Cochrane Library

Cochrane Database of Systematic Reviews

Interventions for eye movement disorders due to acquired brain injury (Protocol)

Rowe FJ, Noonan CP, Garcia-Finana M, Dodridge CS, Howard C, Jarvis KA, MacDiarmid SL, Maan T, North L, Rodgers H

Rowe FJ, Noonan CP, Garcia-Finana M, Dodridge CS, Howard C, Jarvis KA, MacDiarmid SL, Maan T, North L, Rodgers H.
Interventions for eye movement disorders due to acquired brain injury.
Cochrane Database of Systematic Reviews 2014, Issue 9. Art. No.: CD011290.
DOI: 10.1002/14651858.CD011290.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

HEADER 1
ABSTRACT 1
BACKGROUND 2
OBJECTIVES 3
METHODS 4
ACKNOWLEDGEMENTS 7
REFERENCES 8
APPENDICES 9
CONTRIBUTIONS OF AUTHORS 18
DECLARATIONS OF INTEREST 18
SOURCES OF SUPPORT 18

[Intervention Protocol]

Interventions for eye movement disorders due to acquired brain injury

Fiona J Rowe[1], Carmel P Noonan[2], Marta Garcia-Finana[3], Caroline S Dodridge[4], Claire Howard[5], Kathryn A Jarvis[6], Sonia L MacDiarmid[7], Tallat Maan[8], Lorraine North[9], Helen Rodgers[10]

[1]Department of Health Services Research, University of Liverpool, Liverpool, UK. [2]Department of Ophthalmology, Aintree University Hospitals NHS Foundation Trust, Liverpool, UK. [3]Biostatistics, University of Liverpool, Liverpool, UK. [4]Orthoptics, Oxford University Hospitals NHS Trust, Oxford, UK. [5]Orthoptics, Salford Royal NHS Foundation Trust, Manchester, UK. [6]Occupational Therapy, University of Liverpool, Liverpool, UK. [7]Orthoptics, Wrightington Wigan and Leigh NHS Foundation Trust, Wigan, UK. [8]Community Eye Service, Pennine Care NHS Foundation Trust, Ashton-under-Lyne, UK. [9]Orthoptics, Frimley Park NHS Foundation Trust, Frimley, UK. [10]Institute for Ageing and Health, Newcastle University, Newcastle, UK

Contact address: Fiona J Rowe, Department of Health Services Research, University of Liverpool, Whelan Building (1.10), Brownlow Hill, Liverpool, L69 3GB, UK. rowef@liverpool.ac.uk.

Editorial group: Cochrane Eyes and Vision Group.
Publication status and date: New, published in Issue 9, 2014.

Citation: Rowe FJ, Noonan CP, Garcia-Finana M, Dodridge CS, Howard C, Jarvis KA, MacDiarmid SL, Maan T, North L, Rodgers H. Interventions for eye movement disorders due to acquired brain injury. *Cochrane Database of Systematic Reviews* 2014, Issue 9. Art. No.: CD011290. DOI: 10.1002/14651858.CD011290.

ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

The primary objective is to assess the effects of any intervention and determine the effect of timing of any intervention in the treatment of strabismus, gaze deficits and nystagmus due to acquired brain injury in order to align visual axes in primary and/or secondary gaze positions.

The secondary objectives will be to determine whether in patients with eye movement disorders due to acquired brain injury, at what time point or period, using the following interventions and comparators.

- Restitutive treatment is more effective than control, placebo, alternative treatment or no treatment in improving ocular alignment and/or motility.
- Substitutive treatment is more effective than control, placebo, alternative treatment or no treatment in improving ocular alignment and/or motility.
- Compensatory treatment is more effective than control, placebo, alternative treatment or no treatment in improving ocular alignment and/or motility.
- Pharmacological treatment is more effective than control, placebo, alternative treatment or no treatment in improving ocular alignment and/or motility.

BACKGROUND

Description of the condition

Acquired brain injury is brain damage caused by events caused after birth that result in permanent or temporary changes in cognition, physical, emotional and behavioural function. This may be due to trauma, surgery, stroke, brain tumour, infection, inflammation and ischaemia. Eye movement disorders following acquired brain injury may include strabismus, gaze deficits and nystagmus (Rowe 2003). In acquired brain injury, these eye movement disorders are caused by damage to the cranial nerves that supply the extra ocular muscles or to damage of the neurological areas that contribute to the control of eye movements (Pierrot-Deseilligny 2011). It is unknown what the incidence of visual problems is for acquired brain injury but estimates are available for certain types of acquired brain injury. For example, over half of stroke survivors have visual impairments (Freeman 1988), and up to 68% of stroke survivors with visual symptoms have eye movement disorders (Rowe 2009). These impact on daily life by causing a range of difficulties including inability to maintain normal ocular alignment or move the eyes appropriately (Jones 2006; Pedersen 1981; Rowe 2011a). Functional disabilities occur including loss of depth perception, reduced hand-eye coordination and reading impairment (MacIntosh 2003; Rowe 2011b), and these may impede the effectiveness of rehabilitation therapy in regaining mobility, activities of daily living and quality of life (Ciuffreda 2007; MacIntosh 2003).

The true incidence of eye movement disorders in acquired brain injury is unknown and the prevalence varies depending on the cause of brain injury and area of brain involved. Strabismus is a deviation of the ocular alignment where one eye turns and which may be intermittent or constant (Fowler 1996; Rowe 2010). Strabismus occurs in a number of forms including esotropia (in-turning deviation), exotropia (out-turning deviation) or less commonly, hypertropia (up-turning deviation), hypotropia (down-turning deviation) and cyclotropia (rotatory deviation). Gaze deficits include disorders of the eye movement systems which involve saccades (fast movements of the eyes), smooth pursuits (slow, tracking movements of the eyes), vergence (opposite movements of the eyes such as convergence where both eyes turn inwards symmetrically or divergence where both eyes turn outwards), cranial nerve palsy (impairment of III, IV or VI nerve function causing abnormal eye movement and strabismus in the affected eye), bilateral gaze palsy (impaired horizontal, vertical or combined movements in both eyes), unilateral gaze palsy (internuclear ophthalmoplegia, one and a half syndrome) and vestibulo-ocular and opto-kinetic reflexes (involuntary movements of the eyes in response to moving objects and movement of the head and body) (Pedersen 1981; Rowe 2011a; Rowe 2013a). Nystagmus is a condition in which there are frequent involuntary oscillations of the eyes that result in reduced visual function (Rowe 2008).

Symptoms of eye movement disorders can include blurring of vision, diplopia (double vision), impaired depth (3-dimensional) perception, wobbling and jumbling of images, and reading difficulty (Rowe 2013b).

Description of the intervention

There are various treatments associated with strabismus, eye movement disorders and nystagmus. Primarily, treatment is directed at aligning the visual axes and improving the movement of the eyes. Treatments for eye movement disorders can be described as restitution, compensation, substitution or pharmacology (Kerkhoff 2000; Pollock 2011). Restitutive interventions may include convergence training, pursuit training and saccade training. Compensative interventions may include training eye movements for reading, compensatory head posture or movements, use of eye blinks or colour cues and training in activities of daily living. Substitutive interventions may include prisms, eye patches, lens alteration, botulinum toxin and local anaesthetic injections, extra ocular muscle surgery, magnification and environmental modification. Pharmacological interventions may include prescription drugs such as baclofen, memantine and carbamazepine.

Timing of treatment is dependent on the type of treatment option. Treatment options that can be provided early after onset include prisms, eye patches, botulinum toxin, exercises/training programmes, magnifiers and compensatory head posture advice. Treatment options that are provided at later stages (due to a requirement of stable ocular measurements) include extra-ocular muscle surgery and pharmacological drugs.

Commencement of interventions can be at multiple time points. Where an individual is referred immediately following the occurrence of the eye movement disorder, interventions such as prisms or occlusive eye patches to alleviate or reduce visual symptoms can be provided straight away after diagnosis and appropriate measurement of the disorder. Early treatment is considered to occur within one week of onset of eye movement disorder. Where there is a delay in referral, individuals may subconsciously close one eye or turn their head in an attempt to compensate for their visual deficit. Furthermore, interventions such as botulinum toxin and extra-ocular muscle surgery may be appropriate at later time points.

How the intervention might work

Restitution

Restitution includes the biochemical events that help restore functional neural tissue through the reduction of oedema, absorption of blood, restoration of normal neuronal physiology, and restoration of axon transport (Pollock 2011). Treatments of positive fusional

amplitudes and stereopsis through repetition training of specific deficient functions, such as convergence insufficiency, have been reported as effective (Kerkhoff 2000). Restitutive interventions will include those where there is direct training of the impaired function or repetitive stimulation of eye movement.

Compensation

Compensation aims to improve the mismatch between the patients' skills and the demands placed on them by their environment, by teaching patients to compensate or adapt using a spared or intact function (Kerkhoff 1999; Kerkhoff 2000).

Substitution

Substitution involves adaptation of visual components that have been lost or disrupted through the use of optic devices, extra-ocular muscle surgery or environmental modifications (Kerkhoff 1999; Kerkhoff 2000).

Pharmacology

Pharmacology aims to improve visual functioning through alteration of biochemical and/or physiological effects in the body.

Why it is important to do this review

There are many forms of interventions for eye movement disorders that occur following acquired brain injury. Although the natural history of acquired brain injury differs dependent on the cause, the treatment of the resultant eye movement disorder is principally the same regardless of cause. Although the cause may recover or progress, the resultant eye movement disorder may persist and requires treatment to alleviate or reduce visual symptoms. We will consider all interventions for all types of eye movement disorders regardless of cause and evolution of eye movement disorder. We will extract data for improving, stable or deteriorating eye movement disorders. In the early stages, treatment may include conservative options such as eye patching or prisms which are used whilst the eye movement disorder is monitored until it improves or stabilises. Where eye movement disorders persist, further treatment options such as botulinum toxin or extra-ocular muscle surgery may then be considered.

There are multiple time points at which interventions for eye movement disorders that occur following acquired brain injury may be provided. The timing of provision of treatment for eye movement disorders differs for the various treatment options. In the early stages, treatment may include conservative options such as eye patching or prisms which are used whilst the eye movement disorder is monitored until it improves or stabilises. Where eye movement disorders persist, further treatment options such as botulinum toxin or extra ocular muscle surgery may then be considered. There can be delays in referral of patients with acquired brain injury to eye care services and thus patients may not receive treatment early even though treatment options are available. This delay may impede general rehabilitation.

A recent systematic review on interventions for eye movement disorders in stroke found insufficient evidence to reach conclusions about the effectiveness of those interventions for this group of patients (Pollock 2011). There was an absence of relevant evidence with a recommendation for urgent high quality research. Furthermore, there is no consensus for what constitutes the optimum timing for commencing interventions for eye movement disorders due to stroke. Timing may vary dependent on the type of treatment being considered (e.g. eye patch versus extra-ocular muscle surgery) and/or the extent of visual symptoms (minimal versus severe impact on daily life). Because this review only concentrated on stroke populations, one recommendation was for a systematic review of interventions for eye movement disorders in patients with acquired brain injury in order to synthesise the current evidence base, to guide current practice and aid in the development of well-designed randomised controlled trials (RCTs). Other publications reporting efficacy and timing of interventions for eye movement disorders include populations with varied causes of brain damage such as tumours, inflammation, infection, stroke and metabolic causes.

Purpose

We propose to undertake a high-quality systematic review of the existing evidence base in order to determine the evidence for effectiveness and timing of any treatment or management approaches for all adult patients with acquired brain injury with eye movement disorders. This review will directly address the recommendations of the Cochrane systematic review on interventions for eye movement disorders in stroke (Pollock 2011), i.e. conduct a systematic review of interventions for eye movement disorders in patients with acquired brain injury in order to synthesise the current evidence base, and whether the timing of interventions for eye movement disorders has an impact on objective and subjective measures of ocular alignment and motility. This will guide current practice and aid in the development of well-designed RCTs which follow the U.K. Medical Research Council guidance on developing and evaluating complex interventions (Craig 2008).

OBJECTIVES

The primary objective is to assess the effects of any intervention and determine the effect of timing of any intervention in the treatment of strabismus, gaze deficits and nystagmus due to acquired brain injury in order to align visual axes in primary and/or secondary gaze positions.

The secondary objectives will be to determine whether in patients with eye movement disorders due to acquired brain injury, at what time point or period, using the following interventions and comparators.

- Restitutive treatment is more effective than control, placebo, alternative treatment or no treatment in improving ocular alignment and/or motility.

- Substitutive treatment is more effective than control, placebo, alternative treatment or no treatment in improving ocular alignment and/or motility.

- Compensatory treatment is more effective than control, placebo, alternative treatment or no treatment in improving ocular alignment and/or motility.

- Pharmacological treatment is more effective than control, placebo, alternative treatment or no treatment in improving ocular alignment and/or motility.

METHODS

Criteria for considering studies for this review

Types of studies

We will include RCTs and quasi-RCTs.

Types of participants

We will include individuals with eye movement disorders due to acquired brain injury. The type of eye movement disorder may include III, IV, and VI cranial nerve palsy, reduced fixation, gaze holding, horizontal and/or vertica gaze palsy, internuclear ophthalmoplegia, one and a half syndrome, saccadic problems, smooth pursuit problems, strabismus, nystagmus, reduced convergence or divergence, conjugate deviation and skew deviation. The deviation of eye movement may be horizontal, vertical, torsional and the severity of eye movement disorder may be slight, small, moderate, marked, and paralysis, paresis; monocular, binocular.
We will accept studies that included participants based on symptoms which can be assumed to be present as a direct result of an eye movement disorder. Symptoms may include double vision, blurred vision, reading difficulty, wobbling or jumbled vision and excessive head movements. We will consider participants of all ages from studies of adults and children.

Types of interventions

We will include any intervention that aims to improve the defects of eye movement, or alleviating/reducing the visual symptoms associated with the disorder. We will classify interventions as restitution, compensation pharmacological or substitution. We will include any study that documented the timing (recorded as time period from the onset of eye movement disorder) of any intervention that aims to improve the defects of eye movement, or alleviating/reducing the visual symptoms associated with the disorder. We will classify timing as early or late intervention where early constitutes intervention within one month of eye movement disorder onset.

Types of outcome measures

Where possible, we will assess outcome as a dichotomous variable (yes/no) at the end of the intervention period and at a follow-up point (ideally a minimum of three months after the completion of the intervention and maximum of 12 months).

Primary outcomes

- Improvement in ocular motility measured by orthoptic assessments of reduction in the angle of deviation (within 10 prism dioptres of ortho) and/or extent of eye movement range (improvement of one or more grades of limitation ranging from 1 to 4), such that visual axes are aligned in primary and/or secondary gaze positions

Secondary outcomes

- Achievement of binocular single vision as assessed by cover test, motor fusional vergences and stereoacuity
- Reduction of, or alleviation of, patient-reported symptoms assessed by patient record notes or questionnaire
- Improvement in functional ability measured by validated measures such as activity of daily living questionnaires
- Adverse events
    - Intractable permanent diplopia, perforating injury, symptomatic over or under correction, death
    - Assessed by descriptive documentation
- Quality of life data
    - Any measure of patient or parent satisfaction relating to improvement in appearance or improvement to lifestyle

Search methods for identification of studies

Electronic searches

We will search the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group Trials Register) (latest issue), Ovid MEDLINE,

Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to present), EMBASE (January 1980 to present), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1982 to present), Allied and Complementary Medicine Database (AMED) (1985 to present), PsycINFO (1967 to present), Dissertations & Theses (PQDT) database (1861 to present) (http://pqdtopen.proquest.com/search.html), PsycBITE (Psychological Database for Brain Impairment Treatment Efficacy) (http://www.psycbite.com/search.php), the *meta*Register of Controlled Trials (*m*RCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrial.gov), Health Services Research Projects in Progress (HSRProj) (wwwcf.nlm.nih.gov/hsr_project/home_proj.cfm), National Eye Institute Clinical Studies Database (clinicalstudies.info.nih.gov/cgi/protinstitute.cgi?NEI.0.html) and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We will not use any date or language restrictions in the electronic searches for trials.

See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), CINAHL (Appendix 4), AMED (Appendix 5), PsycINFO (Appendix 6), PQDT database (Appendix 8), PsycBITE (Appendix 8), *m*RCT (Appendix 9), ClinicalTrials.gov (Appendix 10), HSRPro (Appendix 11), National Eye Institute Clinical Studies Database (Appendix 12) and the ICTRP (Appendix 13).

Searching other resources

We will search the reference lists of included trials to identify any further studies and will check the references of review articles about vision after acquired brain injury. We will perform citation tracking using Web of Science Cited Reference Search for all included studies and will contact experts in the field - including authors of included trials, and excluded studies identified as possible preliminary or pilot work. We will also search reference material supplied by commercial companies who provide interventions aimed at restoration of eye movements.

We will handsearch the following resources from their inception to the current date at (http://pcwww.liv.ac.uk/~rowef/index_files/Page646.htm):

- British and Irish Orthoptic Journal
- Australian Orthoptic Journal
- Proceedings of the European Strabismological Association (ESA)
- International Strabismological Association (ISA)
- International Orthoptic Association (IOA)

Data collection and analysis

We will follow guidance in Chapter 7 of the *Cochrane Handbook for Systematic Reviews of Interventions* for data collection and Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* for data analysis (Deeks 2011; Higgins 2011a), and also conform to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (Moher 2009). The Cochrane Eye and Vision Group Trials Search Co-ordinator will run all the electronic searches, download references into bibliographic software, and remove duplicates. Two review authors will exclude any titles/abstracts which are obviously not related to acquired brain injury and vision. They will independently consider each of these titles/abstracts and exclude any studies where the intervention is not specifically aimed at improving the eye movement disorder or the patient's ability to cope with the eye movement disorder. We will resolve any disagreements through discussion. We will obtain the full papers for any studies included at this stage.

Selection of studies

Two review authors will independently apply the selection criteria, considering and documenting the type of studies, type of participants, intervention, comparison intervention, and the outcome measures. Each review author will classify each study as include or exclude. If there is disagreement between these two review authors, they will reach consensus through discussion involving a third review author.

We will list all excluded studies that included participants with eye movement disorders in the 'Characteristics of excluded studies' table with the reasons for exclusion. We will not list studies in the 'Characteristics of excluded studies' table that are excluded because they included participants that did not have eye movement disorders (i.e. visual neglect, age-related visual problems, or visual field loss), unless the two review authors agree that there is a clear reason to do so.

Data extraction and management

We will use a pre-designed data extraction form to record data from the included studies. Two review authors will independently document information found in the table in Appendix 14. If there are any discrepancies between data extracted by the two review authors, they will resolve these through discussion.

Assessment of risk of bias in included studies

We will follow the Cochrane Collaboration tool for assessing risk of bias for randomised trials as outlined in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b). We will assess sequence generation, allocation concealment, masking (blinding) of participants, personnel and outcome assessors, incomplete outcome data, selective outcome reporting and other sources of bias. We will judge each domain as "low risk of bias", "high risk of bias" or "unclear".

Measures of treatment effect

We will use the Cochrane Collaboration statistical software, Review Manager 2014, to carry out statistical analyses to determine the treatment and timing effect of restitutive, compensatory, substitutive and pharmacological interventions.

The outcome measures of angle of deviation, range of ocular movements and binocular vision measures versions comprise of either ordinal data from measurement scales (e.g. prism dioptre measurements), count data (e.g. movement grading scales of 1 to 4, -1 to -4), or continuous data (e.g. degree measurements). The threshold for reduction in angle of deviation is +/- 10 prism dioptres (5 degrees) of ortho and for reduction of ocular movements is +/1 one grade. We will analyse these as continuous variables.

Where change (improvement) is reported for angle of deviation, range of ocular movements and binocular vision measures, we will analyse this as dichotomous data with yes/no for reports of improvement.

If reported outcomes have a scale which uses negative values (e.g. divergent ocular deviations recorded as "-"), we will multiply the reported values by -1, so that in all analyses the results are represented as positive values.

If studies report change values and the baseline value is available, we will calculate the value at follow-up (change value - baseline value). If studies report change values and the baseline value is available, we will use these data in meta-analyses, but we plan to conduct sensitivity analyses to investigate the effect of including these data.

We will analyse adverse events and death as dichotomous variables. For dichotomous variables, we will calculate the treatment effects using a fixed-effect model (where there is a small number of trials and where heterogeneity has not been detected) and report as odds ratios (ORs) with 95% confidence intervals (CIs). For continuous data, we will calculate the treatment effect using standardised mean differences (SMDs) and 95% CIs where studies used different scales for the assessment of the same outcome. We will use mean differences (MDs) and 95% CIs where studies have all used the same method of measuring outcome.

Unit of analysis issues

The above interventions will normally be applied at individual level. Some interventions (e.g. prisms for diplopia or field defect, monocular occlusion) are used to treat only one eye. In these instances, there is no unit of analysis issue as the unit of randomisation is the same as the unit of analysis. However, some interventions (e.g. scanning eye exercises, extra-ocular muscle surgery, pharmacological interventions) treat both eyes. In these instances we will report for the person through binocular measurements such as binocular visual acuity, binocular single vision and binocular visual field.

Dealing with missing data

If an included study does not report a particular outcome, we will not include that study in the analyses of that outcome. If an included study has missing data (e.g. it reports the mean but not standard deviations for the follow-up data) we will take logical steps to enter an assumed value. Such steps may include calculating a standard deviation based on a reported standard error, or estimating a follow-up standard deviation based on a baseline value. We plan to do sensitivity analyses to investigate the effect of entering assumed values. Where possible we will contact authors to enquire about missing data to determine differences between groups because of withdrawals, drop-outs and protocol deviations and the extent of this for numbers across the groups, differences across the groups and whether all recruits used in the analysis. We will assess trials that included intention-to-treat analyses to ensure this has been done correctly, ensuring participants have been included even if they did not fully adhere to the protocol and that it is possible to extract the appropriate data for these participants from the results. We will use all trial data even if intention-to-treat analysis was not conducted. However, we will look at which participants dropped out or changed treatment to determine if these relate to one specific group or are dispersed across all groups.

Assessment of heterogeneity

We will check for heterogeneity by examining:

- characteristics of the study;
- forest plot of results of the studies;
- results of the Chi^2 test;
- results of the I^2 statistic.

We will determine heterogeneity using the I^2 statistic. We will consider I^2 greater than 50% as substantial heterogeneity. If I^2 is greater than 50%, we will explore the individual trial characteristics to identify potential sources of heterogeneity, using pre-planned subgroup analyses. If I^2 is less than or equal to 50%, we will used the fixed-effect model for our meta-analyses.

Assessment of reporting biases

We will assess reporting biases as detailed in the Assessment of risk of bias in included studies section. If 10 or more studies are included in analysis, we will use a funnel plot, examining for asymmetry in the assessment of reporting bias.

We will attempt to avoid reporting biases by using a comprehensive search strategy which includes searching for unpublished studies, and searching trials registers. We will carry out sensitivity analyses to explore the effect of publication type. We will evaluate studies for selective reporting of outcomes. Where there is an online protocol for the trial, we will obtain this and compare the reported study outcomes from the publication to the protocol.

Data synthesis

We will combine results to produce a single summary measure using a random-effects model unless there are few trials (three or less), in which case we will use a fixed-effect model. If there is substantial heterogeneity (I^2 > 50%), we will not combine results, unless the effect estimates are all in the same direction. If we do not produce a single summary measure, we will do a narrative summary of the trial results. If multi-arm studies are included, we will ensure that the analysis of multiple intervention groups avoids arbitrary omission of relevant groups and double-counting of participants.

Subgroup analysis and investigation of heterogeneity

For effect of timing, we will compare the effect of interventions at different times points of early intervention (Intervention given within one month of eye movement disorder onset) versus late intervention (intervention given after one month of eye movement disorder onset).

For effect of treatment, we will compare the interventions against each other as outlined above with the different types of treatment (restitutive, compensatory, substitutive and pharmacological) forming a framework for subgroup analysis.

If I^2 is greater than 50%, we will explore the individual trial characteristics to identify potential sources of heterogeneity, using pre-planned subgroup analyses. We intend to explore heterogeneity by subgroup analyses to investigate the effect on the primary outcome of:

- gender (male, female);
- type of acquired brain injury (trauma, surgery, stroke, brain tumour, infection, inflammation, ischaemia);
- side of brain injury (left, right, bilateral);
- type of eye movement disorder (III, IV & VI nerve palsy, reduced fixation/gaze holding, saccadic problems, smooth pursuit problems, strabismus, nystagmus, reduced convergence, conjugate deviation, skew deviation);
- deviation of eye movement (horizontal, vertical, torsional);
- severity of eye movement disorder (slight, small, moderate, marked, paralysis, paresis, monocular, binocular);
- type of treatment (e.g. for compensative interventions - saccadic eye movement, activities of daily living training; for substitutive interventions - prisms, patches, environmental modifications);
- variable timing of treatment (e.g. within one week of onset and upwards).

We will use an established method for subgroup analyses (Deeks 2001).

Sensitivity analysis

We intend to carry out sensitivity analyses to explore the effect of the following methodological features.

- Allocation concealment: we will re-analyse data, excluding trials with inadequate or unclear allocation concealment.
- Masking of outcome assessor: we will re-analyse data, excluding trials without or with unclear masking of outcome assessor.
- Missing outcome data: we will re-analyse data, excluding trials with inadequate or unclear methods of dealing with missing outcome data.
- Other bias: we will re-analyse data, exclude trials assessed to have other bias, or are unclear as to whether they have other bias.
- Publication type (peer-reviewed journal, conference abstract/proceedings, doctoral dissertation): we will re-analyse data including only those trials from peer-reviewed journals.

Methods for future updates

If trials become available in the future we will include them in this review using the methods for the primary review. We will update our systematic review every two years.

Summary of findings

We will include a 'Summary of findings' table according to recommendations described in Chapter 11 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011a). We will include results for one population group, indicate the intervention and the comparison intervention, include seven or fewer patient-important outcomes (e.g. symptoms, adverse events, quality of life), describe the outcomes (e.g. scale, scores, follow-up), indicate the number of participants and studies for each outcome, present at least one baseline risk for each dichotomous outcome (e.g. study population or median/medium risk) and baseline scores for continuous outcomes (if appropriate), summarise the intervention effect (if appropriate), and include a measure of the quality of the body of evidence (independent grading of evidence by two authors) as per the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines described in Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011b).

ACKNOWLEDGEMENTS

The Cochrane Eyes and Vision Group (CEVG) will create and execute the electronic search strategies. We thank Catey Bunce, Tracey Shipman and Jennifer Evans for their comments and Anupa Shah, Managing Editor for CEVG for her assistance throughout the review process.

REFERENCES

Additional references

Ciuffreda 2007
Ciuffreda KJ, Kapoor N, Rutner D, Suchoff IB, Han ME, Craig S. Occurrence of oculomotor dysfunctions in acquired brain injury: a retrospective analysis. *Optometry* 2007;**78**(4):155–61.

Craig 2008
Craig P, Dieppe P, MacIntyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: new guidance. Medical Research Council 2008.

Deeks 2001
Deeks JJ, Altman DG, Bradburn MJ. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman DG editor(s). *Systematic Reviews in Health Care*. 2nd Edition. London: BMJ Books, 2001:300.

Deeks 2011
Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Fowler 1996
Fowler MS, Wade DT, Richardson AJ, Stein JF. Squints and diplopia seen after brain damage. *Neurology* 1996;**243**(1): 86–90.

Freeman 1988
Freeman CF, Rudge NB. Cerebrovascular accident and the orthoptist. *British Orthoptic Journal* 1988;**45**:8–18.

Glanville 2006
Glanville JM, Lefebvre C, Miles JN, Camosso-Stefinovic J. How to identify randomized controlled trials in MEDLINE: ten years on. *Journal of the Medical Library Association* 2006; **94**(2):130–6.

Higgins 2011a
Higgins JPT, Deeks JJ (editors). Chapter 7: Selecting studies and collecting data. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Higgins 2011b
Higgins JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Jones 2006
Jones SA, Shinton RA. Improving outcome in stroke patients with visual problems. *Age and Ageing* 2006;**35**(6): 560–5.

Kerkhoff 1999
Kerkhoff G. Restorative and compensatory therapy approaches in cerebral blindness - a review. *Restorative Neurology and Neuroscience* 1999;**15**(2-3):255–71.

Kerkhoff 2000
Kerkhoff G. Neurovisual rehabilitation: recent developments and future directions. *Journal of Neurology, Neurosurgery and Psychiatry* 2000;**68**(6):691–706.

MacIntosh 2003
MacIntosh C. Stroke re-visited: visual problems following stroke and their effect on rehabilitation. *British Orthoptic Journal* 2003;**60**:10–4.

Moher 2009
Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine* 2009;**6**(7):e1000097.

Pedersen 1981
Pedersen RA, Troost BT. Abnormalities of gaze in cerebrovascular disease. *Stroke* 1981;**12**(2):251–4.

Pierrot-Deseilligny 2011
Pierrot-Deseilligny C. Nuclear, internuclear, and supranuclear ocular motor disorders. *Handbook of Clinical Neurology* 2011;**102**:319–31.

Pollock 2011
Pollock A, Hazelton C, Henderson CA, Angilley J, Dhillon B, Langhorne P, et al. Interventions for disorders of eye movement in patients with stroke. *Cochrane Database of Systematic Reviews* 2011, Issue 10. [DOI: 10.1002/14651858.CD008389.pub2]

Review Manager 2014 [Computer program]
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Rowe 2003
Rowe FJ. Supranuclear and internuclear control of eye movements. A review. *British Orthoptic Journal* 2003;**60**: 2–9.

Rowe 2008
Rowe FJ, VIS Group UK. The spectrum of nystagmus following cerebro-vascular accident. *British and Irish Orthoptic Journal* 2008;**5**:22–5.

Rowe 2009
Rowe FJ, Brand D, Jackson CA, Price A, Walker L, Harrison S, et al. Visual impairment following stroke : do stroke patients require vision assessment?. *Age and Ageing* 2009;**38** (2):188–93.

Rowe 2010
Rowe FJ, VIS Group UK. The profile of strabismus in stroke survivors. *Eye* 2010;**24**(4):682–5.

Rowe 2011a
Rowe FJ, Wright D, Brand D, Jackson C, Price A, Walker L, et al. Reading impairment following stroke: ocular and non ocular causes. *International Journal of Stroke* 2011;**6**(5): 404–11.

Rowe 2011b
Rowe FJ, VIS Group UK. Prevalence of ocular motor cranial nerve palsies and associations following stroke. *Eye* 2011;**25**(7):881–7.

Rowe 2013a
Rowe FJ, Wright D, Brand D, Jackson C, Harrison S, Maan T, et al. Profile of gaze dysfunction following cerebrovascular accident. *ISRN Ophthalmology* 2013;**2013**:264604.

Rowe 2013b
Rowe FJ, VIS Group UK. Symptoms of stroke related visual impairment. *Strabismus* 2013;**21**(2):150–4.

Schünemann 2011a
Schünemann HJ, Oxman AD, Higgins JPT, Vist GE, Glasziou P, Guyatt GH. Chapter 11: Presenting results and 'Summary of findings' tables. In: Higgins JPT, Green S (editors), *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Schünemann 2011b
Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, et al. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JPT, Green S (editors), *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

* *Indicates the major publication for the study*

APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Brain Injuries] explode all trees
#2 brain near/2 injur*
#3 ABI or TBI or non TB
#4 #1 or #2 or #3
#5 MeSH descriptor: [Eye] explode all trees
#6 MeSH descriptor: [Visually Impaired Persons] explode all trees
#7 MeSH descriptor: [Ocular Physiological Processes] explode all trees
#8 MeSH descriptor: [Diagnostic Techniques, Ophthalmological] explode all trees
#9 MeSH descriptor: [Optometry] explode all trees
#10 MeSH descriptor: [Orthoptics] explode all trees
#11 MeSH descriptor: [Eye Diseases] this term only
#12 MeSH descriptor: [Vision Disorders] this term only
#13 MeSH descriptor: [Eye Manifestations] this term only
#14 MeSH descriptor: [Blindness] this term only
#15 MeSH descriptor: [Diplopia] explode all trees
#16 MeSH descriptor: [Vision, Binocular] this term only
#17 MeSH descriptor: [Vision, Monocular] this term only
#18 MeSH descriptor: [Visual Acuity] explode all trees
#19 MeSH descriptor: [Visual Fields] this term only
#20 MeSH descriptor: [Vision, Low] this term only
#21 MeSH descriptor: [Visual Field Tests] explode all trees
#22 MeSH descriptor: [Ophthalmology] this term only
#23 MeSH descriptor: [Vision Screening] this term only
#24 MeSH descriptor: [Eye Diseases, Hereditary] explode all trees
#25 MeSH descriptor: [Ocular Motility Disorders] explode all trees

#26 MeSH descriptor: [Optic Nerve Diseases] explode all trees
#27 MeSH descriptor: [Orbital Diseases] explode all trees
#28 MeSH descriptor: [Pupil Disorders] explode all trees
#29 MeSH descriptor: [Refractive Errors] explode all trees
#30 MeSH descriptor: [Blindness, Cortical] explode all trees
#31 MeSH descriptor: [Hemianopsia] explode all trees
#32 MeSH descriptor: [Scotoma] this term only
#33 MeSH descriptor: [Abducens Nerve] this term only
#34 MeSH descriptor: [Oculomotor Nerve] this term only
#35 MeSH descriptor: [Trochlear Nerve] this term only
#36 nystagmus or smooth pursuit or saccades or depth perception or stereopsis or ophthalmol* or optic nerve
#37 gaze* near/2 (deficit* or palsy or disorder*)
#38 ocular near/2 (muscle* or align*)
#39 esotropi* or exotropi* or hypertropi* or hypotropi* or cyclotropi*
#40 intranuclear ophthalmoplegia or parinaud's syndrome or weber's syndrome or skew deviation or conjugate deviation
#41(visual* or vision or eye or eyes or eyesight or sight) near/5 (problem* or disorder* or impair* or disabilit* or loss or disease* or defect* or manifestation* or screening or test* or examination*)
#42 reading near/2 (difficult* or impair*)
#43 hemianop* or blindness or low vision or refractive errors or scotoma or diplopia or optometr* or ocular or orthoptic*
#44 oscillopsia or visual tracking or fresnel prism*
#45 III or IV or VI or third or fourth or sixth near/3 nerve palsy
#46 (#5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #40 or #41 or #43 or #44 or #45)
#47 #4 and #46

Appendix 2. MEDLINE (OvidSP) search strategy

1. randomized controlled trial.pt.
2. (randomized or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. exp animals/
10. exp humans/
11. 9 not (9 and 10)
12. 8 not 11
13. exp brain injuries/
14. (brain adj2 injur$).tw.
15. (ABI or TBI or non TBI).tw.
16. or/13-15
17. exp Eye/
18. exp Visually Impaired Persons/
19. exp Ocular Physiological Processes/
20. exp Diagnostic Techniques, Ophthalmological/
21. exp Optometry/
22. exp Orthoptics/
23. exp Eye Diseases/
24. exp Vision Disorders/
25. exp Eye Manifestations/

26. exp Blindness/
27. exp Diplopia/
28. Vision, Binocular/
29. Vision, Monocular/
30. exp Visual Acuity/
31. Visual Fields/
32. Vision, Low/
33. exp Visual Field Tests/
34. Ophthalmology/
35. Vision Screening/
36. Eye Diseases, Hereditary/
37. exp Ocular Motility Disorders/
38. exp Optic Nerve Diseases/
39. Enophthalmos/
40. exp Pupil Disorders/
41. exp Refractive Errors/
42. Blindness, Cortical/
43. exp Hemianopsia/
44. Scotoma/
45. Abducens Nerve/
46. Oculomotor Nerve/
47. Trochlear Nerve/
48. (nystagmus or smooth pursuit or saccades or depth perception or stereopsis or gaze disorder$ or ophthalmol$ or optic nerve$).tw.
49. (gaze$ adj2 (deficit$ or palsy or disorder$)).tw.
50. (ocular adj2 (muscle$ or align$)).tw.
51. (esotropi$ or exotropi$ or hypertropi$ or hypotropi$ or cyclotropi$).tw.
52. (intranuclear ophthalmoplegia or parinaud's syndrome or weber's syndrome or skew deviation or conjugate deviation).tw.
53. ((visual$ or vision or eye or eyes or eyesight or sight) adj3 (problem$ or disorder$ or impair$ or disabilit$ or loss or disease$ or defect$ or manifestation$ or screening or test$ or examination$)).tw.
54. (reading adj2 (difficult$ or impair$)).tw.
55. (hemianop$ or blindness or low vision or refractive errors or scotoma or diplopia or optometr$ or ocular or orthoptic$).tw.
56. (oscillopsia or visual tracking or fresnel prism$).tw.
57. ((III or IV or VI or third or fourth or sixth) adj3 nerve palsy).tw.
58. or/17-57
59. 16 and 58
60. 12 and 59

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville et al (Glanville 2006).

Appendix 3. EMBASE (OvidSP) search strategy

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. random$.tw.
6. or/1-5
7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/

13. (clin$ adj3 trial$).tw.
14. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
15. exp placebo/
16. placebo$.tw.
17. random$.tw.
18. exp experimental design/
19. exp crossover procedure/
20. exp control group/
21. exp latin square design/
22. or/12-21
23. 22 not 10
24. 23 not 11
25. exp comparative study/
26. exp evaluation/
27. exp prospective study/
28. (control$ or prospectiv$ or volunteer$).tw.
29. or/25-28
30. 29 not 10
31. 30 not (11 or 23)
32. 11 or 24 or 31
33. exp brain injury/
34. (brain adj2 injur$).tw.
35. (ABI or TBI or non TBI).tw.
36. or/33-35
37. eye/
38. exp visual system function/
39. exp visual system examination/
40. optometry/
41. orthoptics/
42. eye disease/
43. exp visual disorder/
44. exp eye movement disorder/
45. exp visual impairment/
46. exp vision/
47. perimetry/
48. ophthalmology/
49. exp optic nerve disease/
50. exp cranial nerve/
51. (nystagmus or smooth pursuit or saccades or depth perception or stereopsis or gaze disorder$ or ophthalmol$ or optic nerve$).tw.
52. (gaze$ adj2 (deficit$ or palsy or disorder$)).tw.
53. (ocular adj2 (muscle$ or align$)).tw.
54. (esotropi$ or exotropi$ or hypertropi$ or hypotropi$ or cyclotropi$).tw.
55. (intranuclear ophthalmoplegia or parinaud's syndrome or weber's syndrome or skew deviation or conjugate deviation).tw.
56. ((visual$ or vision or eye or eyes or eyesight or sight) adj3 (problem$ or disorder$ or impair$ or disabilit$ or loss or disease$ or defect$ or manifestation$ or screening or test$ or examination$)).tw.
57. (reading adj2 (difficult$ or impair$)).tw.
58. (hemianop$ or blindness or low vision or refractive errors or scotoma or diplopia or optometr$ or ocular or orthoptic$).tw.
59. (oscillopsia or visual tracking or fresnel prism$).tw.
60. ((III or IV or VI or third or fourth or sixth) adj3 nerve palsy).tw.
61. or/37-60
62. 36 and 61
63. 32 and 62

Appendix 4. CINAHL (EBSCO) search strategy

S56 S12 AND S55
S55 S16 AND S54
S54 S51 or S52 or S53
S53 S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51
S52 S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40
S51 S17 or S18 or S19 S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30
S50 nerve palsy
S49 oscillopsia or visual tracking or fresnel prism*
S48 hemianop* or blindness or low vision or refractive errors or scotoma or diplopia or optometr* or ocular or orthoptic*
S47 reading N2 (difficult* or impair*)
S46 (visual* or vision or eye or eyes or eyesight or sight) N5 (problem* or disorder* or impair* or disabilit* or loss or disease* or defect* or manifestation* or screening or test* or examination*)
S45 intranuclear ophthalmoplegia or parinaud's syndrome or weber's syndrome or skew deviation or conjugate deviation
S44 esotropi* or exotropi* or hypertropi* or hypotropi* or cyclotropi*
S43 ocular N2 (muscle* or align*)
S42 gaze* N2 (deficit* or palsy or disorder*)
S41 nystagmus or smooth pursuit or saccades or depth perception or stereopsis or ophthalmol* or optic nerve
S40 (MH "Trochlear Nerve") OR (MH "Trochlear Nerve Diseases")
S39 (MH "Abducens Nerve Diseases+") OR (MM "Abducens Nerve")
S38 (MM "Refractive Errors+")
S37 (MH "Pupil Disorders+")
S36 (MH "Orbital Diseases+")
S35 (MH "Optic Nerve Diseases+")
S34 (MM "Ocular Motility Disorders")
S33 (MM "Eye Diseases, Hereditary")
S32 (MM "Ophthalmology")
S31 (MH "Vision Tests+")
S30 (MH "Visual Perception+")
S29 (MM "Visual Fields")
S28 (MH "Visual Acuity")
S27 (MH "Depth Perception")
S26 (MH "Vision, Subnormal")
S25 (MM "Diplopia")
S24 (MH "Blindness+")
S23 (MH "Eye Manifestations+")
S22 (MH "Vision Disorders+")
S21 (MH "Eye Diseases+")
S20 (MM "Optometry")
S19 (MH "Diagnosis, Eye+")
S18 (MH "Rehabilitation of Vision Impaired+")
S17 (MH "Eye+")
S16 S13 or S14 or S15
S15 ABI or TBI or non TBI
S14 brain N2 injur*
S13 (MH "Brain Injuries+")
S12 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11
S11 TX allocat* random*
S10 (MM "Quantitative Studies")
S9 (MM "Placebos")
S8 TX placebo*
S7 TX random* allocat*

S6 (MM “Random Assignment”)
S5 TX randomi* control* trial*
S4 TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))
S3 TX clinic* n1 trial*
S2 PT Clinical trial
S1 (MH “Clinical Trials+”)

Appendix 5. AMED (OvidSP) search strategy

1. “Randomized controlled trials”/
2. prospective studies/
3. single blind method/
4. random$.tw.
5. placebo$.tw.
6. trial$.tw.
7. groups.tw.
8. ((singl$ or doubl$) adj3 (blind$ or mask$)).tw.
9. or/1-8
10. brain injuries/
11. (brain adj2 injur$).tw.
12. (ABI or TBI or non TBI).tw.
13. or/10-12
14. eye/
15. Blindness/
16. Vision disorders/
17. Vision/
18. Ocular Motility Disorders/
19. Eye Movements/
20. Optic nerve/
21. Refractive Errors/
22. Cranial nerves/
23. (nystagmus or smooth pursuit or saccades or depth perception or stereopsis or gaze disorder$ or ophthalmol$ or optic nerve$).tw.
24. (gaze$ adj2 (deficit$ or palsy or disorder$)).tw.
25. (ocular adj2 (muscle$ or align$)).tw.
26. (esotropi$ or exotropi$ or hypertropi$ or hypotropi$ or cyclotropi$).tw.
27. (intranuclear ophthalmoplegia or parinaud’s syndrome or weber’s syndrome or skew deviation or conjugate deviation).tw.
28. ((visual$ or vision or eye or eyes or eyesight or sight) adj3 (problem$ or disorder$ or impair$ or disabilit$ or loss or disease$ or defect$ or manifestation$ or screening or test$ or examination$)).tw.
29. (reading adj2 (difficult$ or impair$)).tw.
30. (hemianop$ or blindness or low vision or refractive errors or scotoma or diplopia or optometr$ or ocular or orthoptic$).tw.
31. (oscillopsia or visual tracking or fresnel prism$).tw.
32. ((III or IV or VI or third or fourth or sixth) adj3 nerve palsy).tw.
33. or/14-33
34. 13 and 33
35. 9 and 34

Appendix 6. PsychINFO (OvidSP) search strategy

1. exp Treatment Effectiveness Evaluation/
2. exp Clinical Trials/
3. exp Placebo/
4. placebo$.tw.
5. randomly.tw.
6. randomi#ed.tw.
7. trial$.tw.
8. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$ or dummy)).tw.
9. (factorial$ or allocat$ or assign$ or volunteer$).tw.
10. (crossover$ or cross over$).tw.
11. (quasi adj (experimental or random$)).tw.
12. (control$ adj3 (trial$ or study or studies or group$)).tw.
13. or/1-12
14. exp Brain Damage/
15. exp Traumatic Brain Injury/
16. (ABI or TBI or non TB).tw.
17. exp Head Injuries/
18. or/14-17
19. exp Eye Disorders/
20. exp Eye Fixation/
21. exp "Pupil (Eye)"/
22. exp Vision Disorders/
23. exp Vision/
24. exp Blind/
25. exp Optometry/
26. exp Strabismus/
27. exp Amblyopia/
28. exp Binocular Vision/
29. exp Eye Convergence/
30. exp Color Perception/
31. exp Visual Acuity/
32. exp Visual Field/
33. exp Ophthalmology/
34. exp Ophthalmologic Examination/
35. exp Hemianopia/
36. exp Abducens Nerve/
37. exp Cranial Nerves/
38. (nystagmus or smooth pursuit or saccades or depth perception or stereopsis or gaze disorder$ or ophthalmol$ or optic nerve$).tw.
39. (gaze$ adj2 (deficit$ or palsy or disorder$)).tw.
40. (ocular adj2 (muscle$ or align$)).tw.
41. (esotropi$ or exotropi$ or hypertropi$ or hypotropi$ or cyclotropi$).tw.
42. (intranuclear ophthalmoplegia or parinaud's syndrome or weber's syndrome or skew deviation or conjugate deviation).tw.
43. ((visual$ or vision or eye or eyes or eyesight or sight) adj3 (problem$ or disorder$ or impair$ or disabilit$ or loss or disease$ or defect$ or manifestation$ or screening or test$ or examination$)).tw.
44. (reading adj2 (difficult$ or impair$)).tw.
45. (hemianop$ or blindness or low vision or refractive errors or scotoma or diplopia or optometr$ or ocular or orthoptic$).tw.
46. (oscillopsia or visual tracking or fresnel prism$).tw.
47. ((III or IV or VI or third or fourth or sixth) adj3 nerve palsy).tw.
48. or/19-47
49. 18 and 48
50. 13 and 49

Appendix 7. Dissertations and Theses (PQDT) database

Keywords (dissertation topic) = brain injury

Appendix 8. PsycBITE database

PsycBITE was searched using the following options from the search interface:
Neurological Group = Traumatic Brain Injury (TBI) /Head Injury
Method = Randomised Controlled Trials
Target area = Literacy/Numeracy OR Visual Field Loss OR Community Re-entry

Appendix 9. *meta*Register of Controlled Trials search strategy

brain injury AND (vision or eye or ocular or nystagmus or strabismus or gaze or diplopia or reading)

Appendix 10. ClinicalTrials.gov search strategy

Brain Injury AND (Vision OR Eye OR Ocular OR Nystagmus OR Strabismus OR Gaze OR Diplopia OR Reading)

Appendix 11. Health Services Research Projects in Progress

("Brain Injury" AND (Vision OR Eye OR Ocular OR Nystagmus OR Strabismus OR Gaze OR Diplopia OR Reading))

Appendix 12. National Eye Institute Clinical Studies Database

brain AND vision

Appendix 13. ICTRP search strategy

Brain Injury = Condition AND Vision OR Eye OR Ocular OR Nystagmus OR Strabismus OR Gaze OR Diplopia OR Reading = Intervention

Appendix 14. Standardised headings for included studies table

Headings in table in RevMan	Proposed subheadings	
Methods	Study design	• Parallel group RCT i.e. people randomised to treatment • Paired eye or intra-individual RCT i.e. eyes randomised to treatment • Cluster RCT i.e. communities randomised to treatment • Cross-over RCT • Other
	Eyes	• One eye included in study ○ Indicating how the eye was selected • Two eyes included in study, both eyes received same treatment

(*Continued*)

		○ Indicating how data were analysed (best/worst/average/ both and adjusted for within person correlation/both and not adjusted for within person correlation ○ Indicating if a mixture of one eye and two eyes were used • Two eyes included in study, eyes received different treatments (pair matched) ○ Indicating if a correct pair-matched analysis was done
Participants	Country	
	Setting	
	Number of participants	
	Number of men	
	Number of women	
	Average age	
	Age range	
	Ethnic group	
	Inclusion criteria	
	Exclusion criteria	
	Eye movement disorders	Description of the type of eye movement disorder (III, IV, and VI cranial nerve palsy, reduced fixation, gaze holding, gaze palsy, saccadic problems, smooth pursuit problems, strabismus, nystagmus, reduced convergence or divergence, conjugate deviation, skew deviation), the deviation of eye movement (horizontal, vertical, torsional), and the severity of eye movement disorder (slight, small, moderate, marked; paralysis, paresis; monocular, binocular)
	Acquired brain injury	Description of type of brain injury, natural history, side of brain injury
Interventions	Intervention Comparator	We will provide a description of interventions given to each treatment group including, if relevant, the duration, intensity, frequency, or dose. We will classify the type of intervention as restitution, compensation, pharmacological or substitution, type of brain injury, type of eye movement disorder, and the type of control as no treatment, placebo, control, or standard care. We will document the professional background of the person providing the intervention (e.g. ophthalmologist, orthoptist)

(*Continued*)

Outcomes	List	We will document the primary and secondary outcomes relevant to this review as listed in the Types of outcome measures section. Specifically, we will document measurements showing change in angle of deviation and/or extent of eye movement range, measurement of binocular single vision, documentation of patient-reported symptoms, documentation of questionnaires and adverse events. If a study has used a number of different methods of measuring the same outcome (e.g. prisms and degrees for measurement of ocular deviation), we will note each method to be used for any subsequent analysis
Notes	Date conducted	Indicating specific dates of recruitment of participants mm/yr to mm/yr
	Sources of funding	
	Declaration of interest	Indicating any declarations of interest among the primary researchers
	Other	We will record any important confounding variables. If a study includes more than two intervention groups, we will also record the method of including these groups in any subsequent analysis

CONTRIBUTIONS OF AUTHORS

Fiona Rowe will lead this protocol, provide methodological expertise and write the protocol.

Carmel Noonan will act as a second reviewer and provide content expertise.

Sonia MacDiarmid, Kathryn Jarvis, Caroline Dodridge, Tallat Maan, Lorraine North, Marta Garcia-Finana, Claire Howard and Helen Rodgers will provide additional content expertise, will read and comment on final drafts of the protocol.

DECLARATIONS OF INTEREST

Fiona Rowe is an NIHR Research Fellow and has received funding from the NIHR to support research relating to visual problems after stroke (including this Cochrane Review).

The work presented here represents the view of the authors and not necessarily those of the funding bodies.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- National Institute for Health Research (NIHR), UK.

NIHR have funded the research fellowship programme that encompasses this Review.
Richard Wormald (Co-ordinating Editor for the Cochrane Eyes and Vision Group) acknowledges financial support for his Cochrane Eyes and Vision Group research sessions from the Department of Health through the award made by the NIHR to Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology for a Specialist Biomedical Research Centre for Ophthalmology. The views expressed in this publication are those of the authors and not necessarily those of the NIHR, NHS or the Department of Health.