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Ocular motor disorders in children and adults with mTBI: a scoping review protocol

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ABSTRACT

Introduction Ocular motor function is susceptible to neurological injury because it requires a large portion of brain circuitry including every lobe of the brain, brainstem, thalamus, basal ganglia, cerebellum, cranial nerves and visual tracts. While reports of a high frequency of ocular motor dysfunctions after mild traumatic brain injury (mTBI) span multidisciplinary journals, there is no scoping review of the signs, diagnostic assessments and criteria, and appropriate management of ocular motor disorders post-mTBI. Post-mTBI ocular motor dysfunction has been reported to respond to active treatment. The objective of this scoping review is to map the available evidence on the diagnostic assessment and treatment modalities currently used in the management of mTBI-related ocular motor disorders in children and adults. This scoping review also aims to identify gaps in the current literature and provide suggestions for future research.

Methods and analysis This review will include populations with reported concussion and/or mTBI without restrictions on age, race, sex or time since injury. The review will evaluate the reported symptoms related to ocular motor dysfunction, types of assessments and diagnostic criteria used, reported treatments, and the level of evidence supporting the reported treatments. This review will exclude literature on brain injury of non-traumatic aetiology and moderate/severe traumatic brain injury. Ocular motor dysfunction after mTBI appears in journals across multiple disciplines. Thus, multiple databases will be evaluated including Pubmed, Embase, PEDro, OVID, Clinical Key, Google Scholar and REHABDATA. Literature will be searched from inception to present day. Evidence sources will include experimental study designs including randomised controlled trials, non-randomised controlled trials and interrupted time-series. Additionally, analytical observational studies including prospective and retrospective cohort studies, case series, cross-sectional studies and clinical practice guidelines will be considered for inclusion. Data will be extracted on clinical presentation, frequency, assessment, diagnostic criteria management strategies and outcomes of concussion and mTBI-related ocular motor disorders.

Ethics and dissemination This scoping review will use data from existing publications and does not require ethical approval by an institutional review board. Results will be disseminated through publication in a peer-reviewed scientific journal and presented at relevant conferences and as part of future workshops with professionals involved with diagnosis and management of patients with mTBI.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study protocol outlines a rigorous design that includes the use of the established Preferred Reporting Items for Systematic Reviews and Meta-Analyses scoping review methodology and search strategy.
⇒ The broad search strategy is designed to capture all articles relevant to mild traumatic brain injury (mTBI)-related ocular motor disorders.
⇒ The review is limited to articles published in English, which may influence the types of diagnostic and treatment modalities in the studies reviewed.
⇒ A universal definition of mTBI is not currently available and continues to evolve over time, which may result in diagnostic misclassification across studies.

INTRODUCTION

Mild traumatic brain injury (mTBI) is a prevalent injury that impacts up to and possibly more than 600/100 000 population per year globally and represents 70%–90% of all TBI.[1] The most common aetiology of mTBI includes sports, motor vehicle accidents, bicycle accidents, falls and assaults.[1 2] The majority of epidemiological data sources depend on patients seeking medical attention; therefore are often underestimated in national epidemiological studies leading to gaps in the incidence and prevalence of mTBI.[3]

A universal definition of mTBI is not currently available and the definition is consistently being updated by expert working groups.[4] In general, an mTBI is considered clinical sequelae of neurological dysfunction that occurs after an acute traumatic brain injury due to mechanical energy to the head from external physical forces.[5] The acute pathophysiology involves a transient disruption of cellular membranes in the brain due

to focal and/or diffuse damage to neuronal dendrites, axons and astrocytes leading to a release of neurotransmitters. This altered neurotransmission has numerous consequences, including a diffuse change in intracellular and extracellular ionic equilibrium causing subsequent metabolic crisis to re-establish homeostasis, as well as persistent neuroinflammation and cell loss.[6] To be classified as 'mild' TBI, the Glasgow coma scale (if employed) should range from 13 to 15, and if present, loss of consciousness should persist no longer than 30 min, and post-traumatic amnesia should last less than 24 hours postinjury.[7 8] Due to the low risk for intracranial injury, diagnostic neuroimaging like CT and MRI scans are not routinely employed in the acute evaluation of mTBI, unless clinical risk factors support the need for imaging.[9] Concussion is a type of mTBI, and the term is colloquially used interchangeably with mTBI in the scientific literature and clinical care.[8 10] Concussion, a subtype of mTBI, will be included within the scoping review search, and will be hereafter referred to as mTBI.

Due to the complicated pathophysiology and heterogeneity of the condition, patients with mTBI can present with a constellation of symptoms including but not limited to cognitive, psychological/mood, vestibular, headache/migraine and visual.[11] Symptoms of concussion can persist for months and years after injury, impacting quality of life, and causing significant financial burden to individuals and society.[12–14] Visual symptoms are common in up to 68% of patients with chronic mTBI.[15 16] Vision is a crucial neurological sensory and motor system needed to interpret and interact with the world, and therefore visual dysfunction can significantly impact the ability for patients to return to activities like work, sport, school and military duty.[17] Ocular motor impairments like difficulties converging the eyes have been associated with prolonged recovery[18] and worse neurocognitive impairment,[19] directly impacting a patient's ability to learn and work.[20 21] Visual symptoms post-mTBI may include but are not limited to blurry vision, double vision, difficulties with reading, light sensitivity, and physical symptoms like headache or dizziness triggered by visual tasks like computer or reading.[20 22]

Vision problems due to ocular motor dysfunction in mTBI are common.[23–25] A large portion of brain circuitry, including every lobe of the brain, brainstem, thalamus, basal ganglia, cerebellum, cranial nerves and visual tracts, is related to visual function, making the visual system susceptible to neurological injury.[26] Visual symptoms, such as blur, double vision, dizziness and headaches associated with visual tasks, may be signs of post-concussion ocular motor dysfunction.[27] Ocular motor function describes the overall ability of the eyes to focus on objects of interest, track targets and maintain binocular alignment to ensure clear, stable and single vision as an individual moves through space. Ocular motor function includes smooth pursuits (ability for the eyes to track a slowly moving object), saccades (ability to move the eyes from one object to another), vergences (ability for the eyes to turn inward and outward together to fixate far and near objects) and accommodation (ability to change the focus of each eye to objects at different distances from the eyes). The ocular motor system interacts with the vestibular system through the vestibular-ocular reflex, where the eyes move in response to head and body movement as indicated by vestibular input. Post-mTBI ocular motor dysfunction is highly responsive to active participation in treatments.[28 29] Thus, ocular motor dysfunction may serve as an objective biomarker for neurological impairment following mTBI.[30–33]

Reports of a high frequency of ocular motor dysfunction(s) after mTBI span multidisciplinary journals.[23–25 31–34] Comparison of the published research and reports across journals highlights the lack of knowledge of the evaluation of vision, poor standardisation of techniques across studies, and an overall lack of consistency in methodology and diagnostic criteria both across and within disciplines in the assessment and management of visual dysfunctions in mTBI.[33] The objective of this scoping review is to map the available evidence on the diagnostic assessment and treatment modalities that are currently being used in the management of mTBI-related ocular motor disorders in children and adults.[35] This scoping review also aims to identify any gaps in the current literature, provide suggestions for future research and to serve as a precursor to a systematic review.

Review questions

1. What are the criteria used to diagnose ocular motor dysfunction* after mTBI in children and adults?
2. Based on these diagnostic criteria, what is the reported frequency of ocular motor dysfunction and associated symptoms after concussion?
3. What is the natural history of post-concussion ocular motor dysfunction in children and adults?
4. What treatment modalities are currently being used in the management of concussion-related ocular motor disorders in children and adults?
   a. What has been proposed, and what was the reported treatment response?
5. Are there differences across healthcare disciplines in clinical guidelines and recommendations for evaluation and treatment of ocular motor dysfunction after concussion in children and adults?

*Ocular motor dysfunction will include disorders of vergence, accommodation, saccades, smooth pursuit and vestibular-ocular reflex.

Keywords

Concussion; mTBI; vergence dysfunction; accommodative disorders; oculomotor dysfunction, ocular motor.

METHODS

We will perform the scoping review in accordance with the Preferred Reporting Items for Systematic Reviews

Table 1 Search strategy for Pubmed, Results 6045

#1	"craniocerebral trauma"(Mesh:NoExp)OR "Head Injuries, Closed"(Mesh] OR "Brain Injuries, Traumatic"(Mesh:NoExp)OR "Brain Concussion"(Mesh] OR "Brain Contusion"(Mesh] OR "Whiplash Injuries"(Mesh)
#2	(concussion*[tw] OR concussed[tw] OR postconcuss*[tw] OR "post concuss*"[tw] OR postconcuss*[tw] OR subconcuss*[tw] OR "sub concuss*"[tw] OR whiplash[tw] OR "mTBIs"[tw] OR "pmTBI"[tw] OR "c/mTBI"[tw] OR "commotio cerebri*"[tw])
#3	((mild[tw] OR minor[tw] OR "non severe"[tw]) AND ("traumatic brain"[tw] OR tbi[tw] OR tbis[tw] OR "posttraumatic brain"[tw] OR "traumatic head"[tw] OR "posttraumatic head"[tw]))
#4	((mild[tw] OR minor[tw] OR "non severe"[tw]) AND ("brain injur*"[tw] OR "brain trauma*"[tw] OR "brain contusion*"[tw]))
#5	((mild[tw] OR minor[tw] OR "non severe"[tw]) AND ("head injur*"[tw] OR "head trauma*"[tw] OR "head contusion*"[tw] OR "craniocerebral trauma*"[tw] OR "craniocerebral injur*"[tw] OR "craniocerebral contusion*"[tw] OR "cerebral trauma*"[tw] OR "cerebral injur*"[tw] OR "cerebral contusion*"[tw]))
#6	(Neurotrauma*(tw] OR "neuro-trauma*"(tw))
#7	#1 OR 32 OR #3 OR #4 OR #5 OR #6
#8	"Oculomotor Nerve"(Mesh] OR "Ocular Motility Disorders"(Mesh] OR "Ocular Physiological Phenomena"(Mesh] OR "Spasm"(Mesh] OR "Visual Perception"(Mesh] OR "Vision Disorders"(Mesh] OR "Diagnostic Techniques, Ophthalmological"(Mesh] OR "Vestibular Evoked Myogenic Potentials"(Mesh] OR "Reflex, Vestibulo-Ocular"(Mesh] OR "Lenses"(Mesh] OR "Refractive Errors"(Mesh] OR "Pupil Disorders"(Mesh] OR "Botulinum Toxins, Type A"(Mesh] OR "Asthenopia"(Mesh] OR "Eye Pain"(Mesh] OR "Orthoptics"(Mesh)
#9	(oculomotor[tw] OR "ocular motor"[tw] OR vision[tw] OR visual[tw] OR ophthalmologic*[tw] OR ophthalmoplegia*[tw] OR ophthalmopares*[tw] OR "third nerve"[tw] OR "third cranial nerve"[tw] OR "cranial nerve III"[tw] OR vergence[tw] OR convergence[tw] OR accommodation[tw] OR accommodative[tw] OR insufficiency[tw] OR spasm*[tw] OR tracking[tw] OR "eye movement*"[tw] OR saccad*[tw] OR microsaccad*[tw] OR fixation[tw] OR "eye gaze*"[tw] OR "smooth pursuit*"[tw] OR strabismus[tw] OR phoria*[tw] OR squint*[tw] OR esophoria*[tw] OR exophoria*[tw] OR esotropia*[tw] OR esodeviation*[tw] OR "cross eye*"[tw] OR crosseye*[tw] OR exodeviation*[tw] OR lenses[tw] OR refractive[tw] OR tints[tw] OR tinted[tw] OR prism[tw] OR "patching"[tw] OR occlusion[tw] OR binasal[tw] OR pupil[tw] OR pupils[tw] OR pupillary[tw] OR font[tw] OR botox[tw] OR botulinum[tw] OR blur[tw] OR blurry[tw] OR blurred[tw] OR diplopia*[tw] OR polyopsia*[tw] OR asthenopia*[tw] OR "eye strain*"[tw] OR eyestrain*[tw] OR "eye pain*"[tw] OR eyepain*[tw] OR "VOMS"[tw] OR "OMAT"[tw] OR "NPC"[tw] OR "CISS"[tw] OR "BIVSS"[tw] OR orthoptic*[tw] OR pleoptic*[tw] OR photophobia*[tw] OR "light sensitiv*"[tw])
#10	#8 OR #9
#11	#7 AND #10
#12	("Animals"(Mesh] NOT "Humans"(Mesh))
#13	#11 NOT #12

and Meta-Analyses Extension for Scoping Reviews (PRISMA-sCR) methodology.[36]

Eligibility criteria

We will include original research, clinical practice guidelines and reports on ocular motor dysfunction. All databases will be searched from inception to achieve the largest scope possible and to detail early innovations in this field. We will use the Population/Participants, Concept and Context framework to inform our inclusion criteria, search and data charting strategies.[36 37]

Patient and public involvement

None.

Population/Participants

Studies eligible for inclusion in this review include participants with mTBI without restrictions on age, race or sex. There will be no limits on the time from the injury. Studies evaluating brain injury of non-traumatic aetiology or moderate/severe traumatic brain injury will be excluded from this review. This review will classify the severity of mTBI using the categorisations used in the included articles. This will guide the selection of articles that pertain to mTBI.

Concept

Literature will be reviewed regarding the diagnostic assessments currently being performed, the diagnostic criteria used, and the individuals performing these assessments, as well as the translatability of these assessments across disciplines. The symptoms of ocular motor dysfunction and reported relative frequency of these disorders in the post-concussion population will be evaluated. The types of treatment and the evidence supporting the interventions will be reviewed including vision or orthoptic therapy, vestibular-oculomotor and/or vestibular therapy, refractive lenses, patching/occlusion therapy, tinted lenses, prism, school and work accommodations, lifestyle adaptations, surgical interventions, pharmaceutical interventions, other medical interventions and observation.

Context

Articles will be limited to those written in English, but there are no restrictions on the country of origin of the

Table 2 Data extraction instrument for study characteristics

Reference	Study characteristics									
Title, author, year, location	Type of discipline	Study design	Sample size	Age	Sex	Definition criteria for mTBI	Time since injury to evaluation	Dissemination	Aetiology of mTBI	Possible confounding factors (ie, ADHD, LD)**

**ADHD = attention deficit hyperactivity disorder, LD = learning disability
mTBI, mild traumatic brain injury.

study/article. The review will evaluate 'mTBI', including concussion, as diagnosed by clinical standard of care, which is to be further defined after the review of the literature. All time points from the mTBI will be included across disciplines.

This scoping review will consider experimental study designs including randomised controlled trials, non-randomised controlled trials and interrupted time-series studies. In addition, analytical observational studies including prospective and retrospective cohort studies, case series with at least three or more mTBI, cross-sectional studies, as well as clinical practice guidelines will be considered for inclusion. This study will exclude conference proceedings.

Search strategy

Identification of studies relevant to this review will be achieved by searching the following electronic bibliographic databases: Pubmed, Embase, PEDro, OVID, Clinical Key, Google Scholar and REHABDATA. Reference lists of included studies will also be searched to identify additional relevant studies. In addition to the bibliographic database searches, relevant grey literature sources will be searched including: relevant national and international organisations' websites and clinical practice guidelines.

Search terms will be developed with input from the review team in collaboration with an experienced research librarian.

Keywords to be searched will be a combination of one of the following:

1. oculomotor, ocular motor, vergence, convergence, divergence, accommodation, accommodative, insufficiency, spasm, visual, vision, visual dysfunction, visual disorder, visual tracking, tracking, saccade, saccadic, microsaccade, fixation, eye movement, smooth pursuit, vestibular-ocular, vestibular-oculomotor, phoria, esophoria, exophoria, vertical phoria, strabismus, vision therapy, visual therapy, vestibular therapy, lenses, refractive, tints, tinted lenses, prism, patching, occlusion, binasal, font size, Botox, botulinum, blur, blurred vision, double vision, diplopia, eye strain, eyestrain, eye pain, VOMS, OMAT, NPC, King Devick, Developmental eye movement, CISS, BIVSS, oculomotor treatment, oculomotor intervention, oculomotor natural history, orthoptics, vision rehabilitation, ocular motor rehabilitation, ocular motor treatment.

AND one of the following:

1. Concussion, Mild traumatic brain injury, Mild TBI, mTBI, Whiplash.

Study/source of evidence selection

Following the bibliographic searches, all identified citations except grey literature will be collated and uploaded into Covidence and duplicates removed. Following a pilot test, each title and abstract will then be screened by two independent reviewers for assessment against the inclusion criteria for the review. Potentially relevant sources will be retrieved in full and imported into Covidence for further assessment and review. Each full text report will be assessed by two independent reviewers. Reasons for exclusion of sources of evidence at full text that do not meet

Table 3 Data extraction instrument for diagnostic testing

Ocular motor function	Study	Tests used	Symptoms	Criteria of abnormality	Frequency
Accommodation					
Vergence					
Saccades					
Smooth pursuit					
Vestibular-Ocular Reflex					
Other					

Data will be grouped by age.

Table 4 Data extraction instrument for treatment interventions

Ocular motor function	Study	Interventions used	Outcomes
Accommodation			
Vergence			
Saccades			
Smooth pursuit			
Vestibular Ocular Reflex			
Other			

Data will be grouped by age.
Tables may change over time based on literature review.
*Short-term versus long term data will be evaluated if available.

the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion, or with an additional reviewer/s. The aforementioned process will also be performed on grey literature search but not included in Covidence. The results of the search and the study inclusion and exclusion process will be reported in full in the final scoping review and presented in a PRISMA-ScR flow diagram. It will include the number of articles retrieved, description of types of study design and number of studies ultimately included in the review. An example of a database search can be found in table 1, and all databases searched can be found in online supplemental material.

Data extraction

After a piloting step, data will be extracted from papers included in the scoping review by two independent reviewers using Covidence data extraction tool. The data extracted will include specific details about the participants, concept, context, study methods and key findings relevant to the review questions. Specifically, the scoping review will look at any data regarding frequency, prevalence, definitions, diagnostics, and treatment options for ocular motor dysfunction post-mTBI.

Data will be extracted into tables (tables 2–4). Data extracted will include first author, year of publication, study location, sample size, study design, type of discipline/provider involved in the study, age of participants, definition criteria for mTBI, time since injury to evaluation, aetiology of mTBI, and the types of ocular motor dysfunctions evaluated including accommodation, vergence, saccades, smooth pursuits, vestibular-ocular reflex and any others noted. Each ocular motor dysfunction will have further data extracted as applicable to the study including symptoms, diagnostic tests and instruments used, diagnostic criteria including cut-off values, results (including reported frequency and/or prevalence of disorder(s)), treatment type employed and treatment results. There will also be a section to list any confounding factors such as possible comorbidities, including but not limited to repeated mTBI, attention deficit hyperactivity disorder, depression or learning disabilities which could also have concomitant ocular motor disorders and thus influence the data related to exact aetiology of ocular motor disorders. The tables will be modified and revised as necessary during the process of extracting data from each included evidence source. Modifications will be detailed in the scoping review. Any disagreements that arise between the reviewers will be resolved through discussion, or with an additional reviewer/s. If appropriate, authors of papers will be contacted to request missing or additional data, where required. Each ocular motor dysfunction category will have a separate table detailing the diagnostic assessments and criteria used, frequency and prevalence of ocular motor dysfunction studied, treatment options employed and results. Data from clinical practice guidelines including definitions, diagnostic criteria, diagnostic test recommendations and treatment recommendations will be extracted into a separate table.

Data analysis and presentation

A summary table of patient population demographics, discipline and mTBI definition/characteristics will be presented.

Data will be analysed for each type of ocular motor disorder in regards to its frequency post-mTBI, the diagnostic criteria and tests used, symptoms reported, as well as the treatments employed and efficacy of the treatment. Where applicable, quantitative evidence will be aggregated using summary statistics. Data from observational studies or studies with control will be evaluated to assess the natural history of ocular motor dysfunction in mTBI and presented in separate tables (tables 2–4).

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Contributors JT, AC, APB, LDG, AM, ADS, TPY, TR and MS conceived and designed the review, and the search strategies. TR and MS were instrumental in guiding the concept and revising the manuscript for critical intellectual content. JT wrote the first draft of the protocol manuscript, AC, APB, LDG, AM, ADS, TPY, TR and MS edited the manuscript. JT revised the draft(s) into the final manuscript. All authors JT, AC, APB, LDG, AM, ADS, TPY, TR and MS read and approved of the final manuscript prior to submission for publication and agree to be accountable for all aspects of the work in ensuring that all questions related to the accuracy and integrity of the work are investigated and resolved.

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