODS

Search strategy:
Medline (via PubMed)
SPORTDiscus (via EBSCO)
Scopus
Google Scholar
((“physical activity” OR exercise) AND (mTBI OR concussion OR “mild traumatic brain injury” OR “mild TBI” OR “mild head injury”) AND recovery).

Participant or population: Humans that have suffered an mTBI and are engaging in physical activity. All ages, genders and ethnicities.

Intervention: Daily-life physical activity (not structured programmes prescribed by a clinician for example).

Comparator: No physical activity.

Study designs to be included: Observational, Case control.

Eligibility criteria: Human subjects, acute mTBI injury, daily life physical activity (e.g. jogging, walking, running, swimming, etc) as opposed to a structured programme instructed by a clinician or a research group, language is in english, the study is not a pilot, preliminary study, meta-analysis or review, the outcome being studied is symptomatic recovery from mTBI.

Information sources: Medline (via PubMed); SPORTDiscus (via EBSCO); Scopus; Google Scholar.

Main outcome(s): (1) Looking at whether daily-life physical activity impacts recovery from mTBI. Specifically, does it improve recovery (i.e. less symptoms, sooner) or make recovery worse (e.g. more symptoms or lasting longer)

(2) Is there a particular intensity, timing, duration of physical activity that is most beneficial for recovery from mTBI (e.g. moderate activity, within the first 72 hours, for example).

Data management: Rayyan will be used to sort through the possible articles, apply inclusion and exclusion criteria, label studies and store records.

Quality assessment / Risk of bias analysis: AMSTAR-2 risk of bias assessment will be used.

Strategy of data synthesis: Database searches resulted in 970 possible studies to consider for inclusion in the review; Titles and abstracts were read and inclusion/exclusion criteria applied; A total of 382 duplicates were removed; Full text articles were read and inclusion/exclusion criteria applied; This resulted in 15 studies being included in the final review; These studies were re-read and notes were tabulated; Studies were categorised according to their results (e.g. those that found positive benefits of physical activity, those that did not and those with mixed results). Further notes were tabulated in regards to specific intensities, durations and timing or physical activity that the 15 studies analysed.

Subgroup analysis: N/A.

Sensitivity analysis: N/A.

Language restriction: English only.

Country(ies) involved: New Zealand.

Keywords: mTBI; mild TBI; mild traumatic brain injury; concussion; Physical activity; exercise; recovery; symptoms.

Dissemination plans: (1) Publish in a scientific journal (2) Include as part of PhD thesis.

Contributions of each author:
Author 1 - Mayan Bedggood - Background research to discover need for current systematic review; Planning of review;

Creation of search terms; Decision of databases used; Filtering of studies using Rayyan according to inclusion criteria; Reading titles, abstracts; Analysing full articles; Drafting manuscript; Editing manuscript.
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