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Virtual reality for stroke rehabilitation (Protocol)

Laver KE, George S, Thomas S, Deutsch JE, Crotty M



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[Intervention Protocol]

Virtual reality for stroke rehabilitation

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ABSTRACT

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

Primary objective

To determine the effectiveness of virtual reality compared with alternative or no intervention on:

1. upper limb function and activity;
2. gait and balance function and activity;
3. global motor function.

Secondary objective

To determine the effectiveness of virtual reality compared with alternative or no intervention on:

1. cognitive function;
2. activity limitation;
3. participation restriction and quality of life;
4. imaging studies;
5. adverse events.

Additionally, we aim to comment on the feasibility of virtual reality for use with stroke patients by reporting on patient eligibility criteria and recruitment.

BACKGROUND

Description of the condition

Stroke is one of the leading causes of death and disability and has been described as a worldwide epidemic (Feigin 2009). Effects of a stroke may include sensory, motor and cognitive impairment as well as reduced ability to perform self care and participate in social and community activities (Mayo 1999). While most recovery is thought to be made in the first few weeks after stroke, patients may make improvements on functional tasks and experience neural reorganisation up to six months after a stroke (Teasell 2005). Many stroke survivors report long-term disability and reduced quality of life (Patel 2006; Sturm 2004).

Description of the intervention

Repetitive task training has been shown to be effective in some aspects of rehabilitation, such as improving walking distance and speed (French 2007). Virtual reality is a relatively recent approach that may enable simulated practice of functional tasks at a higher dosage than traditional therapies (Merians 2002). Virtual reality has been defined as the 'use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real world objects and events' (Weiss 2006).

Virtual reality has previously been used in a variety of vocational training settings, such as flight simulation training for pilots (Lintern 1990) and procedural training for surgeons (Larsen 2009). Within healthcare the intervention has been used to treat phobias, post-traumatic stress disorder and body image disorders (Schultheis 2001). Although its research in rehabilitation is becoming more prevalent as technology becomes more accessible and affordable (Burdea 2003), the use of virtual reality is not yet commonplace in clinical rehabilitation settings. However, gaming consoles are ubiquitous (Burdea 2003) and so researchers and clinicians are turning to low-cost commercial gaming programs as an alternative way of delivering virtual reality (Deutsch 2008; Rand 2008). These programs, originally designed for the gaming market, are being adapted by clinicians to provide therapeutic activities in rehabilitation.

In virtual rehabilitation, virtual environments and objects provide the user with visual feedback which may be presented through a head-mounted device, projection system or flat screen. Feedback may also be provided through the senses, for example, hearing, touch, movement, balance and smell (Weiss 2006). The user interacts with the environment by a variety of mechanisms. These may be simple devices, such as a mouse or joystick, or more complex systems using cameras, sensors or haptic (touch) feedback devices (Weiss 2006). Virtual reality relies on computer hardware and software that mediates the interaction between the user and the virtual environment (Greenleaf 1994).

Key concepts related to virtual reality are immersion and presence. Immersion refers to the extent to which the user perceives that they are in the virtual environment rather than the real world and is related to the design of the software and hardware (Weiss 2006). Virtual environments can range in their degree of immersion of the user. Systems that include projection onto a concave surface, head-mounted display or video capture in which the user is represented within the virtual environment are generally described as immersive.

Presence is the subjective experience of the user and is dependent on the characteristics of the virtual reality system, the virtual task and the characteristics of the user. People are considered present when they report the feeling of being in the virtual world (Schuemie 2001).

Virtual reality has been used in a neurological rehabilitation population to improve upper (Henderson 2007) and lower extremity function and gait (Deutsch 2007), as well as cognition, perception, and functional tasks such as crossing a street, driving, preparing food and shopping (Rose 2005).

How the intervention might work

Virtual reality may be advantageous as it offers several features, such as goal-oriented tasks and repetition, shown to be important in neurological rehabilitation (Dobkin 2004).

Animal research has shown that training in enriched environments results in better problem solving and performance of functional tasks than training in basic environments (Risedal 2002). Virtual reality is a way of providing an enriched environment in which people with stroke can problem solve and master new skills.

Research with animals and humans has also shown us that intensive task-specific practice is able to induce cortical reorganisation (Nudo 1996; Nudo 2001) and behavioural change (Dean 1997). Virtual reality programs capitalise on this by offering simulated real life functional activities that may provide enhanced ecological validity when compared to traditional rehabilitation tasks (Rizzo 2005). Virtual tasks have been described as more interesting and enjoyable by both children and adults, thereby encouraging higher numbers of repetitions (Bryanton 2006; Thornton 2005).

Grading of tasks and immediate feedback has been shown to optimise motor learning (Sveistrup 2004). Virtual reality offers clinicians the ability to control and grade tasks to challenge the user, and programs often incorporate multimodal feedback provided in real time. Furthermore, clinicians are able to trial tasks that are unsafe to practise in the real world, such as crossing the street. Many programs are designed to be used without supervision, also meaning that increased dosage of therapy can be provided without increased staffing levels (Holden 2005).

Why it is important to do this review

As technology becomes more accessible and affordable, virtual reality is likely to become more widely used in clinical rehabilitation settings. It is important to evaluate the effectiveness of virtual reality in order to guide future design and use. Furthermore, therapeutic interventions that increase the dose of task-specific training without increasing staffing will be sought after as economic pressure and an ageing population impact on health care.

A recent systematic review examined the effectiveness of virtual reality for stroke rehabilitation (Crosbie 2007). The authors included 11 studies, of which only three were randomised controlled trials. These were grouped and presented according to their assessed level of evidence (1 to 5). The authors concluded that while effects were generally positive, the studies were too limited by design and power issues to decide their value. The review could have been strengthened by a more exhaustive search strategy as well as a more rigorous assessment of methodological quality of the included studies.

Another systematic review aimed to evaluate the evidence for the effectiveness of virtual reality in rehabilitation of the upper limb post stroke (Henderson 2007). The authors identified six studies, including two randomised controlled trials, and appraised them using the PEDro rating scale (Maher 2003). The authors were limited by the number and quality of studies identified and, once again, concluded that there was limited but promising information available.

Since the publication of these reviews, several new randomised controlled trials have been published (Jannink 2008; Mirelman 2009; Yang 2008; Yavuzer 2008).

OBJECTIVES

Primary objective

To determine the effectiveness of virtual reality compared with alternative or no intervention on:

1. upper limb function and activity;
2. gait and balance function and activity;
3. global motor function.

Secondary objective

To determine the effectiveness of virtual reality compared with alternative or no intervention on:

1. cognitive function;
2. activity limitation;
3. participation restriction and quality of life;
4. imaging studies;
5. adverse events.

Additionally, we aim to comment on the feasibility of virtual reality for use with stroke patients by reporting on patient eligibility criteria and recruitment.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised or quasi-randomised (e.g. allocation by birth date) controlled trials. We will be looking for studies that compare virtual reality with either an alternative intervention or no intervention. For three-armed trials where two different types of virtual reality are compared with either an alternative intervention or no intervention, we will compare the virtual reality intervention groups with the alternative group individually. If this occurs, we will acknowledge in the review that data from the control group in these studies were double-counted. We will not include studies that compare two different types of virtual reality without an alternative group. We will include trials that evaluate any intensity and duration of virtual reality that exceeds a single treatment session.

Types of participants

The study participants will have a diagnosis of stroke as defined by the World Health Organization (a syndrome of rapidly developing symptoms and signs of focal, and at times global, loss of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin) (WHO 1989), diagnosed by imaging or neurological examination. We will include patients who are 18 years and older with all types of stroke, all levels of severity, and at all stages post stroke, including those patients with subarachnoid haemorrhage. We will exclude studies of participants with mixed aetiology unless data are available relating to the people with stroke only.

Types of interventions

We will include studies using virtual reality interventions that meet the following definition: 'an advanced form of human-computer interface that allows the user to "interact" with and become "immersed" in a computer-generated environment in a naturalistic fashion.' (Schultheis 2001).

We will include studies using any form of non-immersive or immersive virtual reality, and studies that use commercially available gaming consoles.

The comparison group may receive either an alternative intervention or no intervention. There is likely to be a broad range of alternative interventions; however, we will consider these to include any activity designed to be therapeutic at the impairment, activity or participation level that does not include the use of virtual reality.

Types of outcome measures

Primary outcomes

Primary outcomes will be as follows.

1. Upper limb function and activity.
 - i) Arm function and activity: may include assessments such as the Motor Assessment Scale (upper limb), Action Research Arm Test, Wolf Motor Function Test.
 - ii) Hand function and activity: may include the Nine Hole Peg Test, Box and Block Test.
2. Gait and balance function and activity.
 - i) Lower limb function and activity: may include assessments such as walking distance, walking speed, Community Walk Test, functional ambulation, Timed Up and Go Test.
 - ii) Standing reach: may include Berg Balance Scale and laboratory-based force plate measures.
3. Global motor function: may include assessments such as the Motor Assessment Scale.

Secondary outcomes

1. Cognitive function: may include assessments such as Trail making test, Useful Field of View Test.
2. Activity limitation: may include assessments such as the Functional Independence Measure (FIM), Barthel Index, Activities-specific Balance Confidence Scale, On-road driving test.
3. Participation restriction and quality of life: may include assessments such as the SF36, EQ5D, Stroke Impact Scale or other patient reported outcomes.
4. Imaging studies: may include functional magnetic resonance imaging (MRI).
5. Adverse events: including motion sickness, pain, injury, falls and death.

Search methods for identification of studies

Electronic searches

See the 'Specialized register' section in the [Cochrane Stroke Group](#) module.

We will search the Cochrane Stroke Group Trials Register. In addition, we will search the following electronic bibliographic databases: the Cochrane Central Register of Controlled Trials

(CENTRAL) (*The Cochrane Library*, latest issue), MEDLINE (1950 to present) ([Appendix 1](#)), EMBASE (1980 to present), AMED (1985 to present), CINAHL (1982 to present), PsycINFO (1840 to present), PsycBITE (Psychological Database for Brain Impairment Treatment Efficacy, <http://www.psycbite.com/>), and OTseeker (<http://www.otseeker.com/>). We will also search the engineering databases COMPENDEX (1970 to present) and IN-SPEC (1969 to present) for studies from a non-medical background.

We will consult an experienced medical librarian regarding the search strategies for each database. These will include the areas: stroke, virtual reality and a trials filter.

Searching other resources

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

1. search the following ongoing trials registers: Current Controlled Trials (www.controlled-trials.com), National Institute of Health Clinical Trials Database (<http://www.clinicaltrials.gov>) and Stroke Trials Registry (www.strokecenter.org/trials/);
2. use the Cited Reference Search within Science Citation Index (SCI) and Social Science Citation Index (SSCI) to track relevant references;
3. scan the reference lists of all identified studies and reviews;
4. search Dissertation Abstracts and contact the key researchers in the area;
5. scan the abstracts of non-English language studies if they are available in English;
6. handsearch the proceedings of the International Workshop on Virtual Rehabilitation (2003 to 2006), Virtual Rehabilitation Conference (2007 to 2009), International Conference Series on Disability, Virtual Reality and Associated Technologies (2000 to 2009), Artabilitation (2006 to 2009) and Cybertherapy (2003 to 2009);
7. search the IEEE (Institute of Electrical and Electronic Engineers) electronic library;
8. contact the manufacturers of virtual reality equipment to ask for details of trials.

We will search for relevant trials in all languages and arrange translation of trial reports published in languages other than English.

Data collection and analysis

Selection of studies

Two review authors will independently review the titles identified from the database searches. The same two review authors will then assess the trials based on the inclusion criteria (types of studies, participants, interventions and outcome measures) and sort the studies into three groups; included, excluded, and unsure. We will

document the reasons for exclusion. We will seek further information about study methods and interventions from the trial authors if required, particularly for those studies that have been rated as 'unsure'. A third review author will make the final decision regarding studies rated as 'unsure'.

Data extraction and management

Two review authors will independently record information about the included studies on a pre-designed paper data extraction form. We will use the same criteria as those outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008) to evaluate each trial.

We will include the following information on the data extraction form:

1. citation details of the study;
2. the trial setting (e.g. hospital, community, outpatients);
3. inclusion and exclusion criteria;
4. participant details: descriptive characteristics including age, sex, location of stroke, time since onset of stroke, functional abilities of sample, sample size and number of drop outs;
5. methodological quality: according to The Cochrane Collaboration's tool for assessing risk (Appendix 2);
6. interventions: description of the intervention, duration and dosage, comparison intervention;
7. outcome measures: primary and secondary outcome measures and when they were administered, adverse events.

We will contact trial authors for clarification when required, and a third review author will help to resolve disagreements.

Assessment of risk of bias in included studies

Two review authors will independently assess the methodological quality of the studies to be included. The review authors will use the Cochrane risk of bias table (Appendix 2), which covers the domains of sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, and incomplete outcome data. We will complete each domain with 'yes', 'no' or 'unclear', depending on whether they met the criteria for the domain. We will resolve any disagreements with help from a third review author. After using the risk of bias tool the reviewers responsible for data extraction will discuss any modifications that may be required to enhance the assessment of risk of bias. We will give a descriptive report on the overall risk of bias of any findings produced from a meta-analysis.

Measures of treatment effect

Two review authors will independently classify outcome measures in terms of the domain assessed (upper limb function and activity, gait and balance function and activity, global motor function, cognitive function, activity limitation, participation restriction and quality of life, neuroimaging studies). We will not include outcomes measured either immediately after or during virtual reality

intervention. If possible, we will analyse results at both short-term (less than three months) and long-term (three months or more) intervals. If a study presents more than one outcome measure for the same domain, we will include the measure most frequently used across studies in the analysis.

We will calculate relative risks (RR) with 95% confidence intervals (CI) for dichotomous outcomes. We will use standardised mean differences (SMD) for continuous data.

Unit of analysis issues

The unit of randomisation in these trials is the individual patient.

Dealing with missing data

We will contact study authors to obtain any missing data and convert available data when possible (e.g. when reported as a standard error (SE)). Where possible, we will conduct intention-to-treat analyses to include all people randomised, guided by recommendations of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008) and a statistician. Where drop outs have been clearly identified for an outcome assessment, we will use the actual denominator of the patients contributing data. If there are a lot of data missing, we will perform a sensitivity analysis to examine whether the conclusions are affected by inclusion or exclusion of certain data.

Assessment of heterogeneity

We will pool results to present an overall estimate of the treatment effect using a fixed-effect model in the primary analysis. We will assess heterogeneity by visual inspection of the forest plot. We will quantify inconsistency amongst studies using the I^2 statistic (Higgins 2008), where we will consider levels greater than 50% as substantial heterogeneity. We will use a random-effects model as part of a sensitivity analysis. We will explore the reasons if there is a substantial difference between the fixed-effect and random-effects models.

Assessment of reporting biases

If sufficient data are available, we will attempt to assess publication bias by preparing a funnel plot. Our search of clinical trial registers should assist in reducing publication bias. We will investigate selective outcome reporting through the comparison of the methods section of papers with the results reported.

Data synthesis

Where there are acceptable levels of heterogeneity we will conduct a meta-analysis with appropriate data using a fixed-effect model with 95% CI using RevMan 5.0 (RevMan 2008). If meta-analysis is not appropriate due to unacceptable heterogeneity we will present a narrative summary of study results.

Subgroup analysis and investigation of heterogeneity

We will perform subgroup analyses to determine whether outcomes vary according to age, the type and severity of stroke, time since onset of stroke, frequency of intervention (number of sessions per week), intensity of intervention (total hours of intervention) and type of intervention (highly specialised program designed for rehabilitation versus commercial gaming console).

Sensitivity analysis

We will perform sensitivity analyses based on the methodological quality of studies (allocation concealment, blinding of outcome assessor, intention-to-treat analysis) as well as the size of the study to examine the impact of risk of bias in included studies. We will also use a sensitivity analysis to consider the impact of different comparison groups (alternative intervention versus no intervention).

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* Indicates the major publication for the study

APPENDICES

Appendix I. MEDLINE search strategy

We will use the following search strategy for MEDLINE (Ovid) and adapt it to search the other databases.

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ 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/
2. brain injuries/ or brain injury, chronic/
3. (stroke\$ or cva or poststroke or post-stroke).tw.
4. (cerebrovasc\$ or cerebral vascular).tw.
5. (cerebral or cerebellar or brain\$ or vertebrobasilar).tw.
6. (infarct\$ or isch?emi\$ or thrombo\$ or emboli\$ or apoplexy).tw.
7. 5 and 6
8. (cerebral or brain or subarachnoid).tw.
9. (haemorrhage or hemorrhage or haematoma or hematoma or bleed\$).tw.
10. 8 and 9
11. exp hemiplegia/ or exp paresis/
12. (hemipar\$ or hemipleg\$ or paresis or paretic or brain injur\$).tw.
13. Gait Disorders, Neurologic/
14. 1 or 2 or 3 or 4 or 7 or 10 or 11 or 12 or 13
15. user-computer interface/
16. computers/ or exp microcomputers/ or computer systems/ or software/
17. computer simulation/ or computer-assisted instruction/ or therapy, computer-assisted/
18. computer graphics/ or video games/ or *touch/
19. (virtual reality\$ or virtual-reality\$ or VR).tw.
20. (virtual adj3 (environment\$ or world\$ or object\$ or treatment\$ or system\$ or program\$ or rehabilitation\$ or therap\$ or driving or drive\$ or car or tunnel or vehicle)).tw.
21. (computer adj3 (simulat\$ or graphic\$ or game\$ or interact\$)).tw.
22. (computer adj1 assist\$ adj1 (therap\$ or treat\$)).tw.
23. (computer adj1 generat\$ adj1 (environment\$ or object\$)).tw.
24. video game\$.tw.
25. (haptics or haptic device\$).tw.
26. (simulat\$ adj3 (environment\$ or object\$ or driving or drive\$ or car or tunnel or vehicle or event\$)).tw.
27. (user adj1 computer adj1 interface).tw.
28. or/15-27
29. 14 and 28
30. Randomized Controlled Trials as Topic/
31. random allocation/
32. Controlled Clinical Trials as Topic/
33. control groups/
34. clinical trials as topic/
35. double-blind method/
36. single-blind method/
37. Placebos/
38. placebo effect/
39. cross-over studies/
40. Multicenter Studies as Topic/
41. Therapies, Investigational/
42. Research Design/
43. Program Evaluation/
44. evaluation studies as topic/

45. randomized controlled trial.pt.
46. controlled clinical trial.pt.
47. clinical trial.pt.
48. multicenter study.pt.
49. (evaluation studies or comparative study).pt.
50. random\$.tw.
51. (controlled adj5 (trial\$ or stud\$)).tw.
52. (clinical\$ adj5 trial\$).tw.
53. ((control or treatment or experiment\$ or intervention) adj5 (group\$ or subject\$ or patient\$)).tw.
54. (quasi-random\$ or quasi random\$ or pseudo-random\$ or pseudo random\$).tw.
55. ((multicenter or multicentre or therapeutic) adj5 (trial\$ or stud\$)).tw.
56. ((control or experiment\$ or conservative) adj5 (treatment or therapy or procedure or manage\$)).tw.
57. ((singl\$ or doubl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).tw.
58. (coin adj5 (flip or flipped or toss\$)).tw.
59. latin square.tw.
60. versus.tw.
61. (cross-over or cross over or crossover).tw.
62. placebo\$.tw.
63. sham.tw.
64. (assign\$ or alternate or allocat\$ or counterbalance\$ or multiple baseline).tw.
65. controls.tw.
66. (treatment\$ adj6 order).tw.
67. or/30-66
68. 67 and 29
69. limit 68 to humans

Appendix 2. Cochrane risk of bias table

The Cochrane Collaboration's tool for assessing risk of bias

Domain	Description	Review authors' judgement
Sequence generation	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Was the allocation sequence adequately generated? Yes No Unsure
Allocation concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Was allocation adequately concealed? Yes No Unsure

(Continued)

Blinding of participants, personnel and outcome assessors <i>Assessments should be made for each main outcome (or class of outcomes)</i>	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Was knowledge of the allocated intervention adequately prevented during the study? Participants Yes No Unsure Personnel Yes No Unsure Outcome Assessors Yes No Unsure

Incomplete outcome data <i>Assessments should be made for each main outcome (or class of outcomes).</i>	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Were incomplete outcome data adequately addressed? Yes No Unsure
Selective outcome reporting	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Are reports of the study free of suggestion of selective outcome reporting? Yes No Unsure

(Continued)

Other sources of bias	State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.	Was the study apparently free of other problems that could put it at a high risk of bias? Yes No Unsure

HISTORY

Protocol first published: Issue 2, 2010

CONTRIBUTIONS OF AUTHORS

Kate Laver is the guarantor of the review. Contributions include coordinating the review, drafting the protocol, developing the search strategy, searching for trials, obtaining copies of the trials, selecting which trials to include, extracting data from the trials, entering data, carrying out the analysis, interpreting the analysis and drafting the final review.

Stacey George is involved in drafting the protocol, selecting which trials to include, interpreting the analysis and drafting the final review.

Judith Deutsch is involved in drafting the protocol, interpretation of analysis and drafting the final review.

Maria Crotty is involved in drafting the protocol, searching for trials, moderating any disagreements in selection of trials, extracting data from trials, interpreting the analysis and drafting the final review.

DECLARATIONS OF INTEREST

Judith Deutsch is actively researching the use of virtual reality and gaming to improve mobility and balance in individuals post stroke. She is a member of a company and has received research funding to develop a virtual reality cycling kit. She speaks at professional meetings and continuing education courses about the use of virtual reality and gaming to improve mobility and balance.