Environmental enrichment for stroke and other non-progressive brain injury (Protocol)

Ng L, Reid I, Gorelik A, Galea M, Khan F

THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane protocol, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2015, Issue 9

http://www.thecochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Protocol]

Environmental enrichment for stroke and other non-progressive brain injury

Louisa Ng[1], Isabella Reid[1], Alexandra Gorelik[2], Mary Galea[3], Fary Khan[1]

[1]Department of Rehabilitation Medicine, Royal Melbourne Hospital, Royal Park Campus, Melbourne, Australia. [2]Melbourne EpiCentre Melbourne Health, Royal Melbourne Hospital, Melbourne, Australia. [3]Department of Medicine (Royal Melbourne Hospital), The University of Melbourne, Parkville, Australia

Contact address: Louisa Ng, Department of Rehabilitation Medicine, Royal Melbourne Hospital, Royal Park Campus, Poplar Road, Parkville, Melbourne, Victoria, 3052, Australia. louisa.ng@mh.org.au.

Editorial group: Cochrane Stroke Group.
Publication status and date: New, published in Issue 9, 2015.

Citation: Ng L, Reid I, Gorelik A, Galea M, Khan F. Environmental enrichment for stroke and other non-progressive brain injury. *Cochrane Database of Systematic Reviews* 2015, Issue 9. Art. No.: CD011879. DOI: 10.1002/14651858.CD011879.

ABSTRACT

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

To assess the effects of environmental enrichment for patient activity and participation in people who have stroke or non-progressive brain injury.

BACKGROUND

Description of the condition

Stroke is a leading cause of death and disability (Donnan 2008; WHO 2013). One in six people worldwide will have a stroke in their lifetime and in 2012 there were over 420,000 people living with the effects of stroke in Australia (Australian Institute of Health and Welfare 2012). Traumatic brain injury (TBI) is a leading cause of death and disability worldwide (Perel 2006). Annual incidence of TBI is considered to be upwards of 20 to 60 per 100,000 with many of these injuries sustained in young adulthood (Frasca 2013). These conditions often lead to significant functional and psychosocial impairment, causing limitation in mobility and everyday activities. Many patients receive rehabilitation during the first weeks following their injury and it is during this time that most recovery takes place (Frasca 2013; Teasell 2014). There is well established evidence (including Cochrane reviews and overviews) for the effectiveness of various aspects of stroke rehabilitation (Brady 2012; EBRSR 2015; Legg 2006; Pollock 2014a; Pollock 2014b), but questions have been raised as to whether the rehabilitation environment itself, outside of limited therapy hours, is maximally conducive to recovery (King 2011).

Description of the intervention

Within the animal literature, the term 'environmental enrichment' is better established, with standardised categories of enrichment types (social, occupational, physical, sensory and nutritional) (Mench 2010). However, this is a relatively new concept within rehabilitation for humans and the term is less well defined and may be used inconsistently. In this Cochrane review, we define 'environmental enrichment' as an intervention designed to facilitate physical (motor and sensory), cognitive and social activity by pro-

vision of equipment and organisation of a structured, stimulating environment (Nithianantharajah 2006). The environment should be designed to encourage (but not force) activities and verbal encouragement may be provided. The environment itself should be welcoming enough to encourage participation.

The intervention is not therapist dependent as it is not prescribed by a therapist within a tailored, individualised, goal-oriented rehabilitation programme. The intervention is simply 'just there' and easily and freely accessible by patients. Patients who have difficulty with mobility (which is not uncommon in rehabilitation wards) should have access to facilitation (such as from a porter or a nurse) to get to the intervention. The environment is supervised either by a health professional (for example, medical, nursing or therapist) or non-professional (family member, other volunteer) so that assistance may be provided (such as setting up a game or playing a game with the patient). Where the supervision is provided by a therapist, the therapist should not be providing a recognised intervention within his or her field of expertise. For example, if supervision is provided by a music therapist, singing technique or rhythmic auditory stimulation or song-writing should not form part of the activity. The supervisor should easily be replaceable with another with a different skill set or a lay person.

The participant's treating therapists may be asked to approve participation for safety reasons depending on the activity (such as exercise programmes) and the participant is required to choose to engage in structured activity that is cognitively stimulating. Environmental enrichment does not include interventions that do not require participant engagement or choice, such as the provision of background music. Additionally, patients may choose to set their own goals (such as complete a 20 piece jigsaw puzzle). Environmental enrichment should be used to complement, not in lieu of, rehabilitation and patients should be undergoing a concurrent structured individualised rehabilitation programme.

Interventions may include:

- reading material (books, magazines, newspapers);
- easily accessible computers with Internet connection;
- virtual reality and interactive gaming through computers or gaming consoles;
- board games (including puzzles, chess);
- music station;
- audio books;
- art and craft (drawing, painting, craft-work);
- interactive recreational activities (e.g. Bingo);
- exercise.

Interventions may be offered individually (a single activity available only) or collectively (multiple activities available). Settings can be individual (activities available to individuals, for example by the bedside) or communal (the structured stimulating environment is within a communal area, such as a designated area within a ward).

How the intervention might work

Given that stroke recovery is reliant on neuroplasticity, environmental enrichment is a possible alternate option for stimulating neural recovery through functional and cognitive activity. There is evidence suggesting that patients in rehabilitation wards, apart from their scheduled therapy sessions, spend most of their time (waking hours) physically inactive and relatively isolated (Berges 2012a; Berges 2012b; Keith 1987; King 2011; Mackey 1996; Tinson 1989). The amount of practice in functional and cognitive activities therefore needs to be increased to improve their activities and maximise the rehabilitation experience (Janssen 2014). Previous studies after stroke suggest that engagement in higher levels of therapeutically based physical activity is associated with better physical function (Scrivener 2011; Scrivener 2012) and greater independence (Kwakkel 2004); and cognitive or social activity enhances cognitive recovery and improves mood-related disorders such as depressive symptoms (Cheng 2012a; Cheng 2012b; Sakamo 2008). Therefore, it is hypothesised that a more stimulating environment is likely to be more conducive to recovery through improved activity levels that reduce a patient's boredom and in turn improves their mood and engagement in their overall rehabilitation programme. Rehabilitation programmes are generally designed to improve function-whilst mood is often addressed within rehabilitation, it is not usually the primary focus of such programmes. Environmental enrichment therefore should add value to a rehabilitation programme in a different way to conventional therapy, such as through improvement of mood. The positive role of a stimulating environment is supported by evidence in the area of traumatic brain injury, where a lack of environmental enrichment may play a role in post-acute cognitive and neural decline (Frasca 2013).

The effectiveness of environmental enrichment has been investigated extensively in animal models. It facilitates brain physiology and enhances recovery by triggering structural changes within the affected brain, which are significant in the process of neuroplasticity (Hirata 2011; Janssen 2012; Nilsson 2007; Nithianantharajah 2006). Diamond 1964 showed increases in cortical neuron size, number and length of dendrites, and number of dendritic spines in rats exposed to an enriched environment. Moreover, differences were observed in cortical thickness, cortical weight, acetylcholinesterase, cholinesterase and protein and hexokinase levels (Bennett 1964). Beneficial effects of environmental enrichment and exercise have been shown in a wide variety of animal models of brain disorders; these include cognitive enhancement, delayed disease onset, enhanced cellular plasticity and associated molecular processes (Pang 2013). Enriched environments are also associated with improvement in both physical and cognitive function in animal models of neurodegenerative and psychiatric diseases (Laviola 2008; Puurunen 2002).

One recent controlled clinical trial (with 29 participants) of enriched environment and activity in a stroke rehabilitation unit showed significantly increased activity in patients and reduced

time spent inactive and alone (Janssen 2014). They were more likely to be engaged in any activity compared with those in a non-enriched environment (almost twice as likely (1.7) to be engaged in cognitive activities, 1.2 times in social activities, 0.7 times as likely to be inactive and alone).

Why it is important to do this review

If sufficient evidence of effectiveness for environmental enrichment is found, it could potentially be a feasible, low-cost adjunct to conventional rehabilitation. The proposed review has the strong potential of guiding future research and influencing clinical practice. Although some Cochrane reviews have explored the role of similar interventions, such as virtual reality and interactive video gaming (Laver 2015) and music therapy (Bradt 2010) within a rehabilitation programme and other Cochrane reviews have examined the impact of additional exercise on recovery (Galvin 2012), the role of these interventions as part of environmental enrichment has not yet been studied. These reviews do not overlap with the review on environmental enrichment as the interventions studied form part of formal rehabilitation therapy programmes and the interventions are delivered by appropriate health professionals using their specific expertise in the area to attain specific rehabilitation goals through prescription of therapy using these modalities (Bradt 2010; Galvin 2012; Laver 2015). The same modalities (music, virtual reality, exercise) used within an enriched environment would simply be available and accessible to patients for them to use as they wish, as previously described. This review, therefore, aims to identify the existing evidence for interventions for environmental enrichment in people with stroke and other acquired non-progressive brain damage and to identify gaps in current knowledge. This would serve the purpose of informing health professionals, stroke and other acquired non-progressive brain damage survivors and their families and policy makers about the effectiveness of different environmental enrichment interventions and potentially shape the environment in which rehabilitation is delivered in the future.

OBJECTIVES

To assess the effects of environmental enrichment for patient activity and participation in people who have stroke or non-progressive brain injury.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs), including individually randomised trials and cluster-randomised controlled trials.

Types of participants

We will include adults aged 18 and over, men and women, with a definition of stroke as defined by the World Health Organization (WHO) (Hatano 1976), or other acquired non-progressive brain damage. Acquired brain damage includes brain injury, encephalitis, abscess and arteriovenous malformations. We will exclude participants with progressive neurological conditions such as a primary diagnosis of dementia, space-occupying lesions and multiple sclerosis.

We will include studies where at least 75% of participants have a diagnosis of stroke or other non-progressive brain disorders. We will also include studies where data for participants with stroke and other non-progressive brain disorders are reported separately if these diagnostic groups form a minimum of 50% of the participants within the study.

Types of interventions

We will include trials that compare environmental enrichment with standard services. Environmental enrichment is defined as any intervention that facilitates physical, cognitive and social activity by provision of equipment and organisation of a stimulating environment whereby the intervention is not therapist-dependent and exposure alone to such environments encourages patients to perform activities. The intervention is used as an adjunct to a conventional rehabilitation programme; it is not prescribed by a therapist and does not form part of the formal programme. By nature of the intervention being an adjunct to conventional rehabilitation, all patients must therefore also be concurrently undergoing a formal rehabilitation programme (inpatient, outpatient or home-based).

Interventions may include, but are not limited to:

- using easily accessible computers with Internet connection and Skype;
- gaming technology;
- access to library with reading materials;
- board games, puzzles, chess;
- music station (access to a selection of music and an appropriate player).

Interventions may have a single element ('single activity environmental enrichment') only (such as music only or gaming technology) or multiple elements ('multi-activity environmental enrichment') (computers plus gaming technology plus music). Environmental enrichment activities are supervised by an appropriate person (who may or may not be a health professional) and may be facilitated (such as by having a person play board games with the

patient). An appropriate person refers to a responsible person who is willing to be present, to provide encouragement and to assist the patient when necessary.

Within a hospital environment, such interventions might be set up in an area of the ward that is accessible by all patients. Within a home environment, however, an example of environmental enrichment might be an area set up for music with availability of the music and a device that plays the music. Interventions do not have to be provided by the hospital within a hospital environment. For example, if a patient had his own portable laptop computer, this would be an eligible intervention provided use of this was supervised by family members or staff.

The intervention will be compared with standard rehabilitation care. Within three-arm trials, each intervention will be compared to standard rehabilitation care.

Types of outcome measures

Primary outcomes

The primary outcome is psychological well-being and coping at four weeks (short-term) and between four weeks and 12 months (moderate-term). Instruments that measure psychological well-being and coping may include, but are not limited to:

- Depression Anxiety Stress Scale-21 (DASS) (Lovibond 1995);
- Hospital Anxiety and Depression Scale (HADS) (Zigmond 1983);
- Rosenberg Self-Esteem Scale (Rosenberg 1965);
- Multidimensional Health Locus of Control (MHLC) (Wallston 1994).

Secondary outcomes

Secondary outcomes are at four weeks (short-term) and between four weeks and 12 months (moderate-term) and include the following.

- Quality of life. Instruments that measure quality of life may include, but are not limited to:
  - Stroke and Aphasia Quality of Life Scale-39 Generic (SAQOL-39) (Hilari 2003);
  - Euro-Quality of life EQ-5D (EuroQoL 1990);
  - 36-item Short Form Health Survey (SF-36) or the 12-item Short Form Health Survey (SF-12) (Ware 1992; Ware 1995).
- Physical functional improvement (activities of daily living). Instruments that measure physical functional improvement may include, but are not limited to:
  - motor component of Functional Independence Measure (FIM) (Granger 1990).
- Communication and cognitive functional improvement. Instruments that measure communication and cognitive functional improvement may include, but are not limited to:
  - cognitive and language component of Functional Independence Measure (FIM) (Granger 1990);
  - Montreal Cognitive Assessment (MoCA) (Nasreddine 2005).

Search methods for identification of studies

See the 'Specialized register' section in the Cochrane Stroke Group module. We will search for trials in all languages and arrange for the translation of relevant articles where necessary.

Electronic searches

We will search the trials registers of the Cochrane Stroke Group, the Cochrane Injuries Group and the Cochrane Infectious Diseases Group and the following electronic databases.

- Cochrane Central Register of Controlled Trials (CENTRAL) (latest issue).
- MEDLINE (from 1948) (Appendix 1).
- EMBASE (from 1980).
- CINAHL (1982 to present).
- AMED (1985 to present);
- PsycINFO (1806 to present).
- PEDro (Physiotherapy Evidence Database) (http://www.pedro.org.au/).
- Center for International Rehabilitation Research Information and Exchange (CIRRIE) Database of International Rehabilitation Research (http://cirrie.buffalo.edu/search/index.php).
- Database of Abstracts of Reviews of Effects (DARE) (*The Cochrane Library*, latest issue).
- ProQuest Dissertations & Theses Database (PQDT).
- OT Search by the American Occupational Foundation and the American Occupational Therapy Association (http://www1.aota.org/otsearch/).
- Occupational Therapy Systematic Evaluation of Evidence (OTseeker) (http://www.otseeker.com/).
- The National Rehabilitation Information Center REHABDATA Database (http://www.naric.com/?q=en/REHABDATA).
- SPORTDiscus (http://www.ebscohost.com/public/sportdiscus).
- Trials Central (http://www.trialscentral.org/).
- UK Clinical Research Network Portfolio database (http://public.ukcrn.org.uk/search/).
- PsycBite (www.psycbite.com).

We developed the MEDLINE search strategy (Appendix 1) with the help of the Cochrane Stroke Group Trials Search Co-ordinator and will adapt it for the other databases.

We will also search the following ongoing trials registers.

- ClinicalTrials.gov (www.clinicaltrials.gov/).
- Stroke Trials Registry (www.strokecenter.org/trials/).
- EU Clinical Trials Register (https://www.clinicaltrialsregister.eu).
- ISRCTN Registry (http://www.isrctn.com/), previously Current Controlled Trials (www.controlled-trials.com).
- WHO International Clinical Trials Registry Platform (http://www.who.int/ictrp/en/).
- Australian New Zealand Clinical Trials Registry (www.anzctr.org.au/).

Searching other resources

To identify further published, unpublished and ongoing trials, we will:

- handsearch the reference lists of included trials and review articles;
- track citations using Web of Science Cited Reference Search for all included studies;
- contact experts active in this field (including authors of included trials and excluded studies identified as possible preliminary or pilot work);
- search Google Scholar (http://scholar.google.co.uk/).

Data collection and analysis

Selection of studies

Two review authors (LN, IR) will independently screen titles and abstracts of the references obtained as a result of our searching activities and we will exclude obviously irrelevant reports. We will retrieve the full-text articles for the remaining references and two review authors (LN, IR) will independently screen the full-text articles and identify studies for inclusion, and identify and record reasons for exclusion of the ineligible studies. We will resolve any disagreements through discussion or, if required, we will consult a third person (FK). We will collate multiple reports of the same study so that each study, not each reference, is the unit of interest in the review. We will record the selection process and complete a PRISMA flow diagram.

Data extraction and management

Two review authors (LN, IR) will independently extract data from included studies.

We will group studies by intervention type where possible.

We will use a pre-designed data extraction form to extract data from the included studies. Two review authors (LN, IR) will independently document the following.

- Participants: number of participants, age, gender, baseline functional status or level of impairment.
- Methods: inclusion criteria, time since stroke or non-progressive brain injury, and type, nature and location of lesion.
- Interventions: description of interventions given to each treatment group including the duration, type, dose (such as access time to intervention-for example, if a participant is able to access computers and Skype for an hour a day, this will be reported), frequency, supervisor (who supervised the intervention) and setting (inpatient, outpatient or home-based).
- Outcomes: primary and secondary outcomes measured. If a study has used different methods of measuring the same outcome, we will note the outcome to be used for any subsequent analysis.
- Results: number of participants allocated to each intervention group. For each outcome of interest-sample size, missing participants, data for each intervention group.

We will note any important confounding variables. If more than two intervention groups are included in the study, we will note the method of including these groups in any subsequent analysis. We will consider mixed-treatment comparisons/indirect comparisons to determine any differences between various interventions using standard rehabilitation (control) as a common comparator. The two review authors will resolve any data extraction discrepancies through discussion. If disagreement persists, a third author (FK) will independently extract the data.

Assessment of risk of bias in included studies

Two review authors (LN, IR) will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will resolve any disagreements by discussion or by involving another author (FK). We will assess the risk of bias according to the following domains.

- Random sequence generation.
- Allocation concealment.
- Blinding of participants and personnel.
- Blinding of outcome assessment.
- Incomplete outcome data.
- Selective outcome reporting.
- Other bias.

We will grade the risk of bias for each domain as high, low or unclear and provide information from the study report together with a justification for our judgement in the 'Risk of bias' tables. Given the nature of environmental enrichment, it will likely be difficult to blind the participants and personnel. However, it should be possible to have blinded outcome assessment. Additionally, it is likely that randomisation at the individual level would be difficult and that randomisation to intervention or standard care arm may be done at a centre level, which in turn would affect allocation

concealment. We will consider these inherent issues when assessing the risk of bias in these studies.

We will use GRADE to interpret findings and GRADEpro GDT to create a 'Summary of findings' table (Guyatt 2008). The table will provide outcome-specific information concerning the overall quality of evidence from studies included in the comparison, the magnitude of effect of the intervention and the sum of available data on the outcomes considered. When using GRADE, we will downgrade the evidence from 'high quality' by up to three levels (to 'moderate', 'low' or 'very low') for serious study limitations depending on the presence of the following five factors (Higgins 2011).

- Limitations in the design and implementation of available studies suggesting high likelihood of bias.
- Indirectness of evidence (indirect population, intervention, control, outcomes).
- Unexplained heterogeneity or inconsistency of results (including problems with subgroup analysis).
- Imprecision of results (wide confidence intervals).
- High probability of publication bias.

Measures of treatment effect

We will group studies by intervention type where possible and analyse them by single or combined interventions to minimise confounding. For example, we will group single activity studies together (such as music only or board games only) and studies with multi-activity interventions together (such as availability of computers, music, games etc concurrently). We will use the Cochrane Review Manager software to carry out statistical analyses to determine the treatment effect (RevMan 2014). For dichotomous variables we will calculate the treatment effect using a random-effects model and report it 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 different studies used different scales to assess the same outcome, and we will calculate mean differences (MDs) and 95% CIs where studies have all used the same method of measuring outcome.

We will use meta-analysis as the primary point of analysis. We will assess all studies for heterogeneity and in the presence of such, we will use meta-regression to adjust for potential differences between studies. In the absence of a direct comparison between interventions, we will consider mixed-treatment comparisons or indirect comparisons to determine any differences between various interventions, while standard rehabilitation (control) is used as a common comparator. We will do this using either the frequentist or Bayesian approach and using Monte-Carlo Markov simulations.

Unit of analysis issues

The primary outcome of short-term patient psychological well-being and secondary outcomes of short, medium and long-term quality of life and functional improvement comprise either ordinal data from measurement scales or continuous data, and we will analyse these as continuous variables. Where reported outcomes have a scale where a lower value indicates a better outcome we will multiply the reported values by -1 so that in all analyses a higher value will indicate a better outcome.

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 not available, we will use these data in meta-analyses but plan sensitivity analyses to investigate the effect of including these data. We will analyse adverse events as dichotomous variables.

Dealing with missing data

If an included study does not report a particular outcome but it has been included in the battery of measures administered, we will contact the authors for the original data. If we are unsuccessful in obtaining the data, we will not include that study in the analyses of that outcome. We will also contact authors for missing intervention details.

If an included study has missing data (e.g. the study reports means but not standard deviations for the follow-up data) we will contact the authors for the missing data. If we are unsuccessful, then we will take logical steps to enter an assumed value. Such steps may include estimating a standard deviation based on a reported standard error, estimating a follow-up standard deviation based on a baseline value, using the median as a proxy for the mean, and using a multiple of 0.75 times the interquartile range or 0.25 times the range as a proxy for the standard deviation values (Hozo 2005). We plan to do sensitivity analyses to investigate the effect of entering assumed values.

Assessment of heterogeneity

It is anticipated that there will be substantial methodological, statistical and clinical heterogeneity among the trials and we will perform a meta-analysis using a random-effects model.

Assessment of reporting biases

We will attempt to avoid reporting biases by using a comprehensive search strategy that includes searching for unpublished studies and searching trials registers. We will also assess the completeness of outcome data. If possible, we will assess publication bias using a rank correlation test and a funnel plot.

Data synthesis

Where we consider studies to be sufficiently similar (where the same activity, such as music, is used as an intervention, where similar outcomes are sought) and where data are available and of

sufficient quality, we will conduct a meta-analysis by pooling the appropriate data using RevMan 5.3 (RevMan 2014).

Subgroup analysis and investigation of heterogeneity

Given that this area of research is relatively new, it is probably unlikely that we will find a significant body of literature, making subgroup analyses challenging. If possible, we plan to conduct subgroup analyses by intervention, with subgroups that include:

- enriched environments with a variety of communal and individual activities (Internet, reading material, games, Nintendo Wii, music, audio books, books, games, puzzles);
- enriched environments with single activities (such as gaming consoles or music alone).

Sensitivity analysis

We intend to carry out a sensitivity analysis (if necessary) 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 the data, excluding trials with inadequate or unclear methods of dealing with missing outcome data.

ACKNOWLEDGEMENTS

We acknowledge the assistance of Hazel Fraser and Brenda Thomas of the Cochrane Stroke Group with co-ordination and with the search strategy.

REFERENCES

Additional references

Australian Institute of Health and Welfare 2012
Australia's Health 2012. Australian Institute of Health and Welfare 2012.

Bennett 1964
Bennett EL, Diamond MC, Krech D, Rosenzweig MR. Chemical and anatomical plasticity brain. *Science* 1964;**146**(3644):610–9.

Berges 2012a
Berges IM, Kuo YF, Ottenbacher KJ, Seale GS, Ostir GV. Recovery of functional status after stroke in a tri-ethnic population. *PM & R* 2012;**4**(4):290–5.

Berges 2012b
Berges IM, Seale GS, Ostir GV. The role of positive affect on social participation following stroke. *Disability and Rehabilitation* 2012;**34**(25):2119–23.

Bradt 2010
Bradt J, Magee WL, Dileo C, Wheeler BL, McGilloway E. Music therapy for acquired brain injury. *Cochrane Database of Systematic Reviews* 2010, Issue 7. [DOI: 10.1002/14651858.CD006787.pub2]

Brady 2012
Brady MC, Kelly H, Godwin J, Enderby P. Speech and language therapy for aphasia following stroke. *Cochrane Database of Systematic Reviews* 2012, Issue 5. [DOI: 10.1002/14651858.CD000425.pub3]

Cheng 2012a
Cheng ST, Chow PK, Song YQ, Yu EC, Chan AC, Lee TM, et al. Mental and physical activities delay cognitive decline in older persons with dementia. *American Journal of Geriatric Psychiatry* 2014;**22**(1):63–74.

Cheng 2012b
Cheng ST, Chow PK, Yu EC, Chan AC. Leisure activities alleviate depressive symptoms in nursing home residents with very mild or mild dementia. *American Journal of Geriatric Psychiatry* 2012;**20**(10):904–8.

Diamond 1964
Diamond MC, Krech D, Rosenzweig MR. The effects of an enriched environment on the histology of the rat cerebral cortex. *Journal of Comparative Neurology* 1964;**123**:111–20.

Donnan 2008
Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. *Lancet* 2008;**371**:1612–23.

EBRSR 2015
Evidence Based Review of Stroke Rehabilitation 16th edition. Available at: http://www.ebrsr.com/.

EuroQoL 1990
EuroQol. A new facility for the measurement of health-related quality of life. *Health Policy* 1990;**16**:199–208.

Frasca 2013
Frasca D, Tomaszczyk J, McFadyen BJ, Green RE. Traumatic brain injury and post-acute decline: what role does environmental enrichment play? A scoping review. *Frontiers in Human Neuroscience* 2013;**7**:31.

Galvin 2012
Galvin R, Lennon S, Murphy BT, Cusack T, Horgan F, Stokes EK. Additional exercise therapy for the recovery of function after stroke. *Cochrane Database of Systematic Reviews* 2012, Issue 6. [DOI: 10.1002/14651858.CD009859]

Granger 1990
Granger CV, Cotter AC, Hamilton BB, Fiedler RC, Hens MM. Functional assessment scales: a study of persons

with multiple sclerosis. *Archives of Physical Medicine and Rehabilitation* 1990;**71**(11):870–5.

Guyatt 2008

Guyatt GH, Oxman AD, Vist G, Kunz R, Falck-Ytter Y, Alonso-Coello P, the GRADE Working Group. Rating quality of evidence and strength of recommendations GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; **336**:924–6.

Hatano 1976

Hatano S. Experience from a multicentre stroke register: a preliminary report. *Bulletin of the World Health Organization* 1976;**54**(5):541–53.

Higgins 2011

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.

Hilari 2003

Hilari K, Byng S, Lamping DL, Smith SC. Stroke and Aphasia Quality of Life Scale-39 (SAQOL-39): evaluation of acceptability, reliability, and validity. *Stroke* 2003;**34**: 1944–50.

Hirata 2011

Hirata K, Kuge Y, Yokota C, Harada A, Kokame K, Inoue H. Gene and protein analysis of brain derived neurotrophic factor expression in relation to neurological recovery induced by an enriched environment in a rat stroke model. *Neuroscience Letters* 2011;**495**(3):210–5.

Hozo 2005

Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Medical Research Methodology* 2005;**1**(5):13.

Janssen 2012

Janssen H, Ada L, Karayanidis F, Drysdale K, McElduff P, Pollack M. Translating the use of an enriched environment poststroke from bench to bedside: study design and protocol used to test the feasibility of environmental enrichment on stroke patients in rehabilitation. *International Journal of Stroke* 2012;**7**(6):521–6.

Janssen 2014

Janssen H, Ada L, Bernhardt J, McElduff P, Pollack M, Nilsson M. An enriched environment increases activity in stroke patients undergoing rehabilitation in a mixed rehabilitation unit: a pilot non-randomized controlled trial. *Disability and Rehabilitation* 2014;**36**(3):255–62.

Keith 1987

Keith RA, Cowell KS. Time use of stroke patients in three rehabilitation hospitals. *Social Science & Medicine* 1987;**24** (6):529–33.

King 2011

King A, McCluskey A, Schurr K. The time use and activity levels of inpatients in a co-located acute and rehabilitation stroke unit: an observational study. *Topics in Stroke Rehabilitation* 2011;**18 Suppl 1**:654–65.

Kwakkel 2004

Kwakkel G, van Peppen R, Wagenaar RC, Wood Dauphinee S, Richards C, Ashburn A, et al. Effects of augmented exercise therapy time after stroke: a meta-analysis. *Stroke* 2004;**35**(11):2529–39.

Laver 2015

Laver KE, George S, Thomas S, Deutsch JE, Crotty M. Virtual reality for stroke rehabilitation. *Cochrane Database of Systematic Reviews* 2015, Issue 2. [DOI: 10.1002/ 14651858.CD008349.pub3]

Laviola 2008

Laviola G, Hannan AJ, Macri S, Solinas M, Jaber M. Effects of enriched environment on animal models of neurodegenerative diseases and psychiatric disorders. *Neurobiology of Disease* 2008;**31**(2):159–68.

Legg 2006

Legg L, Drummond A, Langhorne P. Occupational therapy for patients with problems in activities of daily living after stroke. *Cochrane Database of Systematic Reviews* 2006, Issue 4. [DOI: 10.1002/14651858.CD003585.pub2]

Lovibond 1995

Lovibond PF, Lovibond SH. The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy* 1995;**33**: 335–43.

Mackey 1996

Mackey F, Ada L, Heard R, Adams R. Stroke rehabilitation: are highly structured units more conducive to physical activity than less structured units?. *Archives of Physical Medicine and Rehabilitation* 1996;**10**:1066–70.

Mench 2010

Mench JN, Millman S, Tucker C, Katz L. *Environmental Enrichment. Guide for the Care and Use of Agricultural Animals in Research and Teaching*. 3rd Edition. Champaign, IL: Federation of Animal Science Societies, 2010.

Nasreddine 2005

Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatric Society* 2005; **53**:695–9.

Nilsson 2007

Nilsson M, Pekny M. Enriched environment and astrocytes in central nervous system regeneration. *Journal of Rehabilitation Medicine* 2007;**39**(5):345–52.

Nithianantharajah 2006

Nithianantharajah J, Hannan AJ. Enriched environments, experience-dependent plasticity and disorders of the nervous system. *Nature Reviews Neuroscience* 2006;**7**(9):697–709.

Pang 2013

Pang TY, Hannan AJ. Enhancement of cognitive function in models of brain disease through environmental enrichment and physical activity. *Neuropharmacology* 2013;**64**:515–28.

Perel 2006
Perel P, Edwards P, Wentz R, Roberts I. Systematic review of prognostic models in traumatic brain injury. *BMC Medical Informatics and Decision Making* 2006;**6**:38.

Pollock 2014a
Pollock A, Baer G, Campbell P, Choo PL, Forster A, Morris J, et al. Physical rehabilitation approaches for the recovery of function and mobility following stroke. *Cochrane Database of Systematic Reviews* 2014, Issue 4. [DOI: 10.1002/14651858.CD001920.pub3]

Pollock 2014b
Pollock A, Farmer SE, Brady MC, Langhorne P, Mead GE, Mehrholz J, et al. Interventions for improving upper limb function after stroke. *Cochrane Database of Systematic Reviews* 2014, Issue 11. [DOI: 10.1002/14651858.CD010820.pub2]

Puurunen 2002
Puurunen K, Sivenius J. Influence of enriched environment on spatial learning following cerebral insult. *Reviews in the Neurosciences* 2002;**13**(4):347–64.

RevMan 2014
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Rosenberg 1965
Rosenberg M. *Society and the Adolescent Self-image*. Princeton NJ: Princeton University Press, 1965.

Sakamo 2008
Sarkamo T, Tervaniemi M, Laitinen S, Forsblom A, Soinila S, Mikkonen M. Music listening enhances cognitive recovery and mood after middle cerebral artery stroke. *Brain* 2008;**131**(3):2529–39.

Scrivener 2011
Scrivener K, Sherrington C, Schurr K. Exercise dose and mobility outcome in a comprehensive stroke unit: description and prediction from a prospective cohort study. *Journal of Rehabilitation Medicine* 2012;**44**(10):824–9.

Scrivener 2012
Scrivener K, Sherrington C, Schurr K, Treacy D. Many participants in inpatient rehabilitation can quantify their exercise dosage accurately: an observational study. *Journal of Physiotherapy* 2011;**57**(2):117–22.

Teasell 2014
Teasell RW, Murie Fernandez M, McIntyre A, Mehta S. Rethinking the continuum of stroke rehabilitation. *Archives of Physical Medicine and Rehabilitation* 2014;**95**(4):595–6.

Tinson 1989
Tinson DJ. How stroke patients spend their days. An observational study of the treatment regime offered to patients in hospital with movement disorders following stroke. *International Disability Studies* 1989;**11**(1):45–9.

Wallston 1994
Wallston KA, Stein MJ, Smith CA. Form C of the MHLC Scales: a condition-specific measure of locus of control. *Journal of Personality Assessment* 1994;**63**:534.

Ware 1992
Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical Care* 1992;**30**:473–83.

Ware 1995
Ware JE Jr, Kosinski M, Bayliss MS, McHorney CA, Rogers WH, Raczek A. Comparison of methods for the scoring and statistical analysis of SF-36 health profile and summary measures: summary of results from the Medical Outcomes Study. *Medical Care* 1995;**33**:AS264–79.

WHO 2013
Research for universal health coverage: World Health Report 2013. World Health Organization 2013.

Zigmond 1983
Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica* 1983;**67**(6):361–70.

* *Indicates the major publication for the study*

APPENDICES

Appendix 1. MEDLINE search strategy

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp cerebrovascular trauma/ or exp intracranial arterial diseases/ or exp intracranial arteriovenous malformations/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or stroke, lacunar/ or vasospasm, intracranial/ or vertebral artery dissection/ or exp hypoxia, brain/
2. (stroke$ or post stroke or poststroke or post-stroke or apoplex$ or cerebral vasc$ or cerebrovasc$ or cva or SAH).tw.
3. ((brain or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebr$ or mca$ or anterior circulation or basilar artery or vertebral artery) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw.
4. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraparenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or putaminal or putamen or posterior fossa or hemispher$ or subarachnoid) adj5 (h?emorrhag$ or h?ematoma$ or bleed$)).tw.
5. exp hemiplegia/ or exp paresis/ or exp aphasia/ or exp gait disorders, neurologic/
6. (hempar$ or hemipleg$ or paresis or paretic or aphasi$ or dysphasi$).tw.
7. exp brain damage, chronic/ or brain injuries/ or exp brain concussion/ or exp brain hemorrhage, traumatic/ or brain injury, chronic/ or diffuse axonal injury/
8. craniocerebral trauma/ or exp head injuries, closed/ or exp intracranial hemorrhage, traumatic/
9. exp brain abscess/ or exp central nervous system infections/ or exp encephalitis/ or exp meningitis/
10. (encephalitis or meningitis or head injur$).tw.
11. ((brain or cerebr$) adj5 (injur$ or hypoxi$ or damage$ or concussion or trauma$ or infection$)).tw.
12. or/1-11
13. environment/ or environment design/ or exp health facility environment/
14. ((enrich$ or stimulat$ or rehabilitat$ or supervised$) adj5 environment$).tw.
15. ((stimulat$ or facilitate$ or equipment or organiz$ or organis$ or participat$ or perform$ or engag$ or encourage$ structured) adj5 (physical or motor or sensory or cognitive or social or functional or recreational) adj5 activit$).tw.
16. exercise/ or exercise therapy/ or exercise movement techniques/
17. ((physical or balance$ or cognit$) adj5 exercis$).tw.
18. user-computer interface/ or computers/ or exp microcomputers/ or computer systems/ or software/
19. computer simulation/ or computer-assisted instruction/ or therapy, computer-assisted/ or computer graphics/ or video games/
20. (virtual reality$ or virtual-reality$ or VR).tw.
21. (virtual adj3 (environment$ or object$ or world$ or treatment$ or system$ or program$ or rehabilitation$ or therap$ or game or gaming)).tw.
22. (computer adj5 (play or access or simulat$ or graphic$ or game$ or interact$)).tw.
23. (computer adj1 assist$ adj1 (therap$ or treat$)).tw.
24. (computer adj1 generat$ adj1 (environment$ or object$)).tw.
25. (video game$ or video gaming or gaming console$ or interactive game or interactive gaming or Nintendo Wii or gaming program$ or gaming technology).tw.
26. skype.tw.
27. (internet adj5 (access or connection)).tw.
28. library materials/ or books/ or periodicals as topic/ or serial publications/ or newspapers/ or libraries/ or libraries, hospital/
29. (read$ adj5 (book or books or newspaper$ or magazine$ or material or materials)).tw.
30. (listen$ adj5 audio book$).tw.
31. music/ or music therapy/ or singing/ or acoustic stimulation/
32. (music$ or rhythmic$ or melod$ or harmon$).tw.
33. ((auditory or acoustic) adj5 (stimulat$ or cue$)).tw.
34. (sing or sings or singing or singer$ or song$ or chant$ or compose or composing or improvis$).tw.
35. (gait adj5 (puls$ or rhythm$)).tw.
36. (music adj5 (background or instrument$ or listen$ or station)).tw.
37. "Play and Playthings"/

38. recreation/ or hobbies/ or leisure activities/
39. art/ or sensory art therapies/ or art therapy/ or play therapy/
40. (art therapy or craft or crafts or craft-work or drawing or painting).tw.
41. (recreation or hobbies or hobby or leisure or board game$ or puzzle$ or jigsaw$ or chess or bingo).tw.
42. ((play or participate) adj5 (game or games)).tw.
43. or/13-42
44. Randomized Controlled Trials as Topic/
45. random allocation/
46. Controlled Clinical Trials as Topic/
47. control groups/
48. clinical trials as topic/ or clinical trials, phase i as topic/ or clinical trials, phase ii as topic/ or clinical trials, phase iii as topic/ or clinical trials, phase iv as topic/
49. double-blind method/
50. single-blind method/
51. Placebos/
52. placebo effect/
53. cross-over studies/
54. randomized controlled trial.pt.
55. controlled clinical trial.pt.
56. (clinical trial or clinical trial phase i or clinical trial phase ii or clinical trial phase iii or clinical trial phase iv).pt.
57. (random$ or RCT or RCTs).tw.
58. (controlled adj5 (trial$ or stud$)).tw.
59. (clinical$ adj5 trial$).tw.
60. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
61. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
62. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
63. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
64. (cross-over or cross over or crossover).tw.
65. (placebo$ or sham).tw.
66. trial.ti.
67. (assign$ or allocat$).tw.
68. controls.tw.
69. or/44-68
70. 12 and 43 and 69
71. exp animals/ not humans/
72. 70 not 71
73. cerebral palsy.tw.
74. 72 not 73

CONTRIBUTIONS OF AUTHORS

Louisa Ng and Isabella Reid will co-lead the review and have an active role in all aspects of the protocol and review, including running the searches, identifying relevant articles, extracting data, analysing risk of bias and writing drafts of the review.

Alex Gorelik will provide statistical expertise.

Fary Khan will provide content expertise, arbitration where necessary during the identification of relevant articles, data extraction and review of papers, as well as comments on the final drafts of the review.

Mary Galea will provide comments on final drafts of the protocol and the review.

DECLARATIONS OF INTEREST

Louisa Ng: none known.

Isabella Reid: none known.

Alex Gorelik: none known

Mary Galea: none known.

Fary Khan: none known.

SOURCES OF SUPPORT

Internal sources

- Royal Melbourne Hospital, Australia.

External sources

- No sources of support supplied