BMJ Open

Effectiveness of non-pharmacological treatments for vestibular and oculomotor dysfunction in patients with persistent post-concussive symptoms: protocol for a systematic review and meta-analysis

Stella Sheeba,[1,2] Rocco Cavaleri ,[2] Simon Summers,[2,3] Cherylea Browne[1,2,4]

To cite: Sheeba S, Cavaleri R, Summers S, *et al*. Effectiveness of non-pharmacological treatments for vestibular and oculomotor dysfunction in patients with persistent post-concussive symptoms: protocol for a systematic review and meta-analysis. *BMJ Open* 2023;**13**:e066634. doi:10.1136/bmjopen-2022-066634

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-066634).

Received 13 July 2022
Accepted 12 December 2022

For numbered affiliations see end of article.

Correspondence to
Dr Cherylea Browne;
C.Browne@westernsydney.edu.au

ABSTRACT

Introduction Concussion is a form of mild traumatic brain injury that disrupts brain function. Although symptoms are mostly transient, recovery can be delayed and result in persistent postconcussive symptoms (PPCS). Vestibular and oculomotor dysfunction are among the most debilitating impairments associated with PPCS. However, pharmacological interventions for these impairments are associated with deleterious side effects. Accordingly, increasing research has examined the utility of non-pharmacological interventions for PPCS. The aim of this review is to synthesise and evaluate the effectiveness of non-pharmacological interventions for the treatment of vestibular and oculomotor dysfunction for patients with PPCS.

Methods and analysis Systematic searches of MEDLINE, PubMed, Web of Science and Scopus will identify randomised controlled trials employing non-pharmacological treatments for vestibular and/or oculomotor dysfunction for PPCS. Such interventions may include, but are not limited to, vestibular rehabilitation, optokinetic stimulation and vestibulo-ocular reflex exercises. Assessments of oculomotor function will include versional eye movements, vergence eye movements, visual-fixation movements and accommodation response. Assessments of vestibular function will include the Fukuda Step test, functional balance tests, force displacement tests, and subjective reports of balance disruption or vertigo. Where appropriate, meta-analyses of standardised mean differences will be conducted using a random effects model for continuous outcomes. For dichotomous outcomes (improved vs not improved following treatment), effects will be expressed as relative risk. The impact of heterogeneity will be calculated using the I^2 statistic. The Physiotherapy Evidence Database scale will be used to determine the methodological quality of individual studies and Grading of Recommendations, Assessment, Development and Evaluations used to assess the certainty and quality of evidence for each outcome.

Ethics and dissemination Ethical approval is not required for this review. Findings will be disseminated through peer-reviewed publications and conference presentations.

PROSPERO registration number CRD42021254720.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This systematic review addresses a gap in the current evidence-base by evaluating the effectiveness of non-pharmacological treatments for vestibular and oculomotor dysfunction in patients with persistent postconcussive symptoms.
⇒ This review will be conducted using rigorous methodology in accordance with the Cochrane handbook and the results will be reported as stated by Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols statement.
⇒ The Grading of Recommendations, Assessment, Development and Evaluations system will be used to ascertain the strength of the evidence base for each outcome.
⇒ This review is limited to evidence from randomised control trials.
⇒ Non-English electronic databases will not be searched, which may introduce language bias during analyses.

BACKGROUND

A concussion, or mild traumatic brain injury (mTBI), is the most common form of traumatic brain injury.[1 2] These injuries are induced by impulsive forces to the head, face or neck, resulting in the disruption of brain function.[3] Common symptoms associated with a concussion include headaches, dizziness, mood changes, light sensitivity, fatigue and impaired concentration.[4–7] While these acute symptoms resolve within days for most people, a subset of individuals do not recover fully and experience symptoms that persist beyond 3 months.[7–10] These individuals are categorised as having 'persistent postconcussive symptoms' (PPCS).[7 9 11] It is estimated that 5%–43% of individuals with concussion experience postconcussive symptoms, with 22% presenting with three or more persistent symptoms.[12 13] Given that there are currently

no universal guidelines for diagnosing PPCS, prevalence rates vary significantly across studies.

Vestibular and oculomotor dysfunction are well-documented in patients with PPCS.[14–18] The vestibulo-ocular reflex (VOR) is a complex reflex that serves to maintain balance and spatial orientation by stabilising the gaze during head movement.[19] Case studies have shown VOR disruption in those with PPCS.[20 21] Common complaints of vestibular dysfunction include dizziness, vertigo, nausea, fogginess, unsteady gait and postural instability.[15 22] The most common oculomotor disorders following a concussion are convergence insufficiency (affecting the ability of eyes to work together to clearly see nearby objects) and accommodative insufficiency (difficulty when focussing on a nearby object).[23] Symptoms associated with oculomotor dysfunction include difficulty tracking objects, motion sensitivity, eye strain or eye fatigue for near vision, and headache.[15 22] Importantly, evidence has shown that these symptoms of vestibular and oculomotor dysfunction are strong predictors of delayed recovery for patients with PPCS.[14 15 18]

Given the impacts of vestibular and oculomotor dysfunction in patients with PPCS, there is a need for effective treatment strategies. Both pharmacological and non-pharmacological interventions are available to treat VOR dysfunction. However, pharmacological treatments have been associated with side effects in up to 16.9% of participants, including sedation, drowsiness and dizziness.[24–28] Further, while pharmacological treatments may alleviate concussive symptoms, research suggests such interventions may mask underlying neural dysfunction,[15] delay central compensatory mechanisms and contribute to delayed recovery.[10] Non-pharmacological interventions are therefore recommended commonly.[10]

Non-pharmacological treatments based on individual disciplines (eg, oculomotor vision treatment or vestibular rehabilitation) have shown mild to moderate effectiveness in treating specific symptoms in patients with PPCS.[29] Other studies have supported interdisciplinary collaboration for patients in this population, such as combining non-invasive brain stimulation with vestibular rehabilitation.[30 31] A previous review by Rytter *et al*[29] on non-pharmacological treatments for patients with PPCS synthesised the effectiveness of interdisciplinary rehabilitation. While the researchers found studies with positive results, the review excluded younger populations.[29] Given that younger age groups are prone to develop PPCS,[32 33] informative studies in this population may have been overlooked. Further, the previous review was conducted on generalised symptoms of PPCS rather than focussing on treatments for specific symptoms. These exclusions may have limited the results of the search strategy and subsequent analysis of their findings. Further investigations of non-pharmacological treatments targeting symptoms such as vestibular and oculomotor dysfunction in the PPCS population is warranted. Novel therapies such as non-invasive brain stimulation have yet to be synthesised in this field. This study presents a protocol for a systematic review and meta-analysis that aims to synthesis and evaluate the effectiveness of non-pharmacological interventions for the treatment of vestibular and oculomotor dysfunction in patients presenting with PPCS.

METHODS

Protocol development and registration

This protocol was prepared in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols.[34] The protocol has been registered with the International Prospective Register of Systematic Reviews. The Cochrane Handbook of Systematic Reviews will also be used to guide the completion of this review.[35]

Review question

What is the effectiveness of non-pharmacological interventions for the treatment of symptoms associated with vestibular and oculomotor dysfunction in patients with postconcussive symptoms compared with sham treatment or control?

Information sources and search strategy

Searches will be conducted in MEDLINE, PubMed, Web of Science and Scopus from database inception. No limits will be placed on language or location of publication. Keywords and Medical Subject Headings related to PPCS treatments for vestibular and oculomotor dysfunction will be used where possible. The core search strategy, which will be modified as needed for each database, is presented in box 1. This core strategy was developed for PubMed and approved by a librarian, experienced in reviews of biomedical literature.

Other resources

The clinical trials registries of the WHO (who.int/ictrp/en), USA (ClinicalTrials.gov), UK (ukctg.nihr.ac.uk) and Australia/New Zealand (anzctr.org.au) will be searched. Google Scholar will also be searched using derivations of "vestibular", "oculomotor" and "post-concussion" for additional studies. Due to the large number of papers retrieved through Google Scholar searches, only the first

Box 1 Advanced search strategy

((Concuss* OR "PCS" OR "PPCS" OR post-concuss* OR "mild traumatic brain injury" OR mTBI OR coup-countercoup OR "head injury" OR "head trauma") AND (exercise OR repositioning OR "physical therapy" OR habituation OR "brain stimulation" OR "magnetic stimulation" OR "transcranial" OR "theta burst" OR "tDCS" OR "tACS" OR "TBS" OR "rTMS" OR "NIBS" OR videonystagmography OR "VNG" OR stimulation OR cortical) AND ("Vestibular ocular reflex" OR "VOR" OR vestibular OR oculomotor OR "VRT" OR gaze OR stabilis* OR stabiliz* OR balance OR postur* OR vergence OR pursuit OR vertigo OR saccades OR accommodation OR optokinetic OR Fukuda OR fixation) AND ("vision therapy" OR "orthoptic" OR "visual training" OR "oculomotor training" OR "oculomotor rehabilitation"))

Table 1 Oculomotor assessment outcomes

Oculomotor assessments	Description of assessment	Unit of measure
Versional (pursuit, saccades)		
Smooth pursuit	Measures smooth eye movement where eyes maintain fixation on a moving target	Speed of eye movement tracking (metres/second or degrees/second), pursuit gain (ratio of eye velocity to target velocity)
Saccades (horizontal/vertical)	Measures rapid eye movements that shifts the centre of gaze from one part of the visual field to another, primarily toward stationary targets	Latency between target movement and eye movement (milliseconds), velocity of eye movement (metres/second or degrees/second), distance between target and performed movement (millimetres), accuracy of eye movement distance relative to the target (%)
King-Devick	Measures the speed of rapid number naming (reading aloud single-digit numbers from three test cards)—a measurement of saccadic movements	Speed of rapid number naming (score 1–15)
Vergence (convergence, divergence)		
Convergence (near point)	The simultaneous inward movement of both eyes toward each other when viewing an object moving towards the viewer	Distance at which both eyes can focus on the target object without double vision (centimetres) or loss of focus
Divergence	The simultaneous outward movement of both eyes away from each other when viewing an object moving away from the viewer	Distance at which both eyes can focus on the target object without double vision (centimetres) or loss of focus
SCAT5	A concussion assessment tool that encompasses a range of measures including symptom evaluation, cognitive and neurological screening	Outcomes on the presence or absence of blurred vision during eye movement side-to-side and up-and-down (found in the neurological screening section) will be extracted
Visual-fixation movements		
Optokinetic nystagmus	The involuntary, side-to-side eye movements that allow the eyes to maintain fixation on a visual target as it moves past an observer (eg, viewing trees while in a moving car)	Velocity of nystagmus (metres/second or degrees/second), OKN performance gain (ratio of eye tracking velocity to target velocity)
Accommodation response		
Accommodation	The process that allows, and maintains, precise focus of an object of interest	The distance at which an eye can focus on an object (centimetres)

OKN, optokinetic nystagmus; SCAT5, Sports Concussion Assessment Tool.

100 articles for each search will be screened for relevance. The reference lists of all full-text articles included in the review will be analysed to identify additional trials. Only peer-reviewed studies from these sources satisfying the eligibility criteria will be included in the systematic review. Where data cannot be extracted from the studies themselves, attempts to contact study authors for primary data will be made. Authors will be contacted two times, 1 week apart. If no response is received in this timeframe, the data will be considered irretrievable.

Eligibility criteria

Only peer-reviewed randomised controlled trials (RCTs) (available as full-text) employing non-pharmacological interventions for the treatment of vestibular and/or oculomotor dysfunction for patients with PPCS will be included. Concussion is defined as temporary unconsciousness or confusion caused when a forceful impact on the head, face or neck alters brain function.[36] For this review, PPCS is defined as the persistence of postconcussive symptoms for greater than 3 months after a concussion.[7 9 11] No restrictions will be placed on participant age or gender. Only RCTs will be included in this review.

Studies of non-pharmacological treatment for vestibular and oculomotor outcomes will be included. A non-pharmacological treatment refers to an intervention where pharmaceutical medications are not considered part of the treatment.[37] Such interventions may include, but are not limited to, vestibular rehabilitation, optokinetic stimulation and VOR exercises. These interventions will be compared with control groups that may be either no treatment or sham conditions. Interventions that have

Table 2 Vestibular assessment outcomes

Assessment	Description of assessment	Unit of measure
Posturography	Measures upright posture, balance and sense of equilibrium by standing on a force platform	Shift in centre of pressure will be used to calculate distance (millimetres), sway (millimetres/second), velocity (millimetres/second) in anterior-posterior/ medial-lateral direction
Fukuda step test	Used to determine if there is unilateral vestibular weakness: subject with eyes closed and arms stretched out, stepping in place	Degree of rotation (from baseline or zero degrees)
SCAT5	A concussion assessment tool that encompasses a wide range of measures including symptom evaluation, cognitive screening, neurological screening and memory recall	Outcomes on the balance examination as 'number of errors' (found in the neurological screening section) will be extracted

SCAT5, Sports Concussion Assessment Tool.

been delivered standalone or in combination with other interventions will also be included. Studies that include participants taking pharmacological treatments that may influence vestibular or oculomotor outcomes, such as gabapentin or memantine (treatments for abnormal eye movements)[38] or vestibular suppressants (such as clonazepam and other benzodiazepines),[39] will be excluded from this review.

Primary outcomes will include measures of oculomotor and vestibular function. Outcomes that assess both constructs concurrently will also be analysed. Assessments of oculomotor function will include analyses of (i) versional eye movements (pursuit, saccades), (ii) vergence eye movements (convergence and divergence), (iii) visual-fixation movements (gaze holding, optokinetic responses, VORs) and (iv) accommodative response. Measurement outcomes of oculomotor function are listed in table 1. Studies presenting continuous data (amplitude, duration, peak velocity and accuracy of eye movements) and dichotomous data ('improved' or 'not improved' following treatment) will be included.

Assessments of vestibular function and balance will include the Fukuda Step test, functional balance tests, force displacement tests with eyes open and/or closed, as well as subjective reports of balance disruption and vertigo. Measurement outcomes of vestibular function are listed in table 2. Studies presenting continuous data (amplitude, duration, error count) and dichotomous data ('improved' or 'not improved' following treatment) will be included.

Assessments of combined vestibulo-oculomotor function will include VORs and vestibular/ocular-motor screening with inclusion of continuous (velocity, accuracy) and dichotomous ('improved' or 'not improved') data. Measurement outcomes of vestibulo-oculomotor function are listed in table 3. A secondary outcome will include any information provided on adverse events associated with the non-pharmacological interventions for PPCS.

Table 3 Combined vestibulo-oculomotor assessment outcomes

Assessment	Description of assessment	Unit of measure
Gaze stability	Ability to maintain a steady gaze on an object while the head is moving	Most rapid head movement velocity where visual acuity is maintained (degrees/second)
VOMS	Subjective measures comparing symptoms at baseline to symptoms after testing smooth pursuits, saccades, convergence, VOR and visual motion sensitivity	Self-reported measures: headache, dizziness, nausea, brain fog
Head impulse testing	Assesses VOR function with eyes fixed on a target while examiner rotates the head	Presence/absence of compensatory saccade back to target after head rotation, or video capture (degrees/second)
Rotational chair test	Eye movements are monitored during a series of tests using videonystagmography goggles while a person is situated in a computerised chair that changes position	Eye movements in response to various head angular accelerations during rotational chair test (degrees/second), nystagmus measured as slow-phase velocity (degrees/ second), VOR suppression (% of gain reduction or degrees/second)

VOMS, vestibular/ocular-motor screening; VOR, vestibulo-ocular reflex.

Data management and extraction

The Cochrane Data Collection Form for Intervention Reviews[40] will be used to extract study characteristics and outcome data. This will include extraction of the following data: study details (author, year, sample size, study design, date of publication, country of publication), participant characteristics (sample size, diagnosis/symptoms, age, sex), treatment characteristics (modality, duration, number of sessions), outcome measures, treatment effects (mean and SD). Two review authors will pilot the form on a randomly selected subset of 10% of included studies.[35] Pilot testing of the forms will include a computation of the reviewers' reliability. Reviewers will extract data independently and in duplicate from each eligible study.

Search results will be exported to EndNote citation software (EndNote X9) for automated removal of duplicates. Duplicates overlooked by the program will be manually removed. After removal of duplicates, two independent reviewers will screen the remaining articles by title and abstract for relevance using Covidence software (https://www.covidence.org/) in accordance with the prespecified eligibility criteria. An additional reviewer will be consulted where any uncertainty or disagreement regarding the eligibility of studies arises. This selection process will be piloted by the two reviewers prior to commencement of the study screening process. Excluded studies and reasons for exclusions will be recorded.

Assessment of methodological and reporting quality

The methodological quality of each RCT will be assessed using the Physiotherapy Evidence Database (PEDro) scale.[41] This tool demonstrates high inter-rater reliability and assesses internal and external validity.[41] Additionally, the PEDro scale has been identified as more relevant than other tools commonly used to appraise rehabilitation-based intervention studies.[42] Items will be scored as either present (1) or absent (0), and a score out of 10 will be achieved via summation. Disagreements will be resolved by discussion. Studies scoring 6 or more will be classified as high quality, studies scoring 4 or 5 will be considered moderate quality and studies scoring less than 3 will be classified as low quality.[41]

The reporting quality of each RCT will be assessed using the Consolidated Standards of Reporting Trials guidelines.[43] These guidelines offer a standard way for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation.[43]

If sufficient data are available for meta-analysis, the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) tool will be used to assess the certainty and quality of evidence[44] in accordance with the guidelines provided in the Cochrane Handbook of Systematic Reviews.[35] The GRADE system uses the following criteria for assigning 'grades' of evidence:

- High: the authors are very confident that the true effect lies close to that of the estimate of the effect.
- Moderate: the authors are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect.
- Low: the authors have limited confidence in the effect estimate; the true effect may be substantially different from the estimate of the effect.
- Very low: the authors have little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

To ensure consistency of GRADE judgements the following criteria will be applied to each domain equally for all key comparisons:

- Limitations of studies: downgrade if less than 75% of included studies are at low risk of bias according to the PEDro checklist.
- Inconsistency: downgrade if heterogeneity is significant ($p<0.05$) and the I^2 value is more than 50%.
- Indirectness: downgrade if any of the participants were outside the target group.
- Imprecision: downgrade if there were fewer than 400 participants for continuous data, fewer than 300 events for dichotomous data[44] or if CIs or SD were not reported across all studies.
- Publication bias: downgrade if there is direct evidence of publication bias.

If insufficient data is available for meta-analysis, the GRADE criteria will be modified for a narrative synthesis in accordance with the guidelines presented by Murad *et al*.[45] The potential influence of publication bias will be evaluated using Begg's funnel plot.[46]

Data synthesis

For continuous data, standardised mean differences between end-scores will be calculated. If studies report baseline differences between active and control groups, relative changes from baseline will be calculated. If data are available from at least two studies, meta-analyses will be performed using the software provided by the Cochrane Collaboration, Review Manager (RevMan V.5.4.1).[47] A random-effects model will be used as methodological heterogeneity is inevitable in practitioner-administered interventions.[48] For dichotomous data ('improved' or 'not improved' following treatment), effect measures will be expressed as relative risk.[49] A p value of <0.05 will be deemed statistically significant.

The impact of heterogeneity will be calculated using the I^2 statistic and interpreted as follows: 0%–40% may be unimportant; 30%–60% may represent moderate heterogeneity; 50%–90% may represent substantial heterogeneity and 75%–100% represents considerable heterogeneity.[35] Separate meta-analyses will be performed for each intervention. If insufficient data is available for meta-analysis, data will be synthesised descriptively.

Patient and public involvement

SSheeba and RC have both worked as on-field health professionals responsible for the assessment and management of sports-related concussions. The initial concept

of this review was inspired by discussions with patients during follow-up assessments in which several indicated a need for additional non-pharmacological management strategies. There has been no further patient or public involvement beyond this early inspiration.

Limitations

Limiting data to full-text published articles may introduce bias through exclusion of data in grey literature. Given that studies with desirable or significant results are more likely to be granted publication, a 'publication bias' may increase estimations of reliable estimates.[50] There is also a possibility of low-level evidence for treatments of vestibular and oculomotor dysfunction in patients with postconcussive symptoms. The methodological appraisals conducted throughout this review will identify if this is the case such that recommendations to strengthen the body of evidence can be made.

ETHICS AND DISSEMINATION

This review does not require ethical approval. Results of this review will be presented at scientific meetings and published in peer-reviewed journals. All publications and presentations related to the study will be authorised and reviewed by the study investigators.

Review status

The reviewers have commenced preliminary searches of relevant databases. This review is expected to be completed by March 2023.

Author affiliations
[1]School of Science, Western Sydney University, Sydney, New South Wales, Australia
[2]Brain Stimulation and Rehabilitation (BrainStAR) Lab, School of Health Sciences, Western Sydney University, Sydney, New South Wales, Australia
[3]Faculty of Health, School of Biomedical Sciences, Queensland University of Technology, Brisbane, Queensland, Australia
[4]Translational Neuroscience Facility, UNSW Sydney, Sydney, New South Wales, Australia

Twitter Stella Sheeba @stella_paramed, Rocco Cavaleri @roccocavaleri, Simon Summers @SimonJSummers and Cherylea Browne @Cherylea_Browne

Contributors All authors, SSheeba, RC, SSummers and CB, contributed equally to the design, writing and editing of the study protocol. All authors agree to be accountable for all aspects of the work to ensure its accuracy and integrity.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD
Rocco Cavaleri http://orcid.org/0000-0001-9499-1703

REFERENCES

1 Dewan MC, Rattani A, Gupta S, *et al*. Estimating the global incidence of traumatic brain injury. *J Neurosurg* 2018:1–18.
2 Cassidy JD, Carroll LJ, Peloso PM, *et al*. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO collaborating centre task force on mild traumatic brain injury. *J Rehabil Med* 2004;43:28–60.
3 Ommaya AK, Rockoff SD, Baldwin M. Experimental concussion; a first report. *J Neurosurg* 1964;21:249–65.
4 Aligene K, Lin E. Vestibular and balance treatment of the concussed athlete. *NeuroRehabilitation* 2013;32:543–53.
5 Alsalaheen BA, Mucha A, Morris LO, *et al*. Vestibular rehabilitation for dizziness and balance disorders after concussion. *J Neurol Phys Ther* 2010;34:87–93.
6 Dean PJA, O'Neill D, Sterr A. Post-concussion syndrome: prevalence after mild traumatic brain injury in comparison with a sample without head injury. *Brain Inj* 2012;26:14–26.
7 Marshall S, Bayley M, McCullagh S, *et al*. Updated clinical practice guidelines for concussion/mild traumatic brain injury and persistent symptoms. *Brain Inj* 2015;29:688–700.
8 Fife TD, Kalra D. Persistent vertigo and dizziness after mild traumatic brain injury. *Ann N Y Acad Sci* 2015;1343:97–105.
9 Ingebrigtsen T, Waterloo K, Marup-Jensen S, *et al*. Quantification of post-concussion symptoms 3 months after minor head injury in 100 consecutive patients. *J Neurol* 1998;245:609–12.
10 Valovich McLeod TC, Hale TD. Vestibular and balance issues following sport-related concussion. *Brain Inj* 2015;29:175–84.
11 Arciniegas DB, Anderson CA, Topkoff J, *et al*. Mild traumatic brain injury: a neuropsychiatric approach to diagnosis, evaluation, and treatment. *Neuropsychiatr Dis Treat* 2005;1:311–27.
12 van der Vlegel M, Polinder S, Toet H, *et al*. Prevalence of post-concussion-like symptoms in the general injury population and the association with health-related quality of life, health care use, and return to work. *J Clin Med* 2021;10:806–18.
13 Voormolen DC, Cnossen MC, Polinder S, *et al*. Divergent classification methods of post-concussion syndrome after mild traumatic brain injury: prevalence rates, risk factors, and functional outcome. *J Neurotrauma* 2018;35:1233–41.
14 Chorney SR, Suryadevara AC, Nicholas BD. Audiovestibular symptoms as predictors of prolonged sports-related concussion among NCAA athletes. *Laryngoscope* 2017;127:2850–3.
15 Ellis MJ, Leddy JJ, Willer B. Physiological, vestibulo-ocular and cervicogenic post-concussion disorders: an evidence-based classification system with directions for treatment. *Brain Inj* 2015;29:238–48.
16 Fino PC, Peterka RJ, Hullar TE, *et al*. Assessment and rehabilitation of central sensory impairments for balance in mTBI using auditory biofeedback: a randomized clinical trial. *BMC Neurol* 2017;17:1–14.
17 Kleffelgaard I, Roe C, Soberg HL, *et al*. Associations among self-reported balance problems, post-concussion symptoms and performance-based tests: a longitudinal follow-up study. *Disabil Rehabil* 2012;34:788–94.
18 Lau BC, Kontos AP, Collins MW, *et al*. Which on-field signs/symptoms predict protracted recovery from sport-related concussion among high school football players? *Am J Sports Med* 2011;39:2311–8.
19 Szentagothai J. The elementary vestibulo-ocular reflex Arc. *J Neurophysiol* 1950;13:395–407.
20 Teare-Ketter A, LaForme Fiss A, Ebert J. The utility of neuromotor retraining to augment manual therapy and vestibular rehabilitation in a patient with post-concussion syndrome: a case report. *Int J Sports Phys Ther* 2021;16:248–58.
21 Ziaks L, Giardina R, Kloos A. Integration of vision and vestibular therapy for vestibulo-ocular post-concussion disorder - a case study. *Internet J Allied Health Sci Pract* 2019;17:1–17.
22 Mucci V, Meier C, Bizzini M, *et al*. Combined optokinetic treatment and vestibular rehabilitation to reduce visually induced dizziness in a professional ice hockey player after concussion: a clinical case. *Front Neurol* 2019;10:1–7.
23 Scheiman M, Grady MF, Jenewein E, *et al*. Frequency of oculomotor disorders in adolescents 11 to 17 years of age with concussion, 4 to 12 weeks post injury. *Vision Res* 2021;183:73–80.
24 Swain SK. Pharmacotherapy for vertigo: a current perspective. *Int J Otorhinolaryngol Head Neck Surg* 2020;6:1400–6.
25 Scholtz A-W, Ilgner J, Loader B, *et al*. Cinnarizine and dimenhydrinate in the treatment of vertigo in medical practice. *Wien Klin Wochenschr* 2016;128:341–7.
26 Kirtane MV, Bhandari A, Narang P, *et al*. Cinnarizine: a contemporary review. *Indian J Otolaryngol Head Neck Surg* 2019;71:1060–8.
27 Pytel J, Nagy G, Tóth A, *et al*. Efficacy and tolerability of a fixed low-dose combination of cinnarizine and dimenhydrinate in the treatment

of vertigo: a 4-week, randomized, double-blind, active- and placebo-controlled, parallel-group, outpatient study. *Clin Ther* 2007;29:84–98.
28 Ganança MM, Caovilla HH, Ganança FF, *et al*. Clonazepam in the pharmacological treatment of vertigo and tinnitus. *Int Tinnitus J* 2002;8:50–3.
29 Rytter HM, Graff HJ, Henriksen HK, *et al*. Nonpharmacological treatment of persistent Postconcussion symptoms in adults: a systematic review and meta-analysis and guideline recommendation. *JAMA Netw Open* 2021;4:e2132221.
30 Koski L, Kolivakis T, Yu C, *et al*. Noninvasive brain stimulation for persistent postconcussion symptoms in mild traumatic brain injury. *J Neurotrauma* 2015;32:38–44.
31 Saki N, Bayat A, Nikakhlagh S, *et al*. Vestibular rehabilitation therapy in combination with transcranial direct current stimulation (tDCS) for treatment of chronic vestibular dysfunction in the elderly: a double-blind randomized controlled trial. *Braz J Otorhinolaryngol* 2022;88:758–66.
32 Babikian T, Satz P, Zaucha K, *et al*. The UCLA longitudinal study of neurocognitive outcomes following mild pediatric traumatic brain injury. *J Int Neuropsychol Soc* 2011;17:886–95.
33 Hessen E, Nestvold K, Anderson V. Neuropsychological function 23 years after mild traumatic brain injury: a comparison of outcome after paediatric and adult head injuries. *Brain Inj* 2007;21:963–79.
34 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
35 Higgins JPT, Thomas J, Chandler J. *Cochrane Handbook for systematic reviews of interventions version 6.2*. Cochrane, 2021. www.training.cochrane.org/handbook
36 Silverberg ND, Iaccarino MA, Panenka WJ, *et al*. Management of concussion and mild traumatic brain injury: a synthesis of practice guidelines. *Arch Phys Med Rehabil* 2020;101:382–93.
37 Ninot G. Non-Pharmacological Interventions: An Essential Answer to Current Demographic, Health, and Environmental Transitions. In: Ninot G, ed. *Defining non-pharmacological interventions (NPIs)*. Cham: Springer International Publishing, 2021: 1–46.
38 Nerrant E, Abouaf L, Pollet-Villard F, *et al*. Gabapentin and memantine for treatment of acquired pendular nystagmus: effects on visual outcomes. *J Neuroophthalmol* 2020;40:198–206.
39 Chaudhry S. Scrupulously managing vertigo. *JPBS* 2021;9:1–6.
40 Cochrane. Data extraction forms The Cochrane Collaboration; 2021. https://dplp.cochrane.org/data-extraction-forms
41 Maher CG, Sherrington C, Herbert RD, *et al*. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther* 2003;83:713–21.
42 Elkins MR, Herbert RD, Moseley AM, *et al*. Rating the quality of trials in systematic reviews of physical therapy interventions. *Cardiopulm Phys Ther J* 2010;21:20–6.
43 Bennett JA. The consolidated standards of reporting trials (consort): guidelines for reporting randomized trials. *Nurs Res* 2005;54:128–32.
44 Guyatt GH, Oxman AD, Vist GE, *et al*. Grade: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–6.
45 Murad MH, Mustafa RA, Schünemann HJ, *et al*. Rating the certainty in evidence in the absence of a single estimate of effect. *Evid Based Med* 2017;22:85–7.
46 Sterne JAC, Sutton AJ, Ioannidis JPA, *et al*. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;343:d4002.
47 Cochrane. *RevMan Analyses [Computer program]*. United Kingdon: London: Review Manager (RevMan) V5, 2020.
48 DerSimonian R, Kacker R. Random-effects model for meta-analysis of clinical trials: an update. *Contemp Clin Trials* 2007;28:105–14.
49 Hancock M, Kent P. Interpretation of dichotomous outcomes: risk, odds, risk ratios, odds ratios and number needed to treat. *J Physiother* 2016;62:172–4.
50 van Assen MALM, van Aert RCM, Nuijten MB, *et al*. Why publishing everything is more effective than selective publishing of statistically significant results. *PLoS One* 2014;9:e84896.