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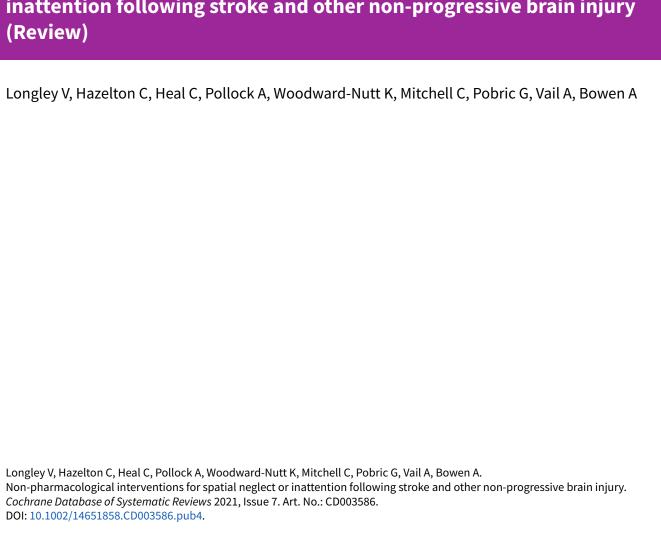
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# Non-pharmacological interventions for spatial neglect or inattention following stroke and other non-progressive brain injury



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#### [Intervention Review]

# Non-pharmacological interventions for spatial neglect or inattention following stroke and other non-progressive brain injury

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# **ABSTRACT**

# **Background**

People with spatial neglect after stroke or other brain injury have difficulty attending to one side of space. Various rehabilitation interventions have been used, but evidence of their benefit is unclear.

# Objectives

The main objective was to determine the effects of non-pharmacological interventions for people with spatial neglect after stroke and other adult-acquired non-progressive brain injury.

### Search methods

We searched the Cochrane Stroke Group Trials Register (last searched October 2020), the Cochrane Central Register of Controlled Trials (CENTRAL; last searched October 2020), MEDLINE (1966 to October 2020), Embase (1980 to October 2020), the Cumulative Index to Nursing and Allied Health Literature (CINAHL; 1983 to October 2020), and PsycINFO (1974 to October 2020). We also searched ongoing trials registers and screened reference lists.

### **Selection criteria**

We included randomised controlled trials (RCTs) of any non-pharmacological intervention specifically aimed at spatial neglect. We excluded studies of general rehabilitation and studies with mixed participant groups, unless separate neglect data were available.

### **Data collection and analysis**

We used standard Cochrane methods. Review authors categorised the interventions into eight broad types deemed to be applicable to clinical practice through iterative discussion: visual interventions, prism adaptation, body awareness interventions, mental function interventions, movement interventions, non-invasive brain stimulation, electrical stimulation, and acupuncture. We assessed the quality of evidence for each outcome using the GRADE approach.



#### **Main results**

We included 65 RCTs with 1951 participants, all of which included people with spatial neglect following stroke. Most studies measured outcomes using standardised neglect assessments. Fifty-one studies measured effects on ADL immediately after completion of the intervention period; only 16 reported persisting effects on ADL (our primary outcome). One study (30 participants) reported discharge destination, and one (24 participants) reported depression. No studies reported falls, balance, or quality of life. Only two studies were judged to be entirely at low risk of bias, and all were small, with fewer than 50 participants per group. We found no definitive (phase 3) clinical trials. None of the studies reported any patient or public involvement.

**Visual interventions versus any control:** evidence is very uncertain about the effects of visual interventions for spatial neglect based on measures of persisting functional ability in ADL (2 studies, 55 participants) (standardised mean difference (SMD) -0.04, 95% confidence interval (CI) -0.57 to 0.49); measures of immediate functional ability in ADL; persisting standardised neglect assessments; and immediate neglect assessments.

**Prism adaptation versus any control:** evidence is very uncertain about the effects of prism adaptation for spatial neglect based on measures of persisting functional ability in ADL (2 studies, 39 participants) (SMD -0.29, 95% CI -0.93 to 0.35); measures of immediate functional ability in ADL; persisting standardised neglect assessments; and immediate neglect assessments.

**Body awareness interventions versus any control:** evidence is very uncertain about the effects of body awareness interventions for spatial neglect based on measures of persisting functional ability in ADL (5 studies, 125 participants) (SMD 0.61, 95% CI 0.24 to 0.97); measures of immediate functional ability in ADL; persisting standardised neglect assessments; immediate neglect assessments; and adverse events.

**Mental function interventions versus any control:** we found no trials of mental function interventions for spatial neglect reporting on measures of persisting functional ability in ADL. Evidence is very uncertain about the effects of mental function interventions on spatial neglect based on measures of immediate functional ability in ADL and immediate neglect assessments.

**Movement interventions versus any control:** we found no trials of movement interventions for spatial neglect reporting on measures of persisting functional ability in ADL. Evidence is very uncertain about the effects of body awareness interventions on spatial neglect based on measures of immediate functional ability in ADL and immediate neglect assessments.

**Non-invasive brain stimulation (NIBS) versus any control:** evidence is very uncertain about the effects of NIBS on spatial neglect based on measures of persisting functional ability in ADL (3 studies, 92 participants) (SMD 0.35, 95% CI -0.08 to 0.77); measures of immediate functional ability in ADL; persisting standardised neglect assessments; immediate neglect assessments; and adverse events.

**Electrical stimulation versus any control:** we found no trials of electrical stimulation for spatial neglect reporting on measures of persisting functional ability in ADL. Evidence is very uncertain about the effects of electrical stimulation on spatial neglect based on immediate neglect assessments.

**Acupuncture versus any control:** we found no trials of acupuncture for spatial neglect reporting on measures of persisting functional ability in ADL. Evidence is very uncertain about the effects of acupuncture on spatial neglect based on measures of immediate functional ability in ADL and immediate neglect assessments.

# **Authors' conclusions**

The effectiveness of non-pharmacological interventions for spatial neglect in improving functional ability in ADL and increasing independence remains unproven. Many strategies have been proposed to aid rehabilitation of spatial neglect, but none has yet been sufficiently researched through high-quality fully powered randomised trials to establish potential or adverse effects. As a consequence, no rehabilitation approach can be supported or refuted based on current evidence from RCTs. As recommended by a number of national clinical guidelines, clinicians should continue to provide rehabilitation for neglect that enables people to meet their rehabilitation goals. Clinicians and stroke survivors should have the opportunity, and are strongly encouraged, to participate in research. Future studies need to have appropriate high-quality methodological design, delivery, and reporting to enable appraisal and interpretation of results. Future studies also must evaluate outcomes of importance to patients, such as persisting functional ability in ADL. One way to improve the quality of research is to involve people with experience with the condition in designing and running trials.

#### PLAIN LANGUAGE SUMMARY

### Non-drug treatments for spatial neglect/inattention following stroke or adult brain injury

### What is the review about?

Spatial neglect, or inattention, is a condition that affects many brain injury survivors, particularly stroke survivors. It reduces a person's awareness of one side of the body or of the surrounding environment. This can affect a person's ability to carry out many everyday tasks such as eating, reading, and getting dressed, which can reduce independence.

#### What did we want to know?



We wanted to find out if non-drug treatments:

- improve patients' ability to complete daily living activities; and
- reduce spatial neglect.

### What did we do?

We reviewed evidence from randomised trials - studies that compared one treatment to another by randomly assigning people with stroke or brain injury to one or the other treatment.

Evidence from 1966 to October 2020 was reviewed.

#### What evidence did we find?

We found 65 studies involving 1951 participants.

All studies included participants with spatial neglect as a result of stroke. It is surprising that only one study included three participants with spatial neglect caused by another type of brain injury.

All studies included participants with right-sided damage to the brain; seven studies also included participants with left-sided damage.

Studies were considered small, with 4 to 69 participants (average 30). Eight studies included 50 or more participants; four studies involved 10 or fewer.

None of the studies reported any patient or public involvement in how the studies were designed, conducted, or reported.

We categorised the studies into eight different types of treatments.

- <u>Visual treatment</u>: 17 studies involving 398 participants explored visual treatments. All treatments encouraged eye movement or scanning by a range of methods including paper-based tasks, computer activities, and daily living activities.
- <u>Prism adaptation training</u>: 8 studies involving 257 participants explored prism adaptation training. This involved participants wearing glasses with prism lenses during a pointing activity.
- <u>Body awareness treatments</u>: 12 studies involving 447 participants explored body awareness treatments. These studies involved various physical, visual, or verbal prompting or cueing aimed at increasing awareness of the affected side.
- <u>Mental function treatments</u>: 7 studies involving 170 participants explored treatments that focused on mental processing/thinking (e.g. mental imagery, virtual reality).
- <u>Movement treatments</u>: 6 studies involving 220 participants explored treatments that used movement of the arm or the whole body. These included the use of robotics, visual and motor feedback, and restricting movement on the side of the body that was not affected.
- <u>Non-invasive brain stimulation</u>: 17 studies involving 467 participants explored non-invasive brain stimulation. These involved different methods of applying electrical or magnetic stimulation to the skull to change brain activity.
- <u>Electrical stimulation</u>: 8 studies involving 270 participants explored electrical stimulation to other parts of the body. These involved sending mild electrical impulses to a particular part of the body (e.g. the arm). Four different types of electrical stimulation were used.
- <u>Acupuncture</u>: 2 studies involving 104 participants explored the use of acupuncture. These involved inserting thin needles into specific points in the body.

# What was the quality of the evidence?

We rated the evidence on use of these treatments and found it to be of very low quality due to:

- the small size of studies;
- differences between studies within each of the eight treatment categories, including participant characteristics, types of treatments, and assessments used to measure changes; and
- concerns about how participants were randomised, and whether people carrying out the assessments were "blinded" (i.e. knew which treatment each patient received).

#### What were the main results?

Most studies used standard tests of spatial neglect. Many also measured effects on daily living activities soon after treatment, but very few reports described longer-term effects.

Other meaningful treatment outcomes were rarely reported.

Overall we found only very low-quality evidence about whether these treatments had benefits or harms for people with spatial neglect.



#### What does this mean?

Despite 65 (small) trials, the benefits or risks of non-drug treatments for reducing neglect and increasing independence remain unknown. It would be a mistake to interpret this review as concluding that the proposed treatments are ineffective. Rather, we conclude that evidence for or against any treatment used within randomised trials conducted worldwide is insufficient. Future trials must be of much higher quality to answer important clinical questions. One way to improve research quality is to involve patients in designing and running the trial. Clinicians should continue to follow national clinical guidelines and are strongly encouraged to participate in trials. People with spatial neglect should continue to receive general stroke or neurological rehabilitation that enables them to meet their rehabilitation goals, including any available intervention for neglect. People with spatial neglect should also have the opportunity to take part in high-quality research.



#### SUMMARY OF FINDINGS

Summary of findings 1. Visual interventions compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Visual interventions compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Patient or population: spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

**Setting:** inpatient or community rehabilitation

**Intervention:** visual interventions **Comparison:** any control

Outcomes	Relative effect (95% CI)	No. of partici- pants (studies)	Certainty of the evidence (GRADE)	Comments
Primary outcome				
Activities of daily living: effects persisting at least 1 month post intervention	SMD -0.04 lower (-0.57 lower to 0.49 high- er)	55 (2 RCTs)	⊕⊝⊝⊝ Very low <sup>a,b,c</sup>	No evidence of benefit or detriment from intervention
Secondary outcomes				
Activities of daily living: immediate effects	SMD -0.15 lower (-0.6 lower to 0.3 higher)	75 (3 RCTs)	⊕⊙⊙⊝ Very low <sup>a,b,c,d</sup>	No evidence of benefit or detriment from intervention
Neglect outcomes: effects persisting at least 1 month post intervention	SMD 0.14 higher (-0.26 lower to 0.55 high- er)	98 (5 RCTs)	⊕⊝⊝⊝ Very lowa,b,c,d	No evidence of benefit or detriment from intervention
Neglect outcomes: immediate effects	SMD 0.08 higher (-0.26 lower to 0.42 high- er)	142 (7 RCTs)	⊕⊙⊙⊝ Very lowa,b,c,d	No evidence of benefit or detriment from intervention
Adverse events	-	No studies	-	

CI: confidence interval; RCT: randomised controlled trial; SMD: standardised mean difference.

#### **GRADE** Working Group grades of evidence.

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

<sup>&</sup>lt;sup>a</sup>Overall, studies contributing to this analysis had limitations regarding risk of bias sufficient to lower certainty regarding the estimate of effect and were downgraded once.

<sup>&</sup>lt;sup>b</sup>Downgraded twice for serious imprecision (very small numbers of participants).

<sup>&</sup>lt;sup>c</sup>Downgraded once for indirectness. Studies included only participants with recent-onset stroke.

<sup>&</sup>lt;sup>d</sup>Downgraded once for indirectness. Studies used different interventions or measured outcomes using different scales.



# Summary of findings 2. Prism adaptation training compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Prism adaptation training compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Patient or population: spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

**Setting:** inpatient or community rehabilitation **Intervention:** prism adaptation training

Comparison: any control

Outcomes	Relative effect (95% CI)	No. of partici- pants (studies)	Certainty of the evidence (GRADE)	Comments
Primary outcome				
Activities of daily living: effects persisting at least 1 month post intervention	SMD -0.29 lower (-0.93 lower to 0.35 higher)	39 (2 RCTs)	⊕⊙⊙o Very low <sup>a,b,c</sup>	No evidence of benefit or detriment from intervention
Secondary outcomes				
Activities of daily living: immediate effects	SMD 0.20 higher (-0.12 lower to 0.51 higher)	158 (5 RCTs)	⊕⊙⊙o Very low <sup>a,b,c</sup>	No evidence of benefit or detriment from intervention
Neglect outcomes: effects persisting at least 1 month post intervention	SMD 0.05 higher (-0.96 lower to 1.06 higher)	16 (1 RCT)	⊕⊙⊙ Very low <sup>a,b,c</sup>	No evidence of benefit or detriment from intervention
Neglect outcomes: immediate effects	SMD 0.28 higher (-0.05 lower to 0.60 higher)	154 (5 RCTs)	⊕⊙⊙⊝ Very low <sup>a,b,c,d</sup>	No evidence of benefit or detriment from interven- tion
Adverse events	-	No studies	-	

CI: confidence interval; RCT: randomised controlled trial; SMD: standardised mean difference.

# **GRADE Working Group grades of evidence.**

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

<sup>&</sup>lt;sup>q</sup>Overall, studies contributing to this analysis had limitations regarding risk of bias sufficient to lower certainty regarding the estimate of effect and were downgraded once.

<sup>&</sup>lt;sup>b</sup>Downgraded twice for serious imprecision (very small numbers of participants).

<sup>&</sup>lt;sup>c</sup>Downgraded once for indirectness. Studies included only participants with recent-onset stroke.

<sup>&</sup>lt;sup>d</sup>Downgraded once for indirectness. Studies used different interventions or measured outcomes using different scales.



Summary of findings 3. Body awareness interventions compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Body awareness interventions compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Patient or population: spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

**Setting:** inpatient or community rehabilitation **Intervention:** body awareness interventions

Comparison: any control

Outcomes	Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
Primary outcome				
Activities of daily living: ef- fects persisting at least 1 month post intervention	SMD 0.61 higher (0.24 higher to 0.97 higher)	125 (5 RCTs)	⊕⊝⊝⊝ Very low <sup>a,b,c,d</sup>	Evidence suggests possible benefit from intervention
Secondary outcomes				
Activities of daily living: im- mediate effects	SMD 0.26 higher (-0.01 lower to 0.53 higher)	221 (7 RCTs)	⊕⊝⊝⊝ Very low <sup>a,b,c,d</sup>	No evidence of benefit or detri- ment from intervention
Neglect outcomes: effects persisting at least 1 month post intervention	SMD 0.36 higher (0.00 lower to 0.72 higher)	125 (5 RCTs)	⊕⊝⊝⊝ Very low <sup>a,b,c,d</sup>	Evidence suggests possible benefit from intervention
Neglect outcomes: immediate effects	SMD 0.16 higher (-0.07 lower to 0.39 higher)	311 (10 RCTs)	⊕⊝⊝⊝ Very low <sup>a,c,d</sup>	No evidence of benefit or detri- ment from intervention
Adverse events	OR 0.36 higher (0.05 to 2.6)	130 (2 RCTs)	⊕⊝⊝⊝ Very low <sup>a,b,d</sup>	No evidence of benefit or detri- ment from intervention

CI: confidence interval; OR: odds ratio; RCT: randomised controlled trial; SMD: standardised mean difference.

# **GRADE Working Group grades of evidence.**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

<sup>&</sup>lt;sup>q</sup>Overall, studies contributing to this analysis had limitations regarding risk of bias sufficient to lower certainty regarding the estimate of effect and were downgraded once.

<sup>&</sup>lt;sup>b</sup>Downgraded twice for serious imprecision (very small numbers of participants).

<sup>&</sup>lt;sup>c</sup>Downgraded once for indirectness. Studies used different interventions or measured outcomes using different scales.

dDowngraded once for indirectness. Studies included only participants with recent-onset stroke.



# Summary of findings 4. Mental function interventions compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Mental function interventions compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Patient or population: spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

**Setting:** inpatient or community rehabilitation **Intervention:** mental function interventions

**Comparison:** any control

Outcomes	Relative effect (95% CI)	No. of participants	Certainty of the evidence (GRADE)	Comments
Primary outcome				
Activities of daily living: effects persisting at least 1 month post intervention		No studies	-	
Secondary outcomes				
Activities of daily living: immediate effects	SMD 0.32 higher (-0.49 lower to 1.12 higher)	24 (1 RCT)	⊕⊙⊙⊝ Very low <sup>a,b,c</sup>	No evidence of benefit or detriment from intervention
Neglect outcomes: effects persisting at least 1 month post intervention	-	No studies	-	
Neglect outcomes: immediate effects	SMD 0.10 higher (-0.32 lower to 0.53 higher)	60 (3 RCTs)	⊕⊝⊝⊝ Very low <sup>a,b,c</sup>	No evidence of benefit or detriment from intervention
Adverse events	-	No studies	-	

CI: confidence interval; RCT: randomised controlled trial; SMD: standardised mean difference.

### **GRADE** Working Group grades of evidence.

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

# Summary of findings 5. Movement interventions compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Movement interventions compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

<sup>&</sup>lt;sup>q</sup>Overall, studies contributing to this analysis had limitations regarding risk of bias sufficient to lower certainty regarding the estimate of effect and were downgraded once.

<sup>&</sup>lt;sup>b</sup>Downgraded twice for serious imprecision (very small numbers of participants).

<sup>&</sup>lt;sup>c</sup>Downgraded once for indirectness. Studies included only participants with recent-onset stroke.



Patient or population: spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

**Setting:** inpatient or community rehabilitation **Intervention:** movement interventions

Comparison: any control

Outcomes	Relative effect (95% CI)	No. of participants	Certainty of the evidence (GRADE)	Comments		
Primary outcome						
Activities of daily living: effects persisting at least 1 month post intervention	-	No studies	-			
Secondary outcomes	Secondary outcomes					
Activities of daily living: immediate effects	SMD 0.57 higher (0.09 higher to 1.04 higher)	75 (3 RCTs)	⊕⊝⊝⊝ Very low <sup>a,b,c</sup>	Evidence suggests possible benefit from intervention		
Neglect outcomes: effects persisting at least 1 month post intervention	-	No studies	-			
Neglect outcomes: immediate effects	SMD 0.57 higher (0.04 higher to 1.10 higher)	58 (2 RCTs)	⊕⊙⊙⊝ Very low <sup>a,b,c</sup>	Evidence suggests possible benefit from intervention		
Adverse events	-	No studies	-			

CI: confidence interval; RCT: randomised controlled trial; SMD: standardised mean difference.

# **GRADE Working Group grades of evidence.**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

# Summary of findings 6. NIBS compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

# NIBS compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

**Patient or population:** spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury **Setting:** inpatient or community rehabilitation

Intervention: NIBS Comparison: any control

<sup>&</sup>lt;sup>q</sup>Overall, studies contributing to this analysis had limitations regarding risk of bias sufficient to lower certainty regarding the estimate of effect and were downgraded once.

<sup>&</sup>lt;sup>b</sup>Downgraded twice for serious imprecision (very small numbers of participants).

<sup>&</sup>lt;sup>c</sup>Downgraded once for indirectness. Studies included only participants with recent-onset stroke.



Outcomes	Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
Primary outcome				
Activities of daily living: effects persisting at least 1 month post intervention	SMD 0.35 higher (-0.08 lower to 0.77 higher)	92 (3 RCTs)	⊕⊙⊙ Very low <sup>a,b,c</sup>	No evidence of benefit or detri- ment from intervention
Secondary outcomes				
Activities of daily living: im- mediate effects	SMD 0.61 higher (0.27 higher to 0.94 higher)	160 (6 RCTs)	⊕⊝⊝⊝ Very low <sup>a,b,c,d</sup>	Evidence suggests possible benefit from intervention
Neglect outcomes: effects persisting at least 1 month post intervention	SMD 0.77 (0.29 higher to 1.24 higher)	102 (3 RCTs)	⊕⊝⊝⊝ Very lowa,b,c,d	Evidence suggests possible benefit from intervention
Neglect outcomes: immediate effects	SMD 0.75 higher (0.47 higher to 1.04 higher)	244 (10 RCTs)	⊕⊝⊝⊝ Very low <sup>a,b,c,d</sup>	Evidence suggests possible benefit from intervention
Adverse events	L.	24 (1 RCT)	-	All adverse events reported deemed to be unrelated to intervention

### CI: Confidence interval

### **GRADE Working Group grades of evidence.**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

# Summary of findings 7. Electrical stimulation compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Electrical stimulation compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Patient or population: spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

**Setting:** inpatient or community rehabilitation

Intervention: electrical stimulation

Comparison: any control

Outcomes	Relative effect	No. of partici-	Certainty of the	Comments
	(95% CI)	pants	evidence	

<sup>&</sup>lt;sup>q</sup>Overall, studies contributing to this analysis had limitations regarding risk of bias sufficient to lower certainty regarding the estimate of effect and were downgraded once.

<sup>&</sup>lt;sup>b</sup>Downgraded twice for serious imprecision (very small numbers of participants).

<sup>&</sup>lt;sup>c</sup>Downgraded once for indirectness. Studies included only participants with recent-onset stroke.

<sup>&</sup>lt;sup>d</sup>Downgraded once for indirectness. Studies used different interventions or measured outcomes using different scales.



		(studies)	(GRADE)	
Primary outcome				
Activities of daily living: effects persisting at least 1 month post intervention		No studies	-	
Secondary outcomes				
Activities of daily living: immediate effects	-	No studies	-	
Neglect outcomes: effects persisting at least 1 month post intervention	-	No studies	-	
Neglect outcomes: immediate effects	SMD 0.99 high- er (0.44 higher to 1.53 higher)	60 (2 RCTs)	⊕⊝⊝⊝ Very lowa,b,c	Evidence sug- gests possible benefit from in- tervention
Adverse events	-	No studies	-	

CI: confidence interval; RCT: randomised controlled trial; SMD: standardised mean difference.

#### **GRADE Working Group grades of evidence.**

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

<sup>q</sup>Overall, studies contributing to this analysis had limitations regarding risk of bias sufficient to lower certainty regarding the estimate of effect and were downgraded once.

<sup>b</sup>Downgraded twice for serious imprecision (very small numbers of participants).

CDowngraded once for indirectness. Studies included only participants with recent-onset stroke.

# Summary of findings 8. Acupuncture compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

Acupuncture compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury

**Patient or population:** spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury **Setting:** inpatient or community rehabilitation

Intervention: acupuncture Comparison: any control

Outcomes	Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
Primary outcome				
Activities of daily living: effects persisting at least 1 month post intervention	-	No studies	-	



#### **Secondary outcomes**

Activities of daily living: immediate effects	SMD 0.65 higher (0.26 higher to 1.05 higher)	104 (2 RCTs)	⊕⊝⊝⊝ Very low <sup>a,b,c</sup>	Evidence suggests possible benefit from intervention
Neglect outcomes: effects persisting at least 1 month post intervention	-	No studies	-	
Neglect outcomes: immediate effects	SMD 0.57 higher (0.18 higher to 0.97 higher)	104 (2 RCTs)	⊕⊙⊙ Very low <sup>a,b,c,d</sup>	Evidence suggests possible benefit from intervention
Adverse events	-	No studies	-	

CI: confidence interval; RCT: randomised controlled trial; SMD: standardised mean difference.

### **GRADE Working Group grades of evidence.**

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

<sup>&</sup>lt;sup>a</sup>Overall, studies contributing to this analysis had limitations regarding risk of bias sufficient to lower certainty regarding the estimate of effect and were downgraded once.

<sup>&</sup>lt;sup>b</sup>Downgraded twice for serious imprecision (very small numbers of participants).

<sup>&</sup>lt;sup>c</sup>Downgraded once for indirectness. Studies included only participants with recent-onset stroke.

<sup>&</sup>lt;sup>d</sup>Downgraded once for indirectness. Studies used different interventions or measured outcomes using different scales.



#### BACKGROUND

#### **Description of the condition**

Brain injury, including stroke, can affect cognitive as well as physical and sensory abilities (Wade 1985). Cognitive deficits include a disorder of spatial awareness or attention known as spatial neglect or inattention. The most widely quoted definition of neglect is a description of the resulting behavioural disabilities: "fails to report, respond, or orient to novel or meaningful stimuli presented to the side opposite a brain lesion" (Heilman 2003). Neglect is not due to a sensory or motor impairment, although these often co-occur. Neglect is a disorder that can reduce a person's ability to look, listen, or make movements towards one-half of their environment. This disorder can also affect an individual's ability to carry out everyday tasks, such as eating, reading, and getting dressed (Nijboer 2013).

Many patients are unaware that they have the disorder (anosognosia), which makes treatment more complex. Brain injury may differentially affect the ability to direct attention in visual, auditory, and tactile modalities. Several different subtypes of neglect have been identified, and little consensus has been reached on how these are identified or categorised (Checketts 2020). As a result, many different terms are used in research and in clinical practice (e.g. visual neglect, hemi-neglect, egocentric neglect, personal neglect, inattention) (Rode 2017). Although neglect of left space is more common than neglect of right space, either can occur and both are disabling.

A majority of cases of adult-acquired spatial neglect occur following stroke. It is not surprising, given the clinical heterogeneity of the neglect syndrome, that the reported incidence of neglect in stroke patients varies hugely. An analysis of recent national audit data from 88,000 UK stroke survivors found that at least 30% screened positive in the acute phase and had a much longer stay in hospital (Hammerbeck 2019). In the light of functional implications of neglect, rehabilitation is an important aim.

For the purposes of this review update, we have chosen to use the term 'neglect' for consistency with previous versions of this review, and to distinguish this review from reviews of attentional deficits after stroke (Loetscher 2019). Based on consultation with stroke survivors who were involved in this update, we have also included the preferred term 'inattention' in the review title and in the Background section of the Plain Language Summary.

# **Description of the intervention**

Many different interventions are used in the rehabilitation of spatial neglect, all of which aim to reduce the adverse effects that cognitive impairments may have on a person's ability to perform everyday activities, as well as on an individual's social participation and quality of life. Traditionally, non-pharmacological rehabilitation is the main treatment method, although pharmacological treatments also exist and have been reviewed elsewhere (Luvizutto 2015). In the current update and expansion of this review of non-pharmacological interventions, we have categorised them into eight types, as described below. We have noted differences in delivery mode (e.g. therapist-delivered, self-directed), professionals involved (e.g. occupational therapists, psychologists), settings (e.g. inpatient, community based), and dose (e.g. length and frequency of intervention sessions).

### How the intervention might work

Interventions for spatial neglect might aim to train individuals to voluntarily compensate for their neglect and require awareness of the disorder; or they might aim to modify underlying factors (i.e. to alter impaired representation of space without requiring awareness of the disorder). For the purposes of this review, we (VL, CH, AB) identified interventions used in each included study; we then developed eight broad groupings through discussion to categorise the non-pharmacological neglect interventions as follows.

- Visual interventions: examples include visual scanning training aimed at active and purposeful exploration of the visual field; training of saccadic or pursuit eye movement using static or moving stimuli; or half-visual field eye-patching, which induces visual exploration of neglected space.
- Prism adaptation training: patients point at a visual target wearing ipsilesional prisms. Patients initially mis-reach, then compensate for this error by recalibrating their pointing movements to point accurately (adaptation). This adaptation persists after removal of the prisms (Rossetti 1998).
- Body awareness interventions: examples include verbal cueing, devices delivering sensory cues, biofeedback, and focused movement - all aimed to cue awareness of the neglected side of the body or space.
- Mental function interventions: these include treatments that focus on mental processing/thinking aimed at improving motor and visual representation without physical activity (e.g. mental imagery, virtual reality).
- Movement-based interventions: examples include upper limb training or balance training, in which specific training of the affected limb or the whole body has an indirect effect on reducing neglect.
- Non-invasive brain stimulation (NIBS): manipulating excitability
  of the motor cortex has been found to cause changes to sensory
  and motor functions post stroke, including neglect symptoms
  (Müri 2013). Methods include repetitive transcranial magnetic
  stimulation (rTMS), including inhibitory or excitatory theta burst
  stimulation (TBS); and transcranial direct current stimulation
  (tDCS).
- Electrical stimulation: examples include passive transcutaneous electrical stimulation to the hand and galvanic vestibular stimulation (GVS), which manipulates stimulation of the vestibular and proprioceptive system. Stimulation used is often below the threshold of perception so differs among patients cued to attend to the stimulated side.
- Acupuncture: a form of complementary stroke treatment that may improve motor function by continually stimulating the nervous system during treatment (Hou 2020).

# Why it is important to do this review

The two main reasons for this review are, first, that neglect is a major problem for people with adult-acquired brain injury, particularly stroke, and second, there is clinical uncertainty about the effectiveness of rehabilitation for this cognitive impairment. Spatial neglect affects long-term outcomes. It can impede active participation in rehabilitation programmes, decrease independence in activities of daily living (ADL) and quality of life, and increase caregiver burden (Bosma 2020; Hammerbeck 2019; Jehkonen 2006). This updated review aimed to systematically consider evidence from randomised controlled trials (RCTs) on the



effectiveness of any non-pharmacological intervention for people with spatial neglect. Previous versions of this review included only cognitive rehabilitation interventions and stroke populations. We have chosen to expand the inclusion criteria (participants and interventions) to increase relevance for clinical practice and to guide future researchers by examining the quality and certainty of existing evidence.

### Stroke survivor involvement in this review

We consulted three stroke survivors with experience of spatial neglect in the analysis and dissemination stages of this review update to improve the relevance of our findings to patients. One co-author (CM or KWN) met with the group regularly to inform group members of progress, and we gathered feedback on results and conclusions. The group provided input to the plain language summary to improve accessibility and relevance to stroke survivors. Our patient involvement was limited to stroke survivors and could have been changed by also including carers.

#### **OBJECTIVES**

The main objective was to determine the effects of non-pharmacological interventions for people with spatial neglect after stroke and other adult-acquired non-progressive brain injury.

#### **Specific objectives**

To assess the effects of non-pharmacological interventions on:

- functional ability in ADL and spatial neglect at an impairment level, (measured at two timepoints: immediately post intervention and persisting at least one month post intervention);
- proportion of patients not discharged to their usual residence;
- falls; balance; depression/anxiety; quality of life persisting at least one month post intervention; and
- adverse events.

#### **METHODS**

### Criteria for considering studies for this review

### Types of studies

We included randomised controlled trials only. As our primary outcome entails persisting effects of treatment (defined as the effect at least one month after completion of the intervention), we excluded trials that could not by design consider this. For example, we excluded early-phase trials that delivered an intervention not intended to have lasting effects as well as trials that crossed participants over to an alternative intervention before persisting effects could be measured. Cross-over trials are not appropriate for rehabilitation for cognitive impairment, as the effects of one approach may contaminate the next. We did not exclude trials that simply failed to record or report persisting effects.

All previously included trials that have been excluded in this update are listed in the Characteristics of excluded studies table.

#### **Types of participants**

We included participants with spatial neglect following any adultacquired non-progressive brain injury. We expected the majority of such individuals to be stroke patients. Stroke was confirmed by neurological examination or by brain scanning, or both, and spatial neglect by neuropsychological assessment. We excluded studies of people with general perceptual problems unless a subgroup with neglect could be identified. A separate review has been published on cognitive rehabilitation for people with perceptual problems (Bowen 2011).

### **Types of interventions**

To be included in the review, a clinical trial had to report a comparison between an active treatment group that received an intervention specifically targeting neglect versus a control group that received either an alternative form of treatment or none. Rehabilitation was broadly defined to include an activity designed to directly reduce the severity of neglect impairment or of the resulting disability. The intervention had to directly target neglect rather than examine whether people with neglect happened to benefit from general rehabilitation services. We excluded pharmacological (drug) treatments and invasive procedures.

#### Types of outcome measures

We were interested in outcomes at two time points: (1) persisting at least one month beyond completion of the intervention (i.e. follow-up outcome), and (2) immediately after completion of an intervention. When more than one follow-up time point was eligible for inclusion, we selected the latest within six months of completion of the intervention. We did not extract data on precise time points.

#### **Primary outcomes**

#### Functional ability in activities of daily living (ADL)

For the primary outcome, we were interested only in the effect of any treatment, measured at the functional level, persisting for at least one month beyond completion of the intervention. We included the following scales: Catherine Bergego Scale (Azouvi 1996), Everyday Neglect Questionnaire (Towle 1991), Nottingham Extended Activities of Daily Living Scale (Nouri 1987), Lawton Instrumental Activities of Daily Living (Graf 2008), Frenchay Activities Index (Holbrook 1983), Rivermead ADL (Lincoln 1990), Edmans EADL (Edmans 1997), Modified Rankin Scale (Wilson 2005), Barthel ADL Index (Collin 1988), Functional Independence Measure (Keith 1987), Katz Index of Activities of Daily Living (Katz 1963), and Rehabilitation Activities Profile (Van Bennekom 1995). When more than one of these scales was reported, we used the scale listed first above. We excluded non-standardised functional measures designed for a specific study (e.g. avoiding obstacles, observing an ADL task).

### Secondary outcomes

We included the following secondary outcomes.

- Ratings on measures of functional ability in ADL (as specified above) recorded immediately after completion of the intervention.
- Performance on a standardised neglect assessment. We separately analysed persisting and immediate effects as defined above. When more than one eligible outcome was presented, we chose the first of target cancellation (single letter, double letter, line, shape) or line bisection. In addition to a conventional subtest score (such as letter cancellation), we used the behavioural summary score from the Behavioural Inattention Test (BIT) when available (Wilson 1987).



- Discharge destination: whether persons were discharged to live in their own home or to a care facility was included when available, with death before discharge treated as not discharged to their own home.
- Balance measured as a persisting effect: Berg Balance Scale (Berg 1992), Functional Reach (Duncan 1990), Get Up and Go Test (Podsiadlo 1991), Standing Balance Test, Step Test (Hill 1996), or other standardised balance measures. We did not include measures of weight distribution or postural sway during standing, as the relationship between ability to maintain balance and these outcomes has not been established.
- Falls measured as a persisting effect: number of reported falls,
   Falls Efficacy Scale (Yardley 2005).
- Depression/anxiety measured as a persisting effect (e.g. Hospital Anxiety and Depression Scale (Zigmond 1983), Beck Depressive Inventory (Beck 1961), General Health Questionnaire (Goldberg 1970), Geriatric Depression Scale (Yesavage 1983)).
- Quality of life and social isolation as a persisting effect: EuroQoL Group Quality of Life Questionnaire based on 5 dimensions (EQ-5D), Health-Related Quality of Life Scale (Flanagan 1978), Quality of Well-Being Scale (Bush 2006), and Short Form Health Survey (SF-36) (Ware 1992).
- Adverse events (excluding falls) such as death or accident before final scheduled follow-up.

#### Search methods for identification of studies

See the 'Specialised Register' section at the Cochrane Stroke Group website. We searched for relevant trials in all languages and arranged translation of trial reports published in languages other than English.

#### **Electronic searches**

We developed search strategies with the help of the Cochrane Stroke Group Trials Information Specialist. We searched the Cochrane Stroke Group Trials Register (October 2020) and the following electronic databases.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2020, Issue 10), in the Cochrane Library (searched 20 October 2020) (Appendix 1).
- MEDLINE Ovid (1946 to 20 October 2020) (Appendix 2).
- Embase Ovid (1974 to 20 October 2020) (Appendix 3).
- Cumulative Index to Nursing and Allied Health Literature (CINAHL; EBSCO; 1982 to 20 October 2020) (Appendix 4).
- PsycINFO Ovid (from 1806 to 20 October 2020) (Appendix 5).

#### **Searching other resources**

In an effort to identify further published, unpublished, and ongoing trials, we searched the following registers of ongoing trials.

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; 20 October 2020) (Appendix 6).
- World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch; 20 October 2020) (Appendix 7).

We searched the ORCID and ResearchGate pages of principal investigators identified from trial registries for relevant

publications. We screened reference lists of all relevant articles and contacted experts in the field. We also checked Cochrane Reviews of NIBS for relevant studies through liaison with those review authors (Elsner 2020).

See Appendix 8 for search methods used in previous versions of this review.

#### Data collection and analysis

The Cochrane Stroke Group Information Specialist ran all electronic searches. One review author (VL or CJH) downloaded references into bibliographic software and removed duplicates. One review author (VL or CJH) excluded any titles that were obviously not related to stroke or other adult-acquired non-progressive brain injury and neglect. We obtained the abstracts for remaining references, and two review authors (of VL, CM, CJH, CH, and AB) independently considered each of these abstracts, excluded any studies that clearly were not RCTs, and excluded any studies for which the intervention was not specifically aimed at improving spatial neglect. Review authors resolved any disagreements through discussion, involving a third review author when necessary. We obtained the full papers for any studies included at this stage.

#### **Selection of studies**

Two review authors (of VL, CM, CH, CJH, AP, or AB) independently selected studies to be included in this review using the four inclusion criteria (types of trials, participants, interventions, and outcome measures). Each review author classified studies as 'include' or 'exclude'. We resolved disagreements by discussion involving a third review author.

# Data extraction and management

We used a pre-designed data extraction form to extract data from the included studies. Four review authors (VL, CM, AV, CJH) independently extracted data from the included trials. We extracted the following: eligibility criteria and baseline characteristics of participants, risk of bias criteria, numbers randomised and analysed, reported results, and publication details. We contacted study authors for further information or for clarification related to randomisation and primary outcomes only. We extracted descriptions of interventions using the Template for Intervention Description and Replication (TIDieR) checklist (Hoffman 2014).

We identified the intervention used in each study; then three review authors (VL, CH, and AB) developed broad groupings through discussion: prism adaptation training, non-invasive brain stimulation, body awareness interventions, visual interventions, movement interventions, electrical stimulation, mental function interventions, and acupuncture. These groupings were developed using an iterative process to cover all intervention types identified.

### Assessment of risk of bias in included studies

Two review authors (AV, CJH) independently documented risk of bias for all studies, classifying each as being at 'high risk', 'low risk', or 'unclear risk' for the following potential biases, using the Cochrane Collaboration Risk of Bias tool 1 for assessing risk of bias (Cochrane Handbook Chapter 8). Any differences were resolved through discussion, involving a third reviewer (VL) when necessary.



- Allocation (selection bias). Studies with adequate allocation included those that reported a method of randomisation using a central system at a site remote from the study, computerised allocation in which records were in a locked readable file that could be assessed only after participant details were entered, or drawing of sequentially numbered, sealed opaque envelopes that allowed retrospective verification of the order. Studies with inadequate allocation included those using open lists or tombola systems.
- Blinding (performance and detection bias). We thought it
  unlikely that any intervention could be blind to those delivering
  it. Adequate masking of participants included studies using a
  sham or placebo procedure and verifying its success. Adequate
  masking of outcome assessment included studies that stated
  that a masked (blinded) outcome assessor was used and
  verified.
- Incomplete outcome data (attrition bias). Studies at low risk for this domain had no missing outcome data; missing outcome data that were unlikely to be related to true outcomes; few missing outcome data that were balanced across intervention groups; or missing data that had been imputed by appropriate methods.
- Selective reporting (reporting bias). Studies were considered at low risk of bias if all recorded outcomes were reported in adequate detail to allow analysis.
- Other potential sources of bias. Studies were considered at low risk if there was no evidence of other sources of bias, such as design flaws or unplanned interim analyses. We planned to study publication bias through funnel plot asymmetry if at least 10 studies were included in subgroup analyses.

#### **Measures of treatment effect**

We anticipated that multiple scales would be used by studies measuring the same underlying constructs. We therefore used the standardised mean difference (SMD) approach and interpreted results as SMD throughout. Our analyses used the fixed-effect approach for all outcomes to provide a simple summary of available evidence.

We treated ADL data, such as the Barthel Index (BI), as continuous measures; we extracted, requested (from study authors), or calculated mean and standard deviation (SD) data. We are aware that there is a difference of opinion regarding how to deal with ordinal level ADL scales. We have treated them as interval level measures, as in practice this makes relatively little difference. This is supported by a study of parametric versus non-parametric methods in stroke trials, which recommended that means and SDs should be reported (Song 2005). We used intention-to-treat analyses when possible.

For all such analyses, we entered data so that a higher score represented a favourable outcome, and the right side of the graph favoured the experimental group. Some of the neglect assessment studies reported outcomes for which a low score was better; for example, for 'number of errors' in cancellation tests and 'line bisection'. In this case, we multiplied these outcomes by -1 to pool them with other neglect assessments for which the direction of effect was opposite.

We used odds ratios (ORs) categorical outcomes. For 'discharge destination', we considered the odds of being discharged to their

own homes. We treated deaths before discharge as 'not discharged to their own home'. We also calculated ORs for the outcome 'falls', comparing the number of participants experiencing at least one fall.

### Unit of analysis issues

As described above, we excluded cross-over trials from consideration as they were unable to assess our primary outcome of persisting differences in this context. When studies had repeated assessments of the same participant, we selected the measure immediately following intervention or, for persisting effect, the latest assessment between one and six months following scheduled completion of the intervention.

#### Dealing with missing data

If an included study did not record a particular outcome, we could not include that study in the analysis of that outcome.

If an included study had missing data (e.g. reported means but not standard deviations for follow-up data), we first tried to calculate this from other statistics (e.g. P value), or we requested the information from study authors. As a last resort, we imputed a value typically equal to the largest SD observed in other studies contributing this outcome.

#### **Assessment of heterogeneity**

We visually assessed heterogeneity by looking at the extent of overlap of the CIs on forest plots. We considered an I<sup>2</sup> statistic over 50% as evidence of substantial heterogeneity. In this case, we explored individual trial characteristics to generate hypotheses regarding potential sources of heterogeneity.

### **Assessment of reporting biases**

We attempted to minimise publication bias by using a comprehensive search strategy that included searching for unpublished studies and searching trials registers. When 10 or more trials contributed to a meta-analysis, we examined the funnel plot for any evidence of asymmetry.

#### **Data synthesis**

One review author (VL) entered the data into RevMan 5.4.1 (RevMan 2020), and another review author (AV) checked entries; we resolved any inconsistencies through discussion, with reference to the original report.

#### Subgroup analysis and investigation of heterogeneity

We re-structured the earlier review of cognitive rehabilitation approaches to separate comparisons for the eight categories of intervention.

- · Visual interventions.
- · Prism adaptation training.
- · Body awareness interventions.
- Mental function interventions.
- · Movement interventions.
- Non-invasive brain stimulation.
- Electrical stimulation.
- Acupuncture.



Within each of these comparisons, we stratified analyses when appropriate by nature of intervention, nature of control group, and a categorisation summarising overall risk of bias to explore likely sources of heterogeneity in the results. No subgroup analyses were planned.

### **Sensitivity analysis**

We planned to carry out sensitivity analyses to explore the effect of any imputation undertaken.

We then considered how results would have been changed if we had restricted eligibility to studies for which the size suggested a definitive phase 3 clinical trial, operationalised as allocating more than 50 participants to each intervention arm.

Finally, we considered how results would have been changed if we had restricted eligibility to those clearly at low risk of allocation bias and without clear evidence of high risk of bias in any other domain aside from blinding, which we believe would be impractical in this context.

# Summary of findings and assessment of the certainty of the evidence

We presented results of the main analyses for each comparison in 'Summary of findings' tables.

We summarised data for our primary outcome of interest (persisting effects on functional ability in activities of daily living),

the three secondary outcomes for which we identified the greatest volume of evidence (immediate effects on functional ability, persisting effects on neglect outcomes, immediate effects on neglect outcome), and any data related to adverse events.

For each of the outcomes, we assessed quality of the evidence using the GRADE approach (Guyatt 2011). One review author (VL) assessed quality of evidence, reported identified concerns, and applied downgrades. Other review authors (AB, AP, AV) checked agreement with these judgements and resolved any disagreements through discussion.

#### RESULTS

### **Description of studies**

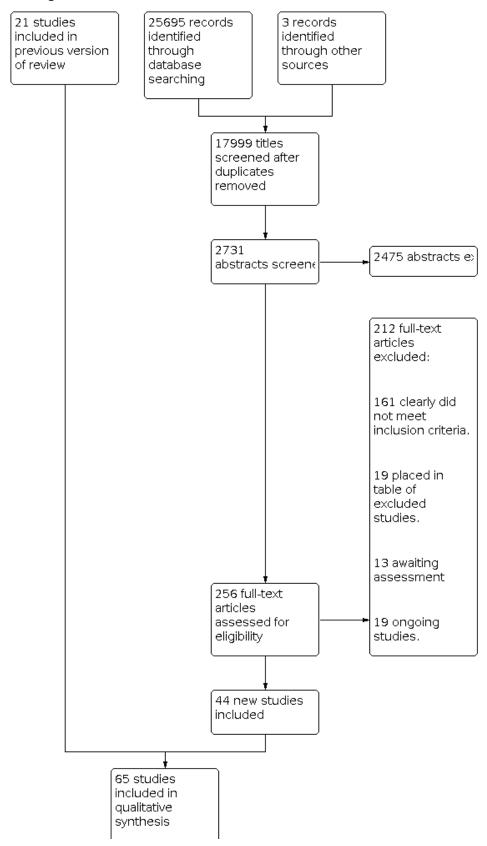
See Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification; and Characteristics of ongoing studies.

### Results of the search

Results of the search are shown in Figure 1. We identified 25,695 records through the database searches. One review author (VL or CJH) eliminated 15,269 irrelevant titles. Two (of VL, CM, CJH, CH, AB) review authors screened the remaining abstracts against our inclusion criteria and reviewed the full text of 256 studies. We identified 65 studies for inclusion. We also identified 19 ongoing studies (see Characteristics of ongoing studies) and 13 studies awaiting assessment (see Studies awaiting classification).

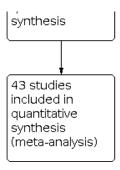


Figure 1. Study flow diagram.





### Figure 1. (Continued)



# **Included studies**

We included in this updated review 65 RCTs involving 1951 participants. Forty-four of these were newly identified studies (Aparicio-Lopez 2016; Bang 2015; Cazzoli 2012; Cha 2016; Choi 2016; Choi 2019; Dolkun 2019; Fong 2013; Fu 2017; Goedert 2020; Iwanski 2020; Karner 2019; Katz 2005; Kerkhoff 2014; Kim 2011; Kim 2013; Kim 2015; Kim 2018; Koch 2012; Kutlay 2018; Learmonth 2020; Li 2017; Machner 2012; Mancuso 2012; Nyfeller 2019; Pandian 2014; Park 2015; Park 2015b; Raghavan 2017; Rode 2015; Rossit 2019; Seniow 2016; Sesh 2018; Song 2009; Ten-Brink 2017; Van Wyk 2014; Varalta 2019; Vatanparasti 2019; Volkening 2016; Wilkinson 2014; Wu 2013; Yang 2015; Yang 2017; Yi 2016). The previous version of this review included 23 RCTs (Cherney 2002; Cottam 1987; Edmans 2000; Fanthome 1995; Ferreira 2011; Fong 2007; Kalra 1997; Kerkhoff 2012; Luukkainen-Markkula 2009; Mizuno 2011; Nys 2008; Polanowska 2009; Robertson 1990; Robertson 2002; Rusconi 2002; Schroder 2008; Tsang 2009; Turton 2010; Welfringer 2011; Wiart 1997; Zeloni 2002). We have excluded two of these studies from this update (Rossi 1990 Weinberg 1977); see Excluded studies for

Full descriptions of the included studies are presented in the Characteristics of included studies table. The table presents 72 entries due to the fact that three studies have multiple entries to enable comparisons when meta-analysis is conducted (Nyfeller 2019; Yang 2015; Yi 2016).

# **Populations studied**

All studies included people with spatial neglect after stroke. Whilst we expanded inclusion criteria for any type of brain injury, only one study also included a small number of non-stroke patients (Robertson 1990). It is unclear whether brain damage in Schroder 2008 was the result of stroke or of other brain injury.

Fifty-one of the 65 included studies included only participants with right hemisphere stroke. Seven included those with either left or right hemisphere lesions, although in each study, there were more people with right hemisphere lesions (Edmans 2000; Kalra 1997; Kutlay 2018; Pandian 2014; Robertson 1990; Ten-Brink 2017; Van Wyk 2014). The remaining seven studies are unclear on the side of the lesion (Bang 2015; Cha 2016; Choi 2019; Park 2015; Varalta 2019; Vatanparasti 2019; Yang 2015). We did not extract data on stroke severity.

# Sample size

All studies had small or extremely small sample sizes, with mean size of 30 participants and range from 4 to 69. Four studies had 10 or fewer participants (Cherney 2002; Ferreira 2011; Kerkhoff 2012;

Zeloni 2002); only eight studies had 50 or more participants (Dolkun 2019; Kalra 1997; Fong 2007; Kutlay 2018; Nyfeller 2019; Ten-Brink 2017; Wilkinson 2014; Yang 2017). No studies met our criterion of a large phase 3 trial (operationalised as allocating more than 50 participants to each intervention arm). Thirteen studies explicitly stated they were intended as pilot or feasibility studies (Cherney 2002; Fanthome 1995; Ferreira 2011; Fong 2013; Fu 2017; Kalra 1997; Learmonth 2020; Nys 2008; Rossit 2019; Turton 2010; Varalta 2019; Vatanparasti 2019; Welfringer 2011).

#### Interventions studied

A range of interventions were investigated (for full details, see Characteristics of included studies and TIDieR (TIDIER)). Fourteen studies explored two different types of interventions (Aparicio-Lopez 2016; Bang 2015; Choi 2019; Ferreira 2011; Fong 2007; Katz 2005; Kim 2018; Learmonth 2020; Luukkainen-Markkula 2009; Park 2015b; Rusconi 2002; Schroder 2008; Wu 2013; Yang 2017) (see Table 1).

#### **Visual interventions**

We identified 17 studies involving 398 participants that explored visual interventions. Two of these compared two different types of visual interventions (Kerkhoff 2012; Kerkhoff 2014), and participants in the intervention arm of Machner 2012 received two different visual interventions during the intervention period. All studies in this category had an underlying rationale to encourage eye scanning or eye movement using a variety of mechanisms. Interventions included visual scanning training (Cherney 2002; Cottam 1987; Ferreira 2011; Katz 2005; Kerkhoff 2012; Kerkhoff 2014; Luukkainen-Markkula 2009; Robertson 1990; Van Wyk 2014), half-field eye patching (Aparicio-Lopez 2016; Fong 2007; Machner 2012; Tsang 2009; Wu 2013; Zeloni 2002), optokinetic stimulation (Kerkhoff 2012; Machner 2012; Schroder 2008), eye movement feedback training (Fanthome 1995), and smooth pursuit eye movement training (Kerkhoff 2014). Studies used a range of methods, such as paper-based tasks (e.g. Cherney 2002), computerbased tasks (e.g. Kerkhoff 2014), and functional tasks (e.g. Van Wyk 2014).

Patients in every arm of seven studies received visual scanning training as an additional intervention (Iwanski 2020; Kim 2015; Polanowska 2009; Robertson 2002; Schroder 2008; Seniow 2016; Volkening 2016), and in one study, all patients received smooth pursuit eye movement training (Nyfeller 2019); therefore these studies were not considered under this comparison.



#### **Prism adaptation training**

Eight studies involving 257 participants explored prism adaptation training (Choi 2019; Goedert 2020; Mancuso 2012; Mizuno 2011; Nys 2008; Rode 2015; Ten-Brink 2017; Turton 2010). Patients in both arms of Vatanparasti 2019 received prism adaptation training; therefore this study was not considered under this comparison.

#### **Body awareness interventions**

We identified 12 studies involving 447 participants that aimed to cue awareness of the affected side of the body. Studies in this category focused on proprioception and awareness of the body in space or in relation to midline. Interventions included sensory cueing (Fong 2013; Kalra 1997; Karner 2019; Yang 2017), limb activation (Luukkainen-Markkula 2009; Robertson 2002), trunk rotation (Fong 2007; Wiart 1997), cueing and feedback (Edmans 2000), mirror therapy (Pandian 2014), neck taping (Varalta 2019), and a combination of visual, auditory, and sensory stimuli (Sesh 2018). Patients in both arms of Bang 2015 received mirror therapy; therefore this study was not considered under this comparison.

#### **Mental function interventions**

We identified seven studies involving 170 participants exploring interventions targeting mental functions, including mental imagery practice (Ferreira 2011; Park 2015; Park 2015b; Welfringer 2011), virtual reality training (Katz 2005; Kim 2011), and general cognitive rehabilitation without a specific visual search focus (Rusconi 2002). All participants in Aparicio-Lopez 2016 received general cognitive rehabilitation; therefore this study was not considered under this comparison.

#### **Movement interventions**

Six studies involving 220 participants explored interventions that used movement of the upper limb or of the whole body to treat neglect. These studies used methods different from those focused on body awareness and included a robotic upper limb treatment (Choi 2016; Kim 2018), a robotic kinaesthetic ability training programme (Kutlay 2018), constraint-induced movement therapy (Wu 2013), and visuomotor feedback training (Learmonth 2020; Rossit 2019).

### Non-invasive brain stimulation (NIBS)

Seventeen studies involving 467 participants explored NIBS. Six of these explored a variety of doses of NIBS (Fu 2017; Kim 2013; Kim 2015; Nyfeller 2019; Yang 2015; Yi 2016), whereas the other 11 did not explore different doses within each study. We identified studies using different stimulation protocols: repetitive transcranial magnetic stimulation (rTMS) (Cha 2016; Iwanski 2020; Kim 2013; Kim 2015; Kim 2018; Raghavan 2017; Song 2009; Yang 2015; Yang 2017), including inhibitory continuous theta burst stimulation (TBS) (Cazzoli 2012; Fu 2017; Koch 2012; Nyfeller 2019; Vatanparasti 2019), and transcranial direct current stimulation tDCS (Bang 2015; Learmonth 2020; Yi 2016).

# **Electrical stimulation**

Eight studies involving 270 participants explored electrical stimulation. One of these explored different doses of the same type of intervention (Wilkinson 2014). Studies used transcutaneous electrical nerve stimulation (TENS) (Polanowska 2009; Schroder 2008; Seniow 2016), galvanic vestibular stimulation (GVS) (Volkening 2016; Wilkinson 2014), functional electrical

stimulation (FES) (Choi 2019; Rusconi 2002), or electromyogram-triggered electrical stimulation (Park 2015b).

#### **Acupuncture**

Two studies involving 104 participants explored acupuncture on specific points as treatment for neglect (Dolkun 2019; Li 2017).

#### Dose of interventions

The nature of the intervention was usually well described, as were the number, frequency, and duration of therapy sessions. The number of sessions varied from one in Choi 2019 to 40 in Rusconi 2002 over a duration of 1 day to 12 weeks. Sessions ranged from 10 times a day to once a week and lasted from 5 minutes to constant application of a wearable device for the entire intervention period. See TIDIER for details.

#### **Comparisons**

Table 1 summarises the interventions delivered in each study alongside the control intervention.

#### **Outcomes**

Table 2 summarises relevant outcome measures used in the included studies and highlights which studies yielded data suitable for inclusion in our meta-analysis.

# **Measures of functional ability**

Fifty-two of the 65 included studies measured functional ability using an 'activities of daily living' scale. Eighteen used the Catherine Bergego Scale (CBS) (Aparicio-Lopez 2016; Cazzoli 2012; Choi 2016; Choi 2019; Goedert 2020; Kim 2011; Kim 2013; Kim 2018; Luukkainen-Markkula 2009; Machner 2012; Mizuno 2011; Nyfeller 2019; Park 2015b; Ten-Brink 2017; Turton 2010; Wu 2013; Yang 2017; Yi 2016); 11 the Functional Independence Measure (FIM) (Ferreira 2011; Fong 2007; Fong 2013; Iwanski 2020; Kutlay 2018; Mizuno 2011; Nyfeller 2019; Pandian 2014; Rode 2015; Tsang 2009; Wiart 1997); 11 the Barthel Index (BI) (Bang 2015; Dolkun 2019; Edmans 2000; Kalra 1997; Li 2017; Nys 2008; Polanowska 2009; Robertson 2002; Rusconi 2002; Van Wyk 2014; Wilkinson 2014); 3 the modified Rankin Scale (Pandian 2014; Sesh 2018; Vatanparasti 2019); and 1 the Frenchay Activities Index (Robertson 1990). The remaining 6 studies reported measures not listed in our protocol: Stroke Impact Scale (Learmonth 2020; Rossit 2019); Unawareness and Behavioural Neglect Index (Kerkhoff 2014); scores on Independence Index for Neurological and Geriatric Rehabilitation (SINGER) (Karner 2019); stroke-specific quality of life scale (Raghavan 2017); and unspecified measures of ADL (Katz

Only 16 studies reported ADL outcomes at least one month post intervention (persisting effects) - our primary outcome of interest (Ferreira 2011; Fong 2007; Goedert 2020; Iwanski 2020; Learmonth 2020; Machner 2012; Pandian 2014; Raghavan 2017; Robertson 2002; Rode 2015; Rossit 2019; Sesh 2018; Turton 2010; Wiart 1997; Wilkinson 2014; Yang 2017).

Kalra 1997, Mizuno 2011, and Tsang 2009 recorded ADL outcomes at the time of hospital discharge, rather than at a set time following completion of the intervention; we omitted these data from meta-analysis, as the time of discharge itself would depend on the participant's recovery.



#### Standardised neglect assessments

All but 2 of the 65 included studies reported a standardised assessment of spatial neglect (Kerkhoff 2014; Wu 2013). Forty-six studies used target cancellation, 35 used line bisection, and 32 used both measures. Ten studies reported neglect assessments that were not our chosen secondary outcomes. Twenty-three studies reported neglect outcomes at least one month post intervention. One study provided data for persisting effect at follow-up but not immediately after treatment (Cottam 1987). Two studies recorded neglect outcomes at the time of hospital discharge (Mizuno 2011; Tsang 2009); we omitted these from meta-analysis as described above.

# Other secondary outcomes

One study reported discharge destination (Kalra 1997). Two studies measured depression using the Beck Depression Inventory (Learmonth 2020; Luukkainen-Markkula 2009), but only Learmonth 2020 provided data post intervention. Five studies recorded adverse events (Choi 2016; Edmans 2000; Ferreira 2011; Kalra 1997; Learmonth 2020). No other relevant outcome data (i.e. falls, balance, quality of life) were reported.

#### **Excluded studies**

We excluded 212 papers after assessment of the full paper in this update (see Figure 1). Of these, 161 clearly did not meet the inclusion criteria. Nineteen of the 212 papers required more indepth appraisal prior to exclusion; we have provided our reasons for exclusion of these studies, as well as those excluded from previous versions of this review, in the Characteristics of excluded studies table. We excluded most of these because the study was not randomised, or because the intervention was not specifically targeted at neglect.

We excluded two studies that were included in previous versions of this review. We excluded Rossi 1990 because less than 50% of participants had neglect. We excluded Weinberg 1977 because we believe participants did not necessarily have neglect but we were unable to obtain clarification due to the age of the study.

#### Risk of bias in included studies

Information on risk of bias is provided in the Characteristics of included studies table and is summarised in Figure 2 and Figure 3. Risk of bias for Nyfeller 2019 Yang 2015 and Yi 2016 is also presented under Nyfeller 2019 16c TBS Yang 2015 10Hz and Yi 2016 anodal to enable presentation of risk of bias in forest plots. We judged only two studies to be entirely at low risk of bias (Rode 2015; Wilkinson 2014).



Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

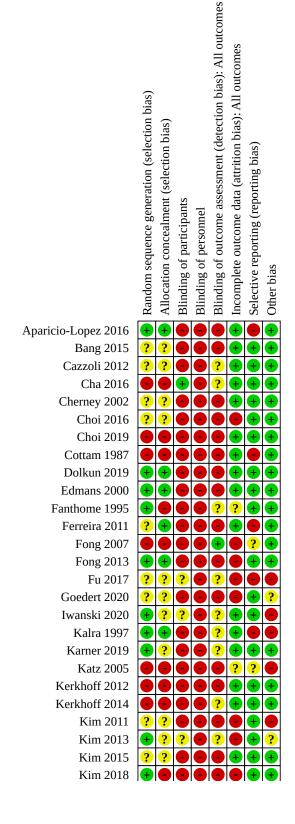




Figure 2. (Continued)

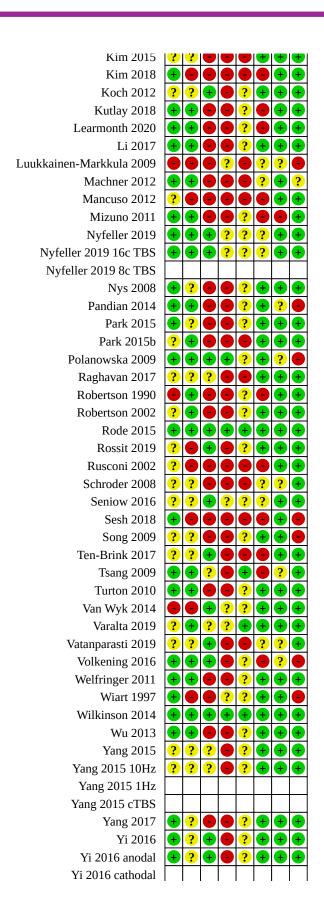


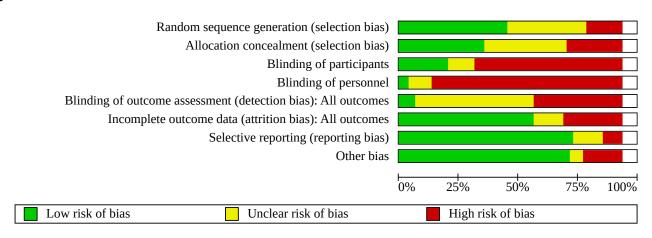


Figure 2. (Continued)





Figure 3.



### Allocation

We assessed 24 of the included RCTs as having low risk of bias with adequate allocation and concealment (Aparicio-Lopez 2016; Dolkun 2019; Edmans 2000; Ferreira 2011; Fong 2013; Kalra 1997; Kutlay 2018; Learmonth 2020; Li 2017; Machner 2012; Mizuno 2011; Nyfeller 2019; Pandian 2014; Park 2015b; Polanowska 2009; Robertson 1990; Robertson 2002; Rode 2015; Tsang 2009; Turton 2010; Volkening 2016; Welfringer 2011; Wilkinson 2014; Wu 2013). Twenty-three studies provided insufficient details for determining adequacy of the allocation process or its concealment without clearly being at high risk in either regard (Bang 2015; Cazzoli 2012; Cherney 2002; Choi 2016; Fu 2017; Goedert 2020; Iwanski 2020; Karner 2019; Kim 2011; Kim 2013; Kim 2015; Koch 2012; Nys 2008; Park 2015; Raghavan 2017; Schroder 2008; Seniow 2016; Song 2009; Ten-Brink 2017; Vatanparasti 2019; Yang 2015; Yang 2017; Yi 2016). The remaining 18 studies reported methods of allocation or concealment that we assessed to be at high risk of bias.

# Blinding

We assessed five of the included RCTs to have adequate blinding of outcome assessors (Fong 2007; Rode 2015; Tsang 2009; Varalta 2019; Wilkinson 2014). This information was unclear for 33 studies (Cazzoli 2012; Cha 2016; Fanthome 1995; Fu 2017; Iwanski 2020; Kalra 1997; Karner 2019; Kerkhoff 2014; Kim 2013; Koch 2012; Kutlay 2018; Learmonth 2020; Li 2017; Mizuno 2011; Nyfeller 2019; Nys 2008; Pandian 2014; Park 2015; Polanowska 2009; Robertson 1990; Robertson 2002; Rossit 2019; Seniow 2016; Song 2009; Turton 2010; Van Wyk 2014; Volkening 2016; Welfringer 2011; Wiart 1997; Wu 2013; Yang 2015; Yang 2017; Yi 2016), and we judged the remaining 27 studies to be at high risk of bias due to not having a blinded outcome assessor or because blinding was not possible.

#### Incomplete outcome data

We assessed 39 of the included RCTs as having low risk of bias arising from incomplete outcome data (Aparicio-Lopez 2016; Bang 2015; Cazzoli 2012; Cha 2016; Cherney 2002; Choi 2019; Cottam 1987; Dolkun 2019; Edmans 2000; Ferreira 2011; Iwanski 2020; Kalra 1997; Karner 2019; Kerkhoff 2012; Kerkhoff 2014; Kim 2015; Koch 2012; Li 2017; Nys 2008; Pandian 2014; Park 2015; Park 2015b; Polanowska 2009; Raghavan 2017; Robertson 2002; Rode 2015; Rossit 2019; Song 2009; Turton 2010; Van Wyk 2014; Varalta 2019; Welfringer 2011; Wiart 1997; Wilkinson 2014; Wu 2013; Yang 2015; Yang 2017; Yi 2016; Zeloni 2002). Eighteen were assessed to be at high risk of bias due to incomplete outcome data (Choi 2016; Fong 2007; Fong 2013; Fu 2017; Goedert 2020; Kim 2011; Kim 2013; Kim 2018; Kutlay 2018; Learmonth 2020; Mancuso 2012; Mizuno 2011; Robertson 1990; Rusconi 2002; Sesh 2018; Ten-Brink 2017; Tsang 2009; Volkening 2016), for example, due to omission of baseline data for dropouts in Choi 2016 and loss of 45% of the control group prior to follow-up in Fong 2013. Insufficient information was available for assessment of the remaining eight studies

### **Selective reporting**

We assessed 50 of the included RCTs to be free of reporting bias. Six had some selective reporting (Aparicio-Lopez 2016; Cottam 1987; Ferreira 2011; Fu 2017; Kalra 1997; Mizuno 2011), for example, they reported subscales to differing levels of detail. For nine studies, this information was unclear (Fong 2007; Katz 2005; Luukkainen-Markkula 2009; Pandian 2014; Polanowska 2009; Schroder 2008; Tsang 2009; Vatanparasti 2019; Volkening 2016).

### Other potential sources of bias

We assessed 49 studies to be free from other potential sources of bias. For 12 studies, we identified some other source of potential bias mainly due to unadjusted baseline differences between



groups (Fu 2017; Iwanski 2020; Kalra 1997; Katz 2005; Kim 2011; Luukkainen-Markkula 2009; Pandian 2014; Polanowska 2009; Sesh 2018; Song 2009; Volkening 2016; Wiart 1997); for four studies, other potential sources of bias were unclear (Goedert 2020; Kim 2013; Machner 2012; Zeloni 2002).

### **Effects of interventions**

See: Summary of findings 1 Visual interventions compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury; Summary of findings 2 Prism adaptation training compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury; Summary of findings 3 Body awareness interventions compared to any control for spatial neglect or inattention following stroke and other adultacquired non-progressive brain injury; Summary of findings 4 Mental function interventions compared to any control for spatial neglect or inattention following stroke and other adultacquired non-progressive brain injury; Summary of findings 5 Movement interventions compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury; Summary of findings 6 NIBS compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury; Summary of findings 7 Electrical stimulation compared to any control for spatial neglect or inattention following stroke and other adult-acquired non-progressive brain injury; Summary of findings 8 Acupuncture compared to any control for spatial neglect or inattention following stroke and other adult-acquired nonprogressive brain injury

#### Studies included in meta-analysis within this review

From the 65 studies included in this review, 43 were included in meta-analysis.

### Studies not included in meta-analysis within this review

Twenty-two studies were not included in meta-analysis. Nine studies compared multiple different active treatments with no control (Ferreira 2011; Katz 2005; Kerkhoff 2012; Kerkhoff 2014; Kim 2015; Luukkainen-Markkula 2009; Park 2015b; Schroder 2008; Wilkinson 2014). We included data from head-to-head comparisons in multi-arm studies in Table 3. Seven studies included no usable data in the published paper, and we were unable to obtain further data (Cazzoli 2012; Fu 2017; Rode 2015; Rusconi 2002; Seniow 2016; Van Wyk 2014; Volkening 2016). Six studies reported change from baseline data for only for outcomes, and we did not obtain raw scores (Ferreira 2011; Kim 2013; Koch 2012; Learmonth 2020; Pandian 2014; Tsang 2009). These studies are presented in Table 4 and are not included in meta-analysis.

### Visual interventions versus any control

# Ratings on measures of functional ability in ADL: persisting effects

Two studies (55 participants) provided usable data for a measure of ADL persisting for at least one month after completion of rehabilitation, one with the Catherine Bergego Scale (CBS) (Machner 2012), the other with the Functional Independence Measure (FIM) (Fong 2007).

Results were consistent ( $I^2 = 0\%$ ), with no evidence of benefit or detriment from intervention (standardised mean difference (SMD) -0.04, 95% confidence interval (CI) -0.57 to 0.49; very low-certainty evidence; Analysis 1.1).

# Ratings on measures of functional ability in ADL: immediate effects

Three studies (75 participants) provided usable data for a measure of ADL immediately after completion of rehabilitation, two with the CBS (Machner 2012; Wu 2013), one with the FIM (Fong 2007).

Results were consistent ( $I^2 = 0\%$ ), with no evidence of benefit or detriment from intervention (SMD -0.15, 95% CI -0.60 to 0.30; very low-certainty evidence; Analysis 1.2).

# Performance on standardised neglect assessment: persisting effects

Five studies (98 participants) provided usable data for a measure of neglect persisting for at least one month after completion of rehabilitation, two with target cancellation (Cottam 1987; Machner 2012), three with the Behavioural Inattention Test (BIT) behavioural subtest (Fanthome 1995; Fong 2007; Robertson 1990).

Results were consistent ( $I^2 = 0\%$ ), with no evidence of benefit or detriment from intervention (SMD 0.07, 95% CI -0.33 to 0.48; very low-certainty evidence; Analysis 1.3).

# Performance on standardised neglect assessment: immediate effects

Seven studies (142 participants) provided usable data for a measure of neglect immediately after completion of rehabilitation, three with target cancellation (Fanthome 1995; Machner 2012; Zeloni 2002), one with line bisection (Aparicio-Lopez 2016), and three with the BIT behavioural subtest (Cherney 2002; Fong 2007; Robertson 1990)

Results were consistent ( $I^2 = 0\%$ ), with no evidence of benefit or detriment from intervention (SMD 0.08, 95% CI -0.26 to 0.42; very low-certainty evidence; Analysis 1.4).

No studies of this intervention recorded other outcomes specified for this review.

### Prism adaptation training versus any control

# Ratings on measures of functional ability in ADL: persisting effects

Two studies (39 participants) provided usable data for a measure of ADL persisting for at least one month after completion of rehabilitation, both using the CBS (Goedert 2020; Turton 2010).

Results were consistent ( $I^2 = 0\%$ ), with no evidence of benefit or detriment from intervention (SMD -0.29, 95% CI -0.93 to 0.35; very low-certainty evidence; Analysis 2.1).

# Ratings on measures of functional ability in ADL: immediate effects

Five studies (158 participants) provided usable data for a measure of ADL immediately after completion of rehabilitation, all with the CBS (Choi 2019; Goedert 2020; Mizuno 2011; Ten-Brink 2017; Turton 2010).



Results were consistent ( $I^2 = 0\%$ ), with no evidence of benefit or detriment from intervention (SMD 0.20, 95% CI -0.12 to 0.51; very low-certainty evidence; Analysis 2.2).

# Performance on standardised neglect assessment: persisting effects

One study (16 participants) provided usable data for a measure of neglect persisting for at least one month after completion of rehabilitation, with target cancellation (Nys 2008).

There was no evidence of benefit or detriment from intervention (SMD 0.05, 95% CI -0.96 to 1.06; very low-certainty evidence; Analysis 2.3).

# Performance on standardised neglect assessment: immediate effects

Five studies (154 participants) provided usable data for a measure of neglect immediately after completion of rehabilitation, four with target cancellation (Choi 2019; Mancuso 2012; Nys 2008; Ten-Brink 2017), one with the BIT behavioural subtest (Mizuno 2011).

Results were not consistent ( $I^2 = 66\%$ ), with no evidence of benefit or detriment from intervention (SMD 0.28, 95% CI -0.05 to 0.60; very low-certainty evidence; Analysis 2.4).

No studies of this intervention recorded other outcomes specified for this review.

#### Body awareness interventions versus any control

# Ratings on measures of functional ability in ADL: persisting effects

Five studies (125 participants) provided usable data for a measure of ADL persisting for at least one month after completion of rehabilitation, two with the CBS (Robertson 2002; Yang 2017), two with the FIM (Fong 2007; Wiart 1997), and one with the modified Rankin Scale (mRS) (Sesh 2018).

Results were consistent ( $I^2 = 11\%$ ) and suggested possible benefit from intervention (SMD 0.61, 95% CI 0.24 to 0.97; very low-certainty evidence; ,Analysis 3.1). The only studies reporting possible benefit were at high or unclear risk of bias for allocation of participants.

# Ratings on measures of functional ability in ADL: immediate effects

Seven studies (221 participants) provided usable data for a measure of ADL immediately after completion of rehabilitation, two with the CBS (Robertson 2002; Yang 2017), one with the Barthel Index (BI) (Edmans 2000), one with the FIM (Fong 2007; Fong 2013; Wiart 1997), and one with the mRS (Sesh 2018).

Results were not consistent ( $I^2 = 51\%$ ), with no evidence of benefit or detriment from intervention (SMD 0.26, 95% CI -0.01 to 0.53; very low-certainty evidence; Analysis 3.2).

# Performance on standardised neglect assessment: persisting effects

Five studies (125 participants) provided usable data for a measure of neglect persisting for at least one month after completion of rehabilitation, two with target cancellation (Sesh 2018; Yang 2017), one with line bisection (Wiart 1997), and two with the BIT behavioural subtest (Fong 2007; Robertson 2002).

Results were a little consistent ( $I^2 = 41\%$ ) and suggested possible benefit from intervention (SMD 0.36, 95% CI 0.00 to 0.72; very low-certainty evidence; Analysis 3.3). The only studies reporting possible benefit were at high or unclear risk of bias for allocation of participants or outcome assessor blinding.

Pandian 2014 (46 participants) reported change from baseline data only (see Table 4) and provided results consistent with the above.

# Performance on standardised neglect assessment: immediate effects

Ten studies (311 participants) provided usable data for a measure of neglect immediately after completion of rehabilitation, seven with target cancellation (Edmans 2000; Fong 2013; Kalra 1997; Karner 2019; Sesh 2018; Varalta 2019; Yang 2017), one with line bisection (Wiart 1997), and two with the BIT behavioural subtest (Fong 2007; Robertson 2002).

Results were a little consistent ( $I^2 = 47\%$ ), with no evidence of benefit or detriment from intervention (SMD 0.16, 95% CI -0.07 to 0.39; very low-certainty evidence; Analysis 3.4).

Pandian 2014 (46 participants) reported change from baseline data only (see Table 4) and provided results not consistent with the above.

### Discharge destination

One study (50 participants) investigated discharge destination as an outcome (Kalra 1997). There was no evidence of benefit or detriment from intervention (odds ratio (OR) 1.4, 95% CI 0.45 to 4.4; very low-certainty evidence; Analysis 3.5).

#### Adverse events

Two studies (130 participants) recorded adverse events. Edmans 2000 reported one death in the control group; Kalra 1997 reported one death in the intervention group and two in the control group. Results were consistent ( $I^2 = 0\%$ ), with no evidence of benefit or detriment from intervention (OR 0.36, 95% CI 0.05 to 2.6; very low-certainty evidence; Analysis 3.6).

No studies of this intervention recorded other outcomes specified for this review.

### Mental function interventions versus any control

# Ratings on measures of functional ability in ADL: persisting effects

No studies of this intervention recorded this outcome.

# Ratings on measures of functional ability in ADL: immediate effects

One study (24 participants) provided usable data for a measure of ADL immediately after completion of rehabilitation, using the CBS (Kim 2011).

There was no evidence of benefit or detriment from intervention (SMD 0.32, 95% CI -0.49 to 1.12; very low-certainty evidence; Analysis 4.2).



# Performance on standardised neglect assessment: persisting effects

No studies of this intervention recorded this outcome.

# Performance on standardised neglect assessment: immediate effects

Three studies (60 participants) provided usable data for a measure of neglect immediately after completion of rehabilitation, all with target cancellation (Kim 2011; Park 2015; Welfringer 2011).

Results were consistent ( $I^2 = 0\%$ ), with no evidence of benefit or detriment from intervention (SMD 0.10, 95% CI -0.32 to 0.53; very low-certainty evidence; Analysis 4.4).

No studies of this intervention recorded other outcomes specified for this review.

#### Movement interventions versus any control

# Ratings on measures of functional ability in ADL: persisting effects

No studies of this intervention recorded this outcome.

# Ratings on measures of functional ability in ADL: immediate effects

Three studies (75 participants) provided usable data for a measure of ADL immediately after completion of rehabilitation, all with the CBS (Choi 2016; Kim 2018; Wu 2013).

Results were a little consistent (I<sup>2</sup> = 46%) and suggested possible benefit from intervention (SMD 0.57, 95% CI 0.09 to 1.04; very low-certainty evidence; Analysis 5.2). The only studies reporting possible benefit were at high risk of bias for allocation of participants or outcome assessor blinding.

Kutlay 2018 (52 participants) provided change from baseline data only (see Table 4) and reported results consistent with the above.

# Performance on standardised neglect assessment: persisting

No studies of this intervention recorded this outcome.

# Performance on standardised neglect assessment: immediate offices

Two studies (58 participants) provided usable data for a measure of neglect persisting for at least one month after completion of rehabilitation, both with target cancellation (Choi 2016; Kim 2018).

Results were consistent ( $I^2 = 0\%$ ) and suggested possible benefit from intervention (SMD 0.57, 95% CI 0.04 to 1.10; very low-certainty evidence; Analysis 5.4). The only studies reporting possible benefit were at high risk of bias for allocation of participants and outcome assessor blinding.

Kutlay 2018 (52 participants) provided change from baseline data only (see Table 4) and reported results consistent with the above..

#### Adverse events

One study recorded adverse events (Choi 2016); none were reported.

No studies of this intervention recorded other outcomes specified for this review.

#### Non-invasive brain stimulation versus any control

# Ratings on measures of functional ability in ADL: persisting effects

Three studies (92 participants) provided usable data for a measure of ADL persisting for at least one month after completion of rehabilitation, two with the CBS (Nyfeller 2019; Yang 2017), one with the FIM (Iwanski 2020).

Results were a little inconsistent ( $I^2 = 21\%$ ), with no evidence of benefit or detriment from intervention (SMD 0.35, 95% CI -0.08 to 0.77; very low-certainty evidence; Analysis 6.1).

# Ratings on measures of functional ability in ADL: immediate effects

Six studies (160 participants) provided usable data for a measure of ADL immediately after completion of rehabilitation, four with the CBS (Kim 2018; Nyfeller 2019; Yang 2017; Yi 2016), one with the FIM (Iwanski 2020), and one with the BI (Bang 2015).

Results were a little inconsistent ( $I^2 = 28\%$ ) and suggested possible benefit from intervention (SMD 0.61, 95% CI 0.27 to 0.94; very low-certainty evidence; Analysis 6.2). In particular, the estimate of effect size from Bang 2015 appears implausible for a clinical outcome and may be a reporting error.

Kim 2013 (27 participants) provided change from baseline data only (see Table 4) but found no evidence of benefit of non-invasive brain stimulation (NIBS).

# Performance on standardised neglect assessment: persisting effects

Three studies (102 participants) provided usable data for a measure of neglect persisting for at least one month after completion of rehabilitation, two with target cancellation (Yang 2015; Yang 2017), one with the BIT behavioural subtest (Iwanski 2020).

Results were not consistent ( $I^2 = 89\%$ ) and suggested possible benefit from intervention (SMD 0.77, 95% CI 0.29 to 1.24; very low-certainty evidence; Analysis 6.3). In particular, estimated effect sizes from Yang 2015 appear implausible for a clinical outcome and may reflect a reporting error.

# Performance on standardised neglect assessment: immediate effects

Ten studies (244 participants) provided usable data for a measure of neglect immediately after completion of rehabilitation, seven with target cancellation (Kim 2018; Koch 2012; Song 2009; Vatanparasti 2019; Yang 2015; Yang 2017; Yi 2016), two with line bisection (Bang 2015; Cha 2016), and one with the BIT behavioural subtest (Iwanski 2020).

Results were not consistent (I<sup>2</sup> = 79%) and suggested possible benefit from intervention (SMD 0.75, 95% CI 0.47 to 1.04; very low-certainty evidence;.Analysis 6.4). In particular, estimated effect sizes from Yang 2015 and Cha 2016 appear implausible for a clinical outcome and may reflect a reporting error.



Kim 2013 (27 participants) provided change from baseline data only (see Table 4) but found no evidence of benefit of NIBS.

#### Adverse events

One study recorded serious adverse events. Learmonth 2020 reported four deaths, one per group, all of which were deemed to be unrelated to the intervention.

No studies of this intervention recorded other outcomes specified for this review.

### Electrical stimulation versus any control

# Ratings on measures of functional ability in ADL: persisting effects

No studies of this intervention recorded this outcome.

# Ratings on measures of functional ability in ADL: immediate effects

No studies of this intervention recorded this outcome.

# Performance on standardised neglect assessment: persisting effects

No studies of this intervention recorded this outcome.

# Performance on standardised neglect assessment: immediate effects

Two studies (60 participants) provided usable data for a measure of neglect immediately after completion of rehabilitation, both with target cancellation (Choi 2019; Polanowska 2009).

Results were consistent ( $I^2 = 0\%$ ) and suggested possible benefit from intervention (SMD 0.99, 95% CI 0.44 to 1.53; very low-certainty evidence; Analysis 7.4). One study reporting possible benefit was at high risk of bias for allocation of participants and outcome assessor blinding.

No studies of this intervention recorded other outcomes specified for this review.

# **Acupuncture versus any control**

# Ratings on measures of functional ability in ADL: persisting effects

No studies of this intervention recorded this outcome.

# Ratings on measures of functional ability in ADL: immediate effects

Two studies (104 participants) provided usable data for a measure of ADL immediately after completion of rehabilitation, both with the BI (Dolkun 2019; Li 2017).

Results were consistent ( $I^2 = 0\%$ ) and suggested possible benefit from intervention (SMD 0.65, 95% CI 0.26 to 1.05; very low-certainty evidence; Analysis 8.2). These studies were at high risk of bias for blinding.

# Performance on standardised neglect assessment: persisting

No studies of this intervention recorded this outcome.

# Performance on standardised neglect assessment: immediate effects

Two studies (104 participants) provided usable data for a measure of neglect immediately after completion of rehabilitation, one with target cancellation (Dolkun 2019), one with line bisection (Li 2017).

Results were consistent ( $I^2 = 0\%$ ) and suggested possible benefit from intervention (SMD 0.57, 95% CI 0.18 to 0.97; very low-certainty evidence; Analysis 8.4). These studies were at high risk of bias for blinding.

#### Sensitivity analyses

No study met our first criterion for conducting sensitivity analyses of sample size suggestive of a definitive clinical trial (more than 50 participants per intervention arm). Nine studies met our second criterion - low risk of allocation bias without clear evidence of high risk of bias in any other domain aside from blinding (Dolkun 2019; Edmans 2000; Nyfeller 2019; Rode 2015; Turton 2010; Welfringer 2011; Wilkinson 2014; Wu 2013; Yi 2016). Neither Rode 2015 nor Wilkinson 2014 contributed data to our meta-analyses, leaving seven 'lower-risk' studies for consideration. Restricting analyses to these seven studies did not alter our overall conclusions, as each reached the same broad conclusion or estimated similar effect sizes as the meta-analyses to which they contributed data.

#### DISCUSSION

In this updated version of the review, we included 44 new randomised controlled trials (RCTs), bringing the total to 65 trials (1951 participants).

### **Summary of main results**

#### Visual interventions versus any control

We found very low-certainty evidence suggesting there may be no benefit or detriment of visual interventions based on measures of persisting functional ability in activities of daily living (ADL) (2 studies, 55 participants); immediate functional ability in ADL (3 studies, 75 participants); persisting standardised neglect assessments (5 studies, 98 participants); and immediate neglect assessments (7 studies, 142 participants).

### Prism adaptation training versus any control

We found very low-certainty evidence suggesting there may be no benefit or detriment of prism adaptation training based on measures of persisting functional ability in ADL (2 studies, 39 participants); and immediate functional ability in ADL (5 studies, 158 participants); nor on persisting standardised neglect assessments (1 study, 16 participants) or immediate neglect assessments (5 studies, 154 participants).

### Body awareness interventions versus any control

We found very low-certainty evidence suggesting there may be benefit from body awareness interventions based on measures of persisting functional ability in ADL (5 studies, 125 participants). In addition to the very small number of participants, not one of these studies reported an adequate allocation process. We similarly found very low-quality evidence from the same studies suggesting there may be benefit based on persisting standardised neglect assessments. There was also marked clinical heterogeneity, with a range of different interventions delivered in these studies.



We found very low-certainty evidence suggesting there may be no benefit or detriment of body awareness interventions based on immediate functional ability in ADL (7 studies, 221 participants) nor on immediate neglect assessments (eleven studies, 357 participants).

### Mental function interventions versus any control

We found no evidence suggesting there may be benefit or detriment of mental function interventions based on measures of persisting functional ability in ADL or on neglect assessments. We found very low-quality evidence suggesting there may be no benefit or detriment of mental function interventions on measures of immediate functional ability in ADL (1 study, 24 participants) nor on immediate neglect assessments (3 studies, 60 participants).

#### Movement interventions versus any control

We found no evidence suggesting there may be benefit or detriment of movement interventions based on measures of persisting functional ability in ADL or on neglect assessments. We found very low-quality evidence suggesting there may be benefit of movement interventions based on measures of immediate functional ability in ADL (3 studies, 75 participants); we similarly found very low-quality evidence suggesting there may be benefit based on immediate neglect assessments (2 studies, 58 participants).

### Non-invasive brain stimulation versus any control

We found very low-certainty evidence suggesting there may be no benefit nor detriment of NIBS based on measures of persisting functional ability in ADL (3 studies, 92 participants). In addition to the very small number of participants, we were concerned about risk of bias in two studies that delivered different types of NIBS. We found very low-quality evidence suggesting there may be benefit from NIBS based on immediate functional ability in ADL (6 studies, 160 participants). We found very low-quality evidence suggesting there may be benefit of NIBS based on persisting standardised neglect assessments (3 studies, 102 participants) or on immediate neglect assessments (10 studies, 244 participants). We had concerns about the accuracy of data reported in three studies included in these analyses.

### **Electrical stimulation versus any control**

We found no evidence suggesting there may be benefit or detriment of electrical stimulation based on measures of persisting functional ability in ADL or neglect assessments, or on immediate functional ability in ADL. We found very low-quality evidence suggesting there may be benefit from electrical stimulation based on immediate neglect assessments (2 studies, 60 participants). In addition to the very small number of participants, these studies were at high risk of bias and explored different types of stimulation.

### **Acupuncture versus any control**

We found no evidence suggesting there may be benefit or detriment of acupuncture based on measures of persisting functional ability in ADL or neglect assessments. We found very low-quality evidence suggesting there may be benefit from acupuncture based on measures of immediate functional ability in ADL and immediate neglect assessments (2 studies, 104 participants). In addition to the very small number of participants, these studies were judged to be at high risk of bias for blinding.

### Key findings from this updated review

- Sixty-five RCTs (1951 participants) evaluated a range of eight types of non-pharmacological interventions for people with neglect after adult-acquired brain injury, all of which included stroke survivors. Most studies measured outcomes using standardised neglect assessments. Many reported immediate effects on ADL, but few reported persisting effects on functional ability in ADL over one month. We acknowledge and welcome an increase in use of persisting ADL assessments since the previous version of this review. Other meaningful outcomes such as discharge destination, falls, mood, quality of life, and adverse events were rarely or never reported
- Methodological quality was generally poor or poorly described, and sample sizes were universally underpowered to detect plausible and important clinical effects. Some were explicitly reported as feasibility or pilot studies, but none has yet resulted in the publication of a moderately sized or large trial
- Interventions were generally well described, and trialists were helpful in providing additional unpublished methodological details. We were able to describe many of the interventions using the Template for Intervention Description and Replication (TIDieR)
- Very low-quality evidence suggests that certain types of interventions may have persisting benefit based on functional ability in ADL and neglect severity (body awareness interventions, based on 5 studies; NIBS, based on 10 studies; movement interventions, based on 3 studies; electrical stimulation, based on 2 studies; acupuncture, based on 2 studies). These types of interventions may warrant prioritisation for further research focus but would benefit from further feasibility/pilot trials, with strong patient and public involvement, before proceeding to costly definitive RCTs
- Despite 65 completed studies, evidence remains insufficient to permit conclusions about the clinical effects of any non-pharmacological interventions for patients with spatial neglect, because as yet, no adequately powered, appropriately designed trials have been undertaken to answer these important questions. Further research must ensure adequate sample size, minimise risk of bias, and evaluate outcomes of importance to patients
- We found no reports of patient and public involvement in any included study

# Overall completeness and applicability of evidence

#### **Methods**

All studies had small underpowered samples, limiting our ability to make generalisations. We observed no trends in sample size over years, with most studies failing to address issues of statistical power. Available studies should provide sufficient data to enable power calculations for future studies, and we urge researchers to design appropriately powered studies.

Authors of both included and excluded studies were helpful in providing unpublished data. This review therefore presents a considerable quantity of unpublished data and previously unpublished clarification of methods used by the original authors. In contrast to problems of methodological reporting, the reporting quality of the rehabilitation approach used has generally improved since the last version of this review.



### **Participants**

Almost all participants in the included studies had right hemisphere stroke, and most studies were completed in inpatient settings. Therefore, it is appropriate to generalise from the results of these studies only to the population of inpatients with neglect following right hemisphere stroke. We did not extract data on stroke severity, which again limits generalisation. Rehabilitation for people with long-term persisting neglect may be different for those at earlier stages of recovery from stroke versus other types of adult-acquired brain injury.

#### Interventions

Included studies investigated a variety of rehabilitation interventions; thus we have not treated them as a single entity. Although studies differed in number, frequency, and duration of therapy sessions, these were generally well described and interventions were similar enough to enable grouping, providing evidence applicable to clinical settings.

#### Comparisons

Fifty-two of the 65 included studies included usual care, sham, no-treatment, or attention control groups. These comparisons are appropriate for evaluating the effectiveness of interventions, providing results that should be generalisable. However we found considerable variation in what constituted usual care across study settings; future studies should provide sufficient detail to allow replication of control interventions.

Nine of the included studies compared multiple interventions with no specific control. Considerable heterogeneity and variation among interventions make it difficult to allow general conclusions from these studies. Further research is clearly required to identify the relative effectiveness of different non-pharmacological interventions. In theory, a network meta-analysis may allow indirect comparison to prioritise classes of intervention for further research. In practice, such an approach would require extreme caution, given the clinical heterogeneity of experimental and control interventions both within and between these classes.

#### **Outcomes**

A majority (51 out of 65) of studies reported a measure of functional ability in ADL, but only 16 reported these outcomes at follow-up (our primary outcome of interest). This lack of follow-up data on functional ability in ADL limited our ability to determine the persistence or maintenance of functional recovery. Almost all (63 out of 65) of the studies reported a standardised neglect assessment. Seven studies reported no usable data and presented results in graphs or gave P values only. Trialists are encouraged to provide appropriate data in accordance with CONSORT guidance to aid interpretation of study results.

We found very few data on other outcomes, such as discharge destination, falls, or depression. These are known to be of importance to stroke survivors, and including these in future research would improve the completeness of the evidence base.

# Quality of the evidence

For this updated review, we judged the quality of evidence using the GRADE approach. We judged all evidence included within meta-analyses to be of very low quality. We were unable to carry out sensitivity analysis because no studies met our pre-planned criteria. Key factors contributing to downgrading of evidence within these comparisons included the following.

#### Risk of bias

We identified concerns about the methods used in a majority of included studies. The method of randomisation used was generally poorly conducted or described, for example, use of unconcealed lists or tombola systems. We assessed 18 of the included studies to be at high risk of bias due to inadequate allocation concealment, and information on 23 further studies was insufficient. We assessed a majority of studies (60 out of 65) to have inadequate evidence of blinding of outcome assessment (see Characteristics of included studies). We did not examine funnel plots because, as pre-specified in our methods, studies for any one comparison were insufficient to make this worthwhile.

#### **Imprecision**

Included studies had small sample sizes, from 4 to 69 participants. Only 8 of the 65 studies had more than 50 participants overall (Dolkun 2019; Fong 2007; Kalra 1997; Kutlay 2018; Nyfeller 2019; Ten-Brink 2017; Wilkinson 2014; Yang 2017), and none had 50 participants per arm (our minimum size for a phase 3 trial adequately powered to investigate longer-term clinical effectiveness). A large quantity of study data could not be combined within analyses due to variations in study design and the fact that the maximum number of participants contributing to a single analysis was 311 (Analysis 3.4). Most studies were unclear about the intended study phase, with few specifying they were pilot studies. The small samples available for inclusion in meta-analysis limit any conclusions drawn from this evidence.

#### **Indirectness**

A number of factors contributed to indirectness of the data included within meta-analyses, particularly the following.

- Population: whilst all studies recruited patients after stroke and only 1 included patients with brain injury from other causes, there remained considerable differences in populations such as time post stroke and baseline differences such as stroke severity. No studies acknowledged the impact of other stroke-related impairments on inclusion, and many studies excluded participants on the basis of previous dementia or stroke, or current cognitive or communication problems, on the grounds that these would adversely affect responsiveness to therapy. These variations contributed to decisions to downgrade the quality of evidence.
- Interventions: we synthesised evidence into categories related
  to a wide range of interventions for neglect to be of greatest use
  for those in clinical practice. However, this meant there were
  substantial variations in the interventions within these different
  categories. For example, our pooled visual interventions include
  paper-based scanning training, computer-based eye movement
  training, hemi-field eye patching, and face-to-face scanning
  training. Studies were too few to warrant subgroup analyses for
  individual interventions, so the variety of interventions included
  in each comparison limits confidence in the pooled result.
- Outcomes: there was substantial variation in measures used for each of our outcomes and how they were reported. For example, studies that included target cancellation as a standardised neglect assessment used a variety of tests involving cancellation



of stars, lines, hearts, letters, numbers, cats, balloons, or bells. There was also variation in whether the number of items cancelled or not cancelled was reported. This variation in type of cancellation test alone highlights limitations when data from individual studies are pooled. Equally, whilst we have seen an increase in use of ADL assessments since the previous version of this review, these are subject to similar levels of heterogeneity, thus limiting certainty in our results.

To summarise, we judged the quality of the evidence synthesised within this review to be very low, which limits our certainty in the results. Future research needs to address factors that contribute to the quality of evidence, particularly around eligibility criteria, risk of bias, and choice of outcome measures, to produce results that are useful and meaningful.

### Potential biases in the review process

#### **Publication bias**

We are confident that we have identified all relevant published studies due to our search methods, which included liaising with authors of relevant Cochrane Reviews; however there is always the potential for human error when screening by title. We sought to obtain unpublished data from study authors and trial registers when appropriate. We last searched trials registers in October 2020; however there may be newly published studies that we did not identify.

#### **Categorisation of interventions**

We categorised interventions into broad types to be of greatest utility for clinicians. We devised and assigned studies to categories through discussion between review authors whose professional backgrounds include psychology, occupational therapy, and optometry, which should limit bias in our categorisation. However, we acknowledge that substantial differences between interventions within each category may reduce the applicability of results. Future updates of this review should pre-plan categories and identify interventions that are clinically relevant to combine. Involvement of key stakeholders is recommended to facilitate this process.

### Outcomes

The primary outcome for this review was persisting functional ability in ADL, measured via standardised assessments. We identified six studies that used measures of ADL not included on our pre-defined list of measures and thus excluded their data from meta-analyses. These standardised measures could be considered for use in future updates of this review.

For this update and for previous versions of this review, we used the Behavioural Inattention Test (BIT) behavioural subtest as a measure of neglect but not the total BIT nor the conventional BIT subtest, and we excluded study data that did not allow calculation of the behavioural subtest. We did this because this subtest is most relevant to functional outcomes. We believe inclusion of total BIT and conventional BIT in future review updates would be of value, as both include cancellation tests and line bisection (our secondary outcomes).

We noted considerable heterogeneity in outcome assessments used (see Quality of the evidence). We believe consensus is needed between stroke survivors, their families and carers, health

professionals, and researchers regarding core outcomes used in trials of interventions for neglect. This would contribute to more meaningful evidence synthesis and meta-analysis.

# Agreements and disagreements with other studies or reviews

# Agreements and disagreements between this updated version and previous version

Our conclusions from the 2013 review were as follows.

- Limited evidence suggests that cognitive rehabilitation may have an immediate effect on neglect impairment. However, considerable heterogeneity and evidence indicates that this effect was not sustained when studies with high risk of bias were removed.
- Some evidence shows subgroup differences between studies with and without an attention control group, highlighting the need for attention control in rehabilitation research.
- Evidence is insufficient to permit generalised conclusions about effects of cognitive rehabilitation interventions on functional ability in ADL or on standardised neglect assessments.

Key changes in the methods of this update include the following.

- Broadened scope of the review to include any nonpharmacological intervention.
- Amendment of inclusion criteria to include participants with any adult-acquired brain injury.
- Updated searches, increasing the number of included studies from 23 to 65.
- Use of the GRADE approach to systematically assess quality of evidence in this updated version.

These changes have increased uncertainty around previous limited evidence.

- Limited very low-quality evidence suggests that certain types of interventions may have benefit for persisting functional ability in ADL. Further research is very likely to have an effect on these conclusions.
- Evidence remains insufficient to permit generalised conclusions about effects of non-pharmacological interventions on functional ability in ADL or on standardised neglect assessments.

### Agreements and disagreements with other published reviews

The UK National Clinical Guidelines for Stroke used evidence provided by the previous version of this review plus three studies now included in this update to conclude, "there is insufficient high-quality evidence to recommend any specific interventions to increase independence" (ISWP 2016). This updated review is in agreement with this guideline. The guidelines also state, "there is some very limited evidence that cognitive rehabilitation may have an immediate beneficial effect on tests of neglect" (ISWP 2016); this is based on evidence from the previous version of this review; this update has highlighted further uncertainty regarding effects of any non-pharmacological interventions on neglect assessments.

The National Institute for Clinical Excellence (NICE) stroke rehabilitation guidelines do not recommend any specific



intervention and suggest "use [of] interventions for visual neglect after stroke that focus on the relevant functional tasks, taking into account the underlying impairment" (NICE 2013). This updated review is in agreement with this guideline.

The Scottish Intercollegiate Guideline Network (SIGN) guidelines for stroke rehabilitation (last updated in 2010) state, "there is insufficient evidence to reach conclusions relating to the effectiveness of any interventions for visual neglect" (SIGN 2010). These guidelines also state, based on evidence from four systematic reviews, that "visual scanning training appears to be the intervention with the most supporting evidence" (SIGN 2010). Our updated review does not directly support this recommendation.

Our review differs from three recent systematic reviews of nonpharmacological interventions for neglect following stroke. A metaanalysis of eight studies of differing intervention types (all of which are included in this update) concluded that intervention had a short-term effect on cognitive function, and that NIBS showed the largest effect size (Kwon 2018). Kwon 2018 analysed studies together in one meta-analysis. We deliberately did not combine different interventions (e.g. NIBS with prism adaptation) because the interventions are too different. Cotoi 2018 conducted a metaanalysis of nine studies using theta-burst stimulation and found improvement but acknowledged that evidence is limited and of low quality. Cotoi 2018 included one cross-over study and one study that we classified as awaiting assessment due to uncertainty around methods. Salazar 2018 conducted a meta-analysis of 10 NIBS studies (including three cross-over studies excluded from this review) and concluded that NIBS is effective; we cannot conclude that NIBS is effective based on uncertainty of the evidence. We are confident that these differences do not impact the conclusions of this updated review.

# **AUTHORS' CONCLUSIONS**

# Implications for practice

As the effectiveness of non-pharmacological interventions for reducing disabling effects of neglect and increasing independence remains unproven, no specific rehabilitation approach can be supported or refuted on the basis of current randomised controlled trials. Until robust evidence is available, clinical practice should follow national clinical guidelines (where these exist). Clinical decisions should always be based on an assessment of the individual stroke survivor and informed by knowledge and critical evaluation of the full range of evidence related to treatment for people with spatial neglect. People with neglect should continue to receive general stroke or neurological rehabilitation services and should have the opportunity to take part in high-quality research. Clinicians are strongly encouraged to participate in high-quality trials. Funding agencies, clinical educators, and policy makers should encourage and facilitate research into spatial neglect to improve clinical practice and outcomes. Appropriate resources are required (e.g. staff, time commitment, data management) to successfully deliver large, long-term trials. The costs of high-quality rehabilitation trials can be recouped, as effective interventions reduce long-term care needs and improve quality of life for people with spatial neglect.

#### Implications for research

Our implications for research are unchanged from those found in the previous version of this review. Evidence is still sufficiently compelling to encourage further trials of non-pharmacological interventions for neglect; however these trials need careful thought. We have identified 65 small underpowered feasibility studies; however before similar studies can be conducted, research and funding are needed to establish what will work in clinical practice, what is important to stroke survivors, and what outcome measures are appropriate to further this field.

A shift in focus to the person rather than the impairment may be required; stroke survivors with cognitive impairments such as neglect are often excluded from general rehabilitation studies. Trialists are encouraged to include these patients in general rehabilitation trials and to include measures of neglect. In addition, we identified 23 studies delivering multiple or combined interventions. Combination interventions may warrant further investigation to establish by means of pragmatic trials whether multiple interventions, such as NIBS plus scanning, provide an advantage over a single intervention.

Future studies must improve on current methodological and reporting issues.

- Prior registration of future trials is essential to allow full assessment. Protocols that sufficiently describe procedural aspects, such as randomisation, concealment, completeness of follow-up, and blinding of assessors, should be made available. Trialists should refer to the Cochrane Handbook (Chapter 8) for a description of acceptable methods of randomisation.
- Future studies must avoid using non-random allocation methods (such as matching) and tombola systems that preclude verification of the allocation process.
- Trialists are encouraged to assess and report whether any attempted blinding of outcome assessors is achieved in practice.
   By its nature, rehabilitation for neglect is likely to be restricted to single-blind trials (of outcome assessors), as blinding of participants and therapists is not usually achievable.
- Cross-over trials are not appropriate for rehabilitation for cognitive impairments, as effects of one approach may contaminate the next; the aim of rehabilitation is to promote independence and maintain treatment effects rather than 'washout' treatment effects.
- Future trials should state their intended purpose (e.g. pilot, feasibility, definitive); a minority of included studies stated they were pilot/feasibility studies. Proof-of-concept studies are essential before studies of effectiveness.
- Adequate statistical power is essential to detect a clinically meaningful difference in definitive trials and will require multicentre collaborations. There is no justification for claims that trials of complex interventions are not appropriate or possible or are too difficult, and suggestions that they would be too expensive should be balanced against long-term care costs.
- Future trials should provide adequate sample description and theoretical justification, and should consider using stratified randomisation to avoid imbalance of any factors likely to confound the trial. Neglect is a heterogeneous condition, and it is unlikely that a single rehabilitation approach is appropriate for all patients with neglect.



- Complete follow-up and intention-to-treat analysis are necessary, as a high dropout rate may be an important indication of effectiveness. Information is provided in the Cochrane Handbook (Chapter 6).
- Researchers must expand the aim of studies; trials aiming to treat or compensate for neglect to improve ADL require different study designs and outcome measures.
- More information about usual care is required, including time and detailed type of therapy received by participants in rehabilitation trials, as this is likely to influence outcomes.
- Whilst we acknowledge an increase in use of ADL assessments since the previous version of this review, trials must assess both functional activities of daily living and neglect at a follow-up assessment at least one month post intervention (i.e. persisting effects). Maintenance of function is of key importance to stroke survivors.
- Trialists should also assess other outcomes that are of importance to stroke survivors, including falls and quality of life.
- Future studies should use patient and public involvement to ensure study design, interventions, and outcomes are acceptable to stroke survivors.

This review is ongoing, and the review authors would be grateful to receive information on ongoing studies for a future update.

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# CHARACTERISTICS OF STUDIES

**Characteristics of included studies** [ordered by study ID]

### **Aparicio-Lopez 2016**

-pariore Lepezzeze	
Study characteristics	
Methods	RCT
	Setting: Spain
Participants	28 right-hemisphere stroke patients Single-treatment = 15, combined treatment = 13 Diagnosis of neglect: suggestive of VSN in the neuropsychological exploration protocol used to assess visuospatial attention Mean age, years: single treatment = 51, combined treatment = 46 Sex (men/women): single treatment = 9/3, combined treatment = 8/5 Days from stroke to admission: single treatment = 80, combined treatment = 85 Exclusion: severe language alteration, significant visual acuity impairment, pre-morbid history of other neurological disease, psychiatric disorder, drug abuse
Interventions	ST group followed a cognitive rehabilitation programme. Exercises included attention, memory, and executive function tasks. In all cases, adequate performance of assigned tasks required visual process-

<sup>\*</sup> Indicates the major publication for the study



# Aparicio-Lopez 2016 (Continued)

ing of stimuli homogeneously distributed across the screen. CT group carried out the same cognitive treatment as ST group, combined with RHEP. RHEP was implemented by using non-prescription glasses specially made for the study. These glasses had a completely opaque right half-field for each eye. This group wore these glasses during all cognitive treatment sessions

# Outcomes

For assessing visuospatial attention

- Bell Cancellation Test
- · Figure Copying of Ogden
- Line Bisection
- Baking Tray Task
- Reading test
- Catherine Bergego Scale

Notes

Breakdown of treatment by sex does not add up to total N  $\,$ 

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A simple randomisation procedure was performed according to a computer-generated random number table based on a uniform distribution (0, 1)
Allocation concealment (selection bias)	Low risk	The research assistant who generated the allocation scheme was not clinically involved in the study (neither in assessment nor in administration of treatment to patients)
Blinding of participants	High risk	Not possible to blind
Blinding of personnel	High risk	Not possible to blind
Blinding of outcome assessment (detection bias) All outcomes	High risk	Before the start of treatment and afterwards, the neuropsychological exploration protocol described in the Instruments section was administered. The researcher in charge of exploration was the same person responsible for planning and monitoring of treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcomes were reported equally
Selective reporting (reporting bias)	High risk	10 primary outcomes
Other bias	Low risk	No baseline imbalance

# Bang 2015

Study characteristics	
Methods	Pilot RCT
	Setting: Republic of Korea
Participants	12 patients unilateral visuospatial neglect admitted to W. University Hospital tDCS + FT (combined) = 6, FT (control) = 6 Diagnosis of neglect: 15% deviation to the right from centre in line bisection test



Bang 2015 (Continued)	Bai	ng 20	015	(Continued)
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Mean age, years: combined = 66, control = 66 Sex (men/women): combined = 2/4, control = 2/4

Weeks from stroke to treatment: combined = 7, control = 7

Exclusion criteria: severe cognitive impairment rendering a person unable to understand instructions given by therapist, contraindications for intervention, unstable medical or neurological condition

#### Interventions

Each participant performed a training programme consisting of 15 sessions lasting 50 minutes/d, 5

days a week, for 3 weeks

Participants in the tDCS + feedback training group received tDCS for 20 minutes, then performed feed-

back training

Both groups received feedback training for 30 minutes a day, 5 times a week, for 3 weeks. Feedback training used a vertical mirror held parallel to the sagittal plane to provide visual feedback on participants' neglected side body. Participants were asked to look at the centre of the mirror, so they could see the reflection of visual input coming from the left side of the body

### Outcomes

- MVPT
- LBT
- MBI

Measured immediately post treatment

#### Notes

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"They were randomly divided into two groups"
Allocation concealment (selection bias)	Unclear risk	"They were randomly divided into two groups"
Blinding of participants	High risk	No attempt at blinding described
Blinding of personnel	High risk	No attempt at blinding described
Blinding of outcome assessment (detection bias) All outcomes	High risk	No attempt at blinding described
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the entire study
Selective reporting (reporting bias)	Low risk	No suggestion of this
Other bias	Low risk	No baseline imbalance

# Cazzoli 2012

Studv	char	acte	rictics

Methods Hybrid 3-arm design. Here, combining first 2 arms "cTBS then sham" and "sham then cTBS" to create 2-arm parallel design without cross-over



Cazzo	li 2012	(Continued)
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Setting: Switzerland, neurorehabilitation clinic

#### **Participants**

24 first-stroke patients with left-sided neglect and normal or corrected-to-normal vision

cTBS-sham = 16, control = 8

Diagnosis of neglect: deficits in at least 2 out of 3 classes of paper-pencil tests

Sex (all patients): 17 men, 7 women Mean age (all patients), years = 58 Stroke type: 14 ischaemic, 10 haemorrhagic

Mean (SE) between stroke and treatment = 27 (4.4) days

Exclusion criteria: history of epilepsy, prior head trauma, drug and alcohol abuse, major psychiatric dis-

order

#### Interventions

Continuous TBS was applied by means of a MagPro X100 stimulator 60 mm outer radius (Magnetic Coil Transducer MC-125). Continuous TBS was delivered with the same protocol described previously (Nyffeler et al, 2008, 2009; Cazzoli et al, 2009a, b). In brief, the continuous TBS protocol comprised 801 pulses, delivered in a continuous train and consisting of 267 bursts. Each burst contained 3 pulses at 30 Hz, repeated at 6 Hz. The total duration of 1 single, continuous TBS train was 44 seconds. Overall, 8 continuous TBS trains were applied over 2 days. Four continuous TBS trains were applied on Day 1 (2 continuous TBS trains with an interval of 15 minutes, third and fourth trains 60 and 75 minutes after first continuous TBS train, respectively; see Nyffeler et al, 2009), and 4 continuous TBS trains on Day 2 (same time intervals as for Day 1). Continuous TBS was applied over P3, according to the International 10–20 EEG System. This site overlies the posterior parietal cortex in proximity of the intraparietal sulcus (Hilgetag et al, 2001). The coil was held tangentially to the scalp, with the handle pointing posteriorly, the current flowing clockwise as viewed from above. Patients were asked to close their eyes during continuous TBS application. Continuous TBS was delivered at 100% of patients' individual resting motor threshold. Sham was applied with the same protocol as described above, except for use of a sham coil (Magnetic Coil Transducer MC-P-B70)

Control group received treatment as usual

# Outcomes

- Vienna Test System (Peripheral Perception)
- CBS

Measured immediately post treatment

Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"were randomly allocated". Split 16:8 could be lucky but suggests structure
Allocation concealment (selection bias)	Unclear risk	No information
Blinding of participants	High risk	Blinding only within groups combined here
Blinding of personnel	High risk	Not clear whether personnel blinded within combined groups, but not applicable to this combined comparison
Blinding of outcome as- sessment (detection bias) All outcomes	Unclear risk	Assessment by "four independent raters who were responsible for the care of each particular patient". Unclear how they could have been blinded for this combined comparison
Incomplete outcome data (attrition bias) All outcomes	Low risk	"All patients included completed the study protocolall patients were assessed with all tests", with limited exceptions



Cazzoli 2012 (Continued)		
Selective reporting (reporting bias)	Low risk	All reported with equal (low) detail
Other bias	Low risk	No evidence of this

# Cha 2016

Study characteristics		
Methods	2-group parallel Setting: South Korea, neurophysiotherapy outpatient clinic	
Participants	30 stroke patients with	
	<ul> <li>No significant cognitive deficit (score &gt; 25 points on the Mini-Mental Status exam)</li> <li>Significant unilateral neglect (score &lt; 16 points on motor free visual perception test (MVPT))</li> <li>No eyesight or hearing problems</li> <li>No psychological or emotional problems</li> </ul>	
	rTMS = 15, control = 15  Sex (women/men): rTMS = 8/7, control = 6/9  Age, mean (SD), years: rTMS = 64 (12), control = 63 (12)  Time from stroke to treatment, mean (SD): rTMS = 4.1 (1.1), control = 3.9 (0.8)  Neglect severity pre-treatment, using LBT mean (SD): rTMS = 35.9 (8.1), control = 38.2 (4.7)	
Interventions	Participants in the experimental group received rTMS and conventional rehabilitation therapy for a to tal of 50 minutes (rTMS: 20 minutes, conventional rehabilitation therapy: 30 minutes) per day, with a 10-minute rest period halfway through the session. Participants in the experimental group received training 5 days per week for 4 weeks. Conventional rehabilitation therapy, consisting of neurodevelopmental facilitation techniques, was administered by therapists blinded to the study protocol and to participants' assignment to groups. The objectives of stroke rehabilitation were to improve patients' functional abilities, such as dressing, transfer, ambulation, and balance, and to provide education to caregivers, so as to help patients achieve earlier and/or greater independence in activities of daily living	
	Participants in the control group received sham therapy and conventional rehabilitation therapy for a total of 50 minutes (sham therapy: 20 minutes, conventional rehabilitation therapy: 30 minutes) per day on the same day	
Outcomes	<ul> <li>LBT</li> <li>Albert test</li> <li>Box and block test</li> <li>Grip strength test</li> </ul>	
	Measured immediately post treatment	
Notes		
Risk of bias		
Bias	Authors' judgement Support for judgement	
Random sequence generation (selection bias)	High risk Assuming tombola system	



Cha 2016 (Continued)		
Allocation concealment (selection bias)	High risk	No oversight of selection order
Blinding of participants	Low risk	Sham treatment
Blinding of personnel	High risk	Physician aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Separate physicians for treatment and assessment but unclear how possible to monitor success of 'blind'
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	ADL not recorded
Other bias	Low risk	No evidence of this

# **Cherney 2002**

Study characteristics	
Methods	RCT: no further information provided Setting: USA
Participants	4 right hemisphere stroke survivors with clinical evidence of neglect at least 6 months post onset Experimental: n = 2, control: n = 2  Mean age (SD), years: experimental = 69.5 (23.3), control = 62.0 (5.7)  Sex (men): experimental = 2, control = 1  Side of damage (RBD): experimental = 2, control = 2  Mean months post onset (SD): experimental = 16 (12.7), control = 7.5 (0.7)  Inclusion: right-handedness, right hemisphere stroke, persisting neglect after 6 months, spoke English as a primary language, passed pure tone audiometry in the better ear, corrected visual acuity sufficient to read newsprint
Interventions	Visual scanning training, practising letter and word cancellation tasks (to address the assumed underlying impairment of selective visual attention) vs repetitive practice of a functional task: oral reading (to represent an approach commonly used in rehabilitation)  Both groups received 20 sessions. Frequency of sessions is not known  Both scanning and reading training included use of visual, verbal, and tactile cues to attend to the left. In both training conditions, task difficulty gradually increased if the participant achieved 90% success (scanning) or 100% success (reading). In reading training, the cues were gradually removed (NB: scanning is coded as 'experimental' in this review)
Outcomes	Study collected 4 types of outcomes, pre-training and post training  MMSE  Stroop Neuropsychological Screening Test  BIT  Functional reading test devised for this study
	The latter task was to identify 5 names from a local telephone book; there was a time limit of 3 minutes per name. BIT was scored in 3 ways: conventional subtests; behavioural subtests; and total. It is assumed this was measured immediately post training



Cherney 2002	(Continued)
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For comparability with other studies, this review used only BIT behavioural subtests post training

Measured immediately post treatment

Notes Comparison of 2 treatments. Intended as a small preliminary study

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear
Allocation concealment (selection bias)	Unclear risk	No details of randomisation provided. Paper states "randomly assigned"
Blinding of participants	High risk	Blinding not possible
Blinding of personnel	High risk	Blinding not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not stated - unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	None reported
Selective reporting (reporting bias)	Low risk	Outcomes reported consistently
Other bias	Low risk	No evidence of this

# Choi 2016

Study ch	aracte	ristics
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Methods	2-group parallel design Setting: South Korea	
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# Participants 38 first-time, right hemisphere stroke

Robot = 20, control = 18

Age, mean (SD), years: robot = 60 (12.5), control = 63 (11.1)

Sex (women/men): robot = 8/12, control = 10/8

Type of stroke: robot = 13 ischaemic, 7 haemorrhagic; control = 12 ischaemic, 6 haemorrhagic Time between stroke and treatment, mean (SD), days: robot = 37 (15.9), control = 38 (16.9) Neglect diagnosis: when bisection deviated 5 mm or more to the right side in the line bisection test

Exclusion criteria: past medical history of brain damage, stroke, and other neurological or neuropsychiatric disease. Also, those who could not undergo robot treatment or hemi-spatial neglect tests due to severe cognitive impairment. Patients with below second-grade left upper extremity muscle strength in a manual muscle test, those who had any visual field defect, those with a seriously declined sitting balance interfering with upper extremity rehabilitation robot treatment in a sitting position on a chair with a back and armrests

Interventions

The Neuro-X system was used for robotic treatment of hemi-spatial neglect. During treatment, each patient sat on the right side of the robot, so the monitor was located to the left side of the patient. In this



#### Choi 2016 (Continued)

position, the patient could focus continuously on the left side. The robot treatment programme was implemented through games that induce passive and active assistive exercises of the wrist, elbow, and shoulder joints; games consisted of 2 types of isometric exercises and 2 types of range of motion exercises. Isometric exercises comprised an archery game, which was programmed to hit apples appearing on left and right sides of the monitor without any determined order, and a goalkeeper game, which was programmed to block a ball randomly approaching bottom left and right sides of the monitor. Range of motion exercises were conducted in a passive or an active assistive mode and consisted of a dolphin circus game and a skateboard game. All game programmes prompted participants' concentration through sound effects

During robotic treatment, occupational therapists monitored patients for diligently following progression of the robot programmes, measured patients' muscle strength before robotic programmes began, and helped patients when games had to be changed from time to time

Control group received treatment as usual

#### Outcomes

- MVPT-3
- LBT
- Star cancellation
- CBS
- MMSE
- K-MBI

All taken immediately post intervention with no longer-term follow-up

#### Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"patients were randomly assigned"
Allocation concealment (selection bias)	Unclear risk	No information
Blinding of participants	High risk	Blinding not possible
Blinding of personnel	High risk	Blinding not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	"therapists who did not participate first hand in the treatment"; not clear how possible to validate or prevent communication
Incomplete outcome data (attrition bias) All outcomes	High risk	> 20% attrition from controls. All dropout informative – either early discharge or medical decline. Baseline data not reported for these participants
Selective reporting (reporting bias)	Low risk	Outcomes presented equally
Other bias	Low risk	No evidence of this



# Choi 2019

3-group parallel RCT Setting: hospital, South Korea
Inclusion: individual with diagnosis of unilateral neglect from a medical doctor and number of lines neglected in Albert test > 70%; individual without brain lesions other than stroke; individual with less than 3 months since stroke; individual with Korean version of Mini-Mental Status Examination (K-MMSE) score ≥ 20, who can follow directions and does not have hearing or vision impairment Age: mean, SD
<ul> <li>62.90 ± 8.64, Group A</li> <li>67.70 ± 9.76, Group B</li> <li>66.00 ± 12.09, Group C</li> </ul>
Sex: 17 women, 13 men Hemisphere damaged: not specified Time since stroke: 1 to 3 months
This study has 3 intervention groups
<ul> <li>PA plus FES group (Group A)</li> <li>PA group (Group B)</li> <li>FES group (Group C)</li> </ul>
- Group A received 30 minutes of conventional occupational therapy, followed by FES application on upper limb on the affected side and PA treatment for 20 minutes, for a total of 50 minutes. Conventional occupational therapy was conducted for 30 minutes and included joint movement, task-oriented training, and daily life activity training. Joint movement was conducted and included passive joint movement, active adjuvant joint movement, and active joint movement. Task-oriented training considered functional level of patients and used tools to sequentially conduct activities such as cup-stacking and skateboarding. Daily life activity training included using the restroom, eating a meal, performing personal hygiene activities, wearing and taking off clothes, and transferring to chair or bed. Participants wore prism glasses that deflect the axis of vision to the right by 15 degrees, with the proximal surface shaped like a triangle facing the left. For FES, a product from Microstim was used. One channel was used and was set to apply, in shifts, 10 seconds of rest and 10 seconds of stimulation. It was attached below the elbow on the affected side. Although an intensity of 20 Hz is normally recommended, the threshold for electrical stimulation is different for each participant. Therefore, it was set to contract muscles enough to produce sufficient finger and wrist movements
- Group B received 30 minutes of conventional occupational therapy, followed by PA on the upper limb on the affected side for 20 minutes, for a total of 50 minutes
- Group C received 30 minutes of conventional occupational therapy, followed by FES application for 20 minutes, for a total of 50 minutes
<ul><li>K-MMSE</li><li>Albert test</li><li>MVPT</li><li>CBS</li></ul>
All taken immediately post intervention with no longer-term follow-up
Authors' judgement Support for judgement



Choi 2019 (Continued)		
Random sequence generation (selection bias)	High risk	No detail offered. Exactly 10 per group
Allocation concealment (selection bias)	High risk	No detail offered. Exactly 10 per group
Blinding of participants	High risk	Outcome group: all Blinding not possible
Blinding of personnel	High risk	Outcome group: all Blinding not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome group: all Blinding not possible
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	No suggestion of this
Other bias	Low risk	Not obvious

# **Cottam 1987**

Study characteristics	5
Methods	2-group parallel RCT Setting: rehabilitation centre, USA
Participants	12 stroke rehabilitation inpatients with left hemi-spatial neglect Experimental: n = 6, control = 6 Mean age, years: experimental = 66.2, control = 71.3 Sex (men/women): 7/5 Side of damage: all had right middle cerebral artery lesions Time post onset, mean, weeks: experimental = 6, control = 16.3 Inclusion: right-handedness; visual acuity > 20/100 corrected on Snellen's; oriented in person, place, and time; evidence of left hemi-spatial neglect on ≥ 3 of the tests used; either WAIS-R VIQ > 80 or minimum scaled score = 8 on 4/6 verbal subtests; arm and leg able to propel wheelchair
Interventions	<ul> <li>3-phase intervention, each phase consisting of 5 half-hour sessions per day</li> <li>Visually scanning a light board when stationary, taught to verbally self-prompt to start on left and scan from left to right</li> <li>Same activity but while self-propelling</li> <li>Did not use the light board, but participants named objects presented on both sides while self-propelling</li> <li>vs no information other than participants were inpatients at a rehabilitation facility and were assessed after same periods as experimental group</li> </ul>
Outcomes	<ul> <li>Study collected 3 types of outcomes:</li> <li>Data scanning and attention skills: single target cancellation (3 minutes letter H) and double target cancellation (3 minutes letters C and E); scores are for average number of far left-sided omissions</li> </ul>



#### Cottam 1987 (Continued)

- Light board: point at light and say the colour, allowing 10 seconds; scores are for average number of left-sided omissions
- ADL: avoidance of obstacles on wheelchair course, as rated by 2 observers

Assessed pre-intervention, after each phase (5 days), and at follow-up 6 weeks post discharge from hospital

This review used only cancellation data, immediate and persisting effects

Notes

Single-letter cancellation outcome data are entered as left-sided omissions (i.e. low score is better outcome)

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	No detail given; exactly 6 per group
Allocation concealment (selection bias)	High risk	No detail given; exactly 6 per group
Blinding of participants	High risk	Blinding not possible
Blinding of personnel	High risk	Blinding not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not stated. Not mentioned so unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 control lost to follow-up
Selective reporting (reporting bias)	High risk	Comprehensive dissertation report with massive multiplicity. Apparently post-hoc combinations of quintiles (far left, left, centre, right, far right) of areas on visual tasks
Other bias	Low risk	Nothing obvious

# Dolkun 2019

Study characteristics	
Methods	RCT, 2-group parallel
	Setting: outpatient department and hospital ward, China
Participants	Patients with left hemiplegia after first stroke who met diagnostic criteria for unilateral spatial neglect of stroke. Patients with first cerebral infarction with course of disease within 2 weeks to 3 months. Muscle strength of the affected hand was reduced to at least level 4 and > 48 hours. Motor function of upper limbs was restored at the time of enrolment, and muscle strength at proximal end of the upper limbs was > grade 1. Right-handedness (according to Chinese handedness)  Age: intervention = range 37 to 80, mean $61 \pm 13$ ; control = range 41 to 79, mean $63 \pm 12$ Sex: intervention = $23/9$ men/women; control = $22/10$ men/women

Hemisphere damaged: right



#### Dolkun 2019 (Continued)

#### Interventions

Intervention group received acupuncture at specific points. Acupoints selection: Bai Hui, Feng Fu, Feng Chi, Xuan Zhong, Nie San Zhen. Operation: patient was in the supine position, and local skin was routinely disinfected. Acupuncture needles of 0.25 mm × 25 mm or 0.25 mm × 40 mm were used. After needle insertion at the acupoint Bai Hui, horizontal insertion subcutaneous 15~20 mm. Insert into Feng Fu to jaw direction slowly 15~25 mm. After inserting the needle at the acupoint Feng Chi, towards throat direction oblique insert 15~25 mm. Insert into Xuan Zhong straight 15~30 mm. Temporal Three Needles: acupoint 1, 2 cun above tip of ear; acupoint 2, 1 cun forward acupoint 1; acupoint 3, 1 cun backward acupunct 1; when the needle is inserted, the tip of the needle is downward at an angle of 15°~20° with the scalp, slowly twirling and piercing into 25~30 mm. After insertion into acupoints, the needle is twisted and is retained for 30 minutes after De Qi

Control group received standard acupuncture. Both groups received acupuncture at 10:00 to 13:00 Beijing time, once a day, 5 times per course of treatment, for a total of 4 courses of treatment

#### Outcomes

- · Line cancellation test
- · Digit cancellation test
- · Line bisection
- Clock drawing test
- Copy drawing test
- B
- · Simplified Fugl-Meyer motor function score

All taken immediately post intervention with no longer-term follow-up

#### Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Statistical software cited for sequence generation
Allocation concealment (selection bias)	Low risk	"Opaque craft envelopes with serial numbers"
Blinding of participants	High risk	No mention and not straightforward
Blinding of personnel	High risk	No mention and not straightforward
Blinding of outcome assessment (detection bias) All outcomes	High risk	No mention and not straightforward
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	Tables for all presented in equal detail
Other bias	Low risk	Nothing obvious



# Edmans 2000

Study characteristics	
Methods	RCT Setting: UK
Participants	42 (see Notes) stroke patients with visual neglect from those with general perceptual problems admitted to an inpatient SU Experimental: n = 24, control: n = 18  Mean age (SD), years: experimental = 69.17 (11.35), control = 66.61 (14.5)  Sex (men/women): experimental = 10/14, control = 8/10  Mean time post onset: 37 days  Inclusion: a subset of those with neglect from those with general perceptual problems from consecutive admissions to a stroke unit trial. SU trial criteria were medically stable, able to transfer with maximum 2 nurses, no discharge date planned, able to tolerate 30-minute treatments, able to carry out some independent ADL pre-stroke
Interventions	ToT approach to treat the 'cause of the perceptual problem'. Underlying assumption is that practising a perceptual task will treat the underlying impairment and if successful will improve performance of other tasks that depend on the skills. Personal communication suggests that cueing and feedback were used to teach participants to compensate vs FA to treat the 'symptom rather than the cause' and involved practising ADL tasks  Both groups received 2.5 hours per week for 6 weeks in addition to standard OT (NB: ToT is coded as experimental in this review)
Outcomes	The broader study of perceptual problems completed the following measures by different assessors immediately after the 6-week treatment: an independent blinded assessor completed the BI, Edmans ADL Scale, and RPAB. This assessor completed the ADL scales following interviews with unblinded nursing staff. The unblinded ward OT also completed the BI and Edmans ADL Scale. An unblinded physiotherapist completed the RMA gross motor scale. Additionally, assessments by other clinical staff were analysed: speech and language therapists, psychologists, physiotherapists.  For comparability with other studies, this review used only the RPAB letter cancellation subtest score (number correctly cancelled) and the blinded assessor's BI
Notes	Personal communication supplied further data and clarification of methods. Study authors provided unpublished data on 42 neglect patients from a larger RCT of 80 left and right (35) hemisphere strokes with perceptual problems, who was themselves taken from the stroke unit admission arm (n = 158) of an RCT of stroke unit vs general medical care. No pre-randomisation differences between groups, except that the ToT group was a little longer post stroke (40/33 days) than the FA group
Risk of bias	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number tables
Allocation concealment (selection bias)	Low risk	The researcher used random number tables to prepare sequentially numbered opaque sealed envelopes. The random number tables were then returned; due to the large number randomised (80 to the full perception trial), it was unlikely that the sequence would be remembered. The envelopes were opened only in the presence of a witness. Random number tables were used. Concealment was highly likely to have been achieved, although this could not be guaranteed
Blinding of participants	High risk	Blinding not possible
Blinding of personnel	High risk	Blinding not possible
Blinding of outcome assessment (detection bias)	High risk	Assessor blinded but required to discuss with ward staff



# Edmans 2000 (Continued)

All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	"No patients withdrew from the study but one patient (in the functional approach group) died before completing his six weeks of perceptual treatment."  Data from this patient are included in analyses
Selective reporting (reporting bias)	Low risk	All outcomes were reported equally
Other bias	Low risk	No evidence of this

# Fanthome 1995

Study characteristics	
Methods	RCT Setting: UK
Participants	18 (see Notes) RH stroke patients admitted to hospital Experimental: n = 9, control: n = 9 (The following data describe the 18 initial participants: see Notes) Mean age (SD), years: experimental = 66.3 (10.7), control = 71.1 (7.6) Sex (men/women): experimental = 6/3, control = 6/3 Time post onset (mean months): experimental = 1.0, control = 0.6 Inclusion: not blind, < 80 years of age, no history of dementia or psychiatric problems, not ill, right-handedness, score > 6 on Abbreviated Mental Test, RH stroke, score < 130 on BIT
Interventions	4 weeks (2 hours 40 minutes per week) of feedback on eye movements (wearing specially adapted glasses with auditory signal) vs 4 weeks of no treatment
Outcomes	Study collected 3 types of outcomes: eye movements, conventional BIT subtests, and behavioural BIT subtests, immediately post treatment (4 weeks) and 4 weeks later (8 weeks)  For this review, we used the 4-week single-letter cancellation test (for immediate outcomes) and 8-week BIT summary behavioural subtest scores (for persisting outcomes)
Notes	Personal communication supplied group data on BIT subtests for all but 1 control participant at 4 weeks (missing data; therefore n = 18 - 1) and the information that assessor was blinded to allocation. BIT behavioural data are for all 18 at 4 weeks but for only 13 at 8 weeks. 8 weeks = post start of treatment, i.e. 4-week follow-up post end of treatment  Single-letter cancellation data are for number cancelled, i.e. higher numbers indicate better outcomes Experimental and control groups appeared adequately matched on demographic and clinical data, although control group was slightly older than experimental group; no baseline BIT data

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sealed opaque envelopes prepared from random number tables
Allocation concealment (selection bias)	High risk	Concealment of allocation cannot be guaranteed, as this was not done by a third party. The combination of a small sample size with no external randomisation meant there was potential risk to concealment
Blinding of participants	High risk	Impossible to blind



Fanthome 1995 (Continued)		
Blinding of personnel	High risk	Impossible to blind
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinded outcome assessor stated, although no detail given
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	1 participant was recruited but was not included, as "he could not move his eyes to the fixation points". 1 participant from the control group was excluded, as he was discharged home outside the area of the hospital
Selective reporting (reporting bias)	Low risk	Outcomes were reported equally
Other bias	Low risk	Groups appeared similar at baseline, and no significant differences were found

# Ferreira 2011

Study characteristics		
Methods	RCT Setting: Brazil	
Participants	10 ischaemic, right cerebral hemisphere stroke > 3/12 duration  Mental practice = 5, visual scanning = 5  Detection of neglect: score < 129 (out of 146) on BIT  Sex (women/men): mental practice = 2/3, visual scanning = 3/2  Age (range), years: mental practice = 46 to 73, visual scanning = 62 to 80  Time between stroke and treatment, range, months: mental practice = 3 to 62, visual scanning = 4 to 132  Exclusion criteria: locomotor problems or ataxia interfering with task completion, dysphasia, Parkinson's disease, dementia, any neurodegenerative condition	
Interventions	Group 1: visual scanning Group 2: mental practice	
Outcomes	BIT conventional su     FIM  Intervention groups we	btests ere assessed at end of intervention period and at 3 months
Notes	"Five patients not willing to participate in the experimental protocols were submitted to a follow-up exam 2 months later and were included in a control group." We did not include this group in analysis because it was non-randomised; data only from the 2 intervention groups are presented We used imputation to calculate post-intervention scores using 3 of the 5 values provided in each group: minimum, median, maximum	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Ten patients were randomly allocated"



Ferreira 2011 (Continued)		
Allocation concealment (selection bias)	Low risk	Randomisation (information from study authors): "Concealed envelopes for every patient (0 or 1). Then patients as they were recruited/included and subsequently randomised by the same method" $\frac{1}{2} \left( \frac{1}{2} \right) = \frac{1}{2} \left( \frac{1}{2} \right) \left$
Blinding of participants	High risk	Not possible
Blinding of personnel	High risk	Not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	States: "the evaluations were always done by a physical therapist not directly involved in patients' treatment." However, correspondence with study authors confirms: "there were two therapists involved, each one directly responsible for a different treatment strategy (mental practice or visual scanning). For instance, whenever a patient was randomised to mental practice, treatment was done by one and assessments by the other therapist. Hence, the assessor was always the therapist who would not be involved in treatment but he always knew the treatment allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All complete
Selective reporting (reporting bias)	High risk	Total FIM reported more briefly than 'significant' subscale (self-care items)
Other bias	Low risk	Groups appeared similar at baseline, and no significant differences were found

#### Fong 2007

ong 2007	
Study characteristics	
Methods	3-arm RCT Setting: rehabilitation hospital, Hong Kong
Participants	Experimental 1: n = 20; experimental 2: n = 20; control: n = 20  Number lost to follow-up: immediate post treatment (Day 30) assessments on 19, 20, and 15, respectively  Also lost 5, 0, and 3, respectively to follow-up (Day 60), so final analysis of 14, 20, and 12  Adequacy of matching at baseline? yes: P values are reported for all demographics and for baseline data - there are no significant differences  Mean age, mean (SD): experimental 1 = 69.9 (11.0), experimental 2 = 69.9 (9.8), control = 73.8 (9.9)  Sex (men/women): 34/20  Side of damage: all had right brain damage  Time post onset, days (SD): experimental 1 = 12.1 (9.4), experimental 2 = 11.6 (5.1), control = 12.1 (7.1)  Inclusion criteria: first or second unilateral right lesion stroke confirmed by imaging and examination, admitted to rehabilitation hospital, < 8 weeks since stroke onset, right-handedness, left visual inattention or neglect diagnosed by < 51/54 on Star Cancelled of BIT and GCS = 15 at recruitment Exclusion criteria: severe aphasia, significantly impaired visual acuity, hemianopia  Visual sensory deficit: hemianopia and visual acuity assessed (method of assessment not stated)
Interventions	Experimental 1: voluntary trunk rotation 1 hour per day, 5 days per week for 30 days = 30 hours; OT present throughout Each hour composed of 15 minutes ADL + 45 voluntary trunk rotations with setup equipment (supine, unsupported sitting, and standing frame) reaching with ipsilateral hand into contralateral space and therefore rotating upper body/trunk by 15 to 35 degrees from midline. Used setup apparatus (pegboard or shoulder arc). Voluntary or if necessary therapist-provided verbal or motor prompting for 15 minutes



#### Fong 2007 (Continued)

Experimental 2: voluntary trunk rotation and half-field eye-patching

Same amount and content as experimental group 1 but wearing half-field eye-patches to ipsilesional (right) hemi-field wearing patches on plastic goggles (over own glasses if necessary)

Control: same amount of time as experimental groups 1 and 2. Conventional OT for hemiplegia (15 minutes ADL + 45 minutes training upper extremity). No mention of any neglect-specific treatment, implying treated as if had only hemiplegia

For analysis, voluntary trunk rotation with half-field eye-patching was classed as the experimental condition, and control as the control condition

Profession of outcome provider: OT

#### Outcomes

Used 3 (some with multiple subtests) at 2 follow-up time points (Day 30 immediately post therapy + Day 60)

- Full BIT (15 subtests with 2 category scores and an overall score)
- · Clock drawing task "using the Watson system"
- FIM motor subscale (4 subtests with 1 motor subscale score)

Did not measure serious adverse events; excluded anyone re-hospitalised or with deteriorating health

#### Notes

"Recruitment hypothesis" target both spatial representation and motor intentional deficits of personal and peri-personal space - this is the voluntary rotation plus eye-patches
"Inexpensive and easily integrated into use in day-to-day rehabilitation"

Lack of intention to treat analysis, no baseline data for those follows:

Lack of intention-to-treat analysis, no baseline data for those allocated, baseline data for those followed up suggests pre-therapy differences described in 'Risk of bias' table below

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Patients were "allocated to different groups according to their orders of admission to the study"
Allocation concealment (selection bias)	High risk	Personal communication with study authors: "we didn't have concealment of allocation of participants from the person who was recruiting"
Blinding of participants	High risk	Not mentioned and not practicable
Blinding of personnel	High risk	"The investigators were not blinded to group membership, and were also responsible for the intervention as allocated by the data manager"
Blinding of outcome as- sessment (detection bias) All outcomes	Low risk	"Two independent blinded assessors, who were blinded to group membership, were responsible for all repeated measures throughout the duration of the study"
Incomplete outcome data (attrition bias) All outcomes	High risk	Although reasons for post-randomisation exclusions are stated, it would have been preferable if all participants had been included in intention-to-treat analysis
Selective reporting (reporting bias)	Unclear risk	Unclear
Other bias	Low risk	P values reported for all demographic and baseline data - no significant differences



# **Fong 2013**

Study characteristics	
Methods	Multi-centre, randomised, sham-controlled RCT Setting: rehabilitation hospitals, Hong Kong
Participants	Stroke patients: (1) cerebral vascular disease diagnosed by computed tomography scan or magnetic resonance imaging in a medical report and compatible with unilateral hemispherical involvement; (2) evidence of unilateral neglect from neurological testing or Behavioural Inattention Test (BIT) conventional subtest score < 129; (3) right-handedness; (4) within 8 weeks after stroke; (5) ability to understand verbal instructions and to follow 1-step commands; (6) severe to moderate unilateral upper limb paresis, defined as levels 1 to 5 in the Functional Test for the Hemiplegic Upper Extremity (FTHUE) with the range of some beginning voluntary motion of the hemiplegic shoulder and elbow to beginning ability of the hand to combine components of strong mass flexion and strong mass extension patterns Age, years: intervention = $66.2 \pm 14.8$ , control = $68.6 \pm 10.6$ Sex: men/women: intervention = $16 (84.2)/3 (15.8)$ , control = $9 (56.2)/7 (43.8)$ Hemisphere damaged: right, basal ganglia, internal capsule, corona radiate, or other Time since stroke, mean and SD, days: intervention = $24.3 \pm 18.5$ , control = $22.3 \pm 12.0$
Interventions	Experimental group wore a wristwatch device emitting vibration cue with actometer for 3 consecutive waking hours on weekdays for 3 weeks. In the experimental group, patients had to press the acknowledgement button on the device with their right hand as soon as possible after each cue. Patients were told to follow every sensory cue with customary consecutive movements of the hemiplegic arm. They were instructed to perform the movement consecutively 5 times after each sensory cue. Cues came at intervals of 5 minutes for 3 hours. There were 2 kinds of customary movements tailored for participants according to the severity of their arm impairment: patients in levels 3 to 5 of the FTHUE who had partial use of their shoulders or arms were instructed to flex or extend their elbows; those in levels 2 to 3 of the FTHUE who had some voluntary motion of the shoulder were told to flex or abduct their shoulders  Control group wore a sham wristwatch device with actometer
Outcomes	<ul><li>BIT-C</li><li>Fugl-Meyer</li><li>FTHUE</li><li>FIM</li></ul>
	Outcomes were reported as follow-up but only 3 weeks following end of intervention, and therefore not meeting our definition of 'persisting' for this review
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Computerised random number generators"
Allocation concealment (selection bias)	Low risk	"Allocation to treatment sequences [was] concealed from all investigators"
Blinding of participants	High risk	Sham clearly ineffective: lost 20% of controls and none from active group for "lost interest"
Blinding of personnel	High risk	Ineffective sham
Blinding of outcome assessment (detection bias) All outcomes	High risk	Ineffective sham



Fong 2013 (Continued)		
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost 45% of control group before follow-up assessment
Selective reporting (reporting bias)	Low risk	Consistent reporting of key outcomes
Other bias	Low risk	Nothing obvious

Study characteristics		
Methods	RCT Setting: Korea, inpatient rehabilitation unit	
Participants	13 right-handed patients who had a first-ever stroke in the right hemisphere and VSN with normal or corrected-to-normal vision rTMS = 7, control = 6 Diagnosis of neglect: average rightward bias of 12% Age, years: intervention = 60.17 ± 14.05, control = 62.00 ± 9.78 Sex: 3 women Time post stroke, days: intervention = 41.83 ± 20.56, control = 36.17 ± 17.50	
Interventions	cTBS group received continuous TBS with the coil placed tangentially to the scalp at P3 over the left posterior parietal cortex (according to the 10–20 electrode position system of the American Electroencephalographic Association). Magnitude of the pulses was maintained at 80% resting motor threshold. On each day for 10 consecutive days, 4 sessions of stimulation were delivered, with an interval of 15 minutes between every 2 sessions. Each session lasted 40 seconds and contained 600 pulses delivered in 200 bursts at 5 Hz (theta rhythm). Each burst included 3 pulses delivered at 30 Hz	
Outcomes	LBT     SCT     Baseline inter-regional RSFC	
Notes	Measured immediately post treatment  Fu (2017) and Cao (2016) used the same participants but reported different outcomes	
Risk of bias	ru (2017) and Cao (201	o) used the same participants but reported different outcomes
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No detail beyond "patients were randomly assigned"
Allocation concealment (selection bias)	Unclear risk	As above
Blinding of participants	Unclear risk	"Patients were blinded to the frequency of cTBS used"
		Clearly attempted with sham treatment but in direct contact with unblinded

All/staff needed to know to set up

staff

High risk

Blinding of personnel



Fu 2	017	(Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome group: imaging  Not clear when or how 'regions of interest' were identified. Looks more like hypothesis-generating (exploratory) than hypothesis-testing  Outcome group: clinical  Not clear how successful blinding attempt was or whether personnel administering tasks were the same as those involved in treatment, or otherwise had knowledge of group assignment
Incomplete outcome data (attrition bias) All outcomes	High risk	Cao 2016 contains additional participant omitted without explanation from Fu 2017
Selective reporting (reporting bias)	High risk	Cao 2016 cites t-tests for comparison at baseline but non-parametric tests for comparison at outcome. Suggests absence of prospective or coherent analysis plan
Other bias	High risk	Massive multiplicity issues in imaging data, e.g. 78 hypothesis tests reported in each of Tables 1 and 2 (and these only in defined 'regions of interest')

# **Goedert 2020**

Study characteristics	
Methods	RCT Setting: inpatient rehabilitation facility, USA
Participants	Less than 60 days post stroke, first clinical stroke, unilateral right brain Event as confirmed by clinical computed tomography or magnetic resonance imaging, and BIT score at screening indicative of neglect (< 129) Age, years: 65.6 control, 61.8 prism Sex: 5 men/4 women = control, 4/4 = prism Hemisphere damaged: right Time since stroke: 9 to 50 days post stroke
Interventions	Prism adaptation. Those randomised to the prism group received prism adaptation treatment once a day for 10 days (5 days per week for 2 weeks). Prism adaptation sessions were timed and each lasted approximately 15 to 20 minutes. Control group received usual care
Outcomes	<ul> <li>BIT</li> <li>CBS</li> <li>Outcomes were measured up to 24 weeks post intervention. For comparability with other studies, we used outcomes at week 6 post intervention</li> </ul>

# Notes

Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	No information on process used despite detailed appendix	
Allocation concealment (selection bias)	Unclear risk	Administrative (likely junior?) staff member tasked with list. Unblinded allocation and possibly post-hoc evaluation "approximately half-way through data collection" imply absence of proper quality control process	



Goedert 2020 (Continued)		
Blinding of participants	High risk	Not possible
Blinding of personnel	High risk	Not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not attempted
Incomplete outcome data (attrition bias) All outcomes	High risk	Omission of 2 (11%) cases from prism arm, who did not (could not?) do more than 4 of planned 10 sessions
Selective reporting (reporting bias)	Low risk	No evidence of this
Other bias	Unclear risk	<ul> <li>Data-driven inclusion of co-variates in analysis and omission of outliers</li> <li>Change to randomisation ratio may favour prism group if (as likely) care improved during trial</li> </ul>

# lwanski 2020

Study characteristics		
Methods	Setting: Poland, inpatient or outpatient rehabilitation	
Participants	Inclusion criteria: (1) MRI or CT (in case of contraindications to MRI) confirming a first-ever stroke in the right hemisphere; (2) time after onset 2 to 12 weeks (early subacute stroke; Bernhardt et al, 2017); (3) severe to moderate VSN recognised in a neuropsychological assessment; (4) age 18 to 75 years Age, mean $\pm$ SD, years: intervention = 65 $\pm$ 7.5, control = 64.6 $\pm$ 7.7 Sex (men/women): intervention: 11/3, control: 11/3 Days since stroke, mean $\pm$ SD: intervention = 49.2 $\pm$ 27, control = 35.4 $\pm$ 17	
Interventions	Inhibiting stimulation parameters were chosen according to safety guidelines for rTMS (Rossi, Hallett, Rossini, & Pascual-Leone, 2009). Stimulation was applied at 90% of the RMT at 1 Hz frequency. A total of 1800 pulses were generated during a 30-minute session. Control group received sham stimulation performed with a sham coil that looked and sounded similar to real stimulation. To target the left angular gyrus, we positioned the coil on the scalp using the neuronavigation system and Talairach coordinates (x: –41; y: –66; z: 38; Cattaneo, Silvanto, Pascual-Leone, & Battelli, 2009). During the long-lasting rTMS, accuracy of the stimulation was constantly monitored by neuronavigation, while coil position error was recorded every 10 pulses. Deviation of up to 4 mm from the target was considered acceptable. For every participant, the percentage of pulses "in target" was estimated for each session	
	Behavioral therapy of visuospatial neglect	
	VSN therapy was focused mainly on visuospatial scanning with active and purposeful direction of sight to the left visual field in cognitive tasks performed in 2 computer programmes: RehaCom (HASOMED GmbH, Magdeburg, Germany) and CogniPlus (SCHUHFRIED GmbH, Modling, Austria). Additionally, paper-and-pencil tasks were used to improve visual scanning. Patients were asked to draw, copy, and analyse complex visual stimuli. Visual-scanning training was guided by verbal instruction, contralesional cues (e.g. visual stimuli), and therapist feedback to orient attention to the neglected part of space	
Outcomes	<ul> <li>BIT</li> <li>FIMFAM</li> <li>Bespoke Visuospatial Scale</li> </ul>	
	Measured up to 3 months post intervention	



# Iwanski 2020 (Continued)

Notes

Study authors reported median scores only for persisting neglect assessment. We imputed median for mean and used highest observed scores for SD

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Bespoke minimisation routine
Allocation concealment (selection bias)	Unclear risk	Insufficient detail; from correspondence with study author: "we allocated participants using Excel sheet. The file was protected by a password, which was known only for researchers (KP, ML), who were responsible for performing rT-MS/sham sessions"
Blinding of participants	Unclear risk	Stated no previous experience and unaware of allocation but without evidence
Blinding of personnel	High risk	"Group assignments were known to the researchers who administered rTMS"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome group: all  "The neuropsychologist responsible for the cognitive assessment and leading therapy (SI) was blind to all patient treatment allocation"
		Assumes no communication within research team and success of participant blinding. Communication with study author reveals the following: "the neuropsychologist responsible for cognitive assessment and leading visuospatial scanning therapy was blind to rTMS/sham allocation. Participants also were not informed about the rTMS/sham allocation. Only two researchers knew the allocation because they administered the stimulation. The cooperation in the research team was close but due to blinding procedure information of allocation of the participants was known only form researchers who perform rT-MS/sham procedure"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only 1 loss to follow-up (death)
Selective reporting (reporting bias)	Low risk	Primary and secondary outcomes identified
Other bias	High risk	Data-driven analyses seemingly according to misunderstanding of 'non-significant' and required assumptions for methods

# **Kalra 1997**

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Study Characteristics		
Methods RCT Setting: UK		
Participants	50 (see Notes) stroke patients with visual neglect admitted to an SU The following data are for the 47 surviving patients: Experimental: n = 24, control: n = 23 Mean age (SD), years: experimental = 78 (9), control = 76 (10) Sex (male): experimental = 11, control = 9	



Ka	ılra	1997	(Continued)
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Side of damage (RBD): experimental = 16, control = 17 Median time post onset, days (range): 6 (2 to 14)

Inclusion: infarcts; partial anterior circulation, known to be sensitive to rehabilitation on basis of impairment of power, balance, proprioception, and cognition at 1 to 2 weeks after stroke

Exclusion: TIAs, reversible neurological deficits, hemianopsia, severe dysphasia

# Interventions

Spatio-motor cueing based on 'attentional-motor integration' model and early emphasis on restoration of function vs conventional therapy input concentrating on restoration of tone, movement pattern, and motor activity before addressing skilled functional activity

#### Outcomes

Study collected 6 types of outcomes:

- Mortality
- BI at discharge
- Discharge destination
- Length of hospital stay
- Duration of therapy input
- RPAB after 12 weeks

This review used only BI, RPAB letter cancellation subtest, and discharge home. All were analysed as immediate effects

#### Notes

Principle behind approach: movement of affected limb in the deficit hemi-space led to summation of activation of affected receptive fields of 2 distinct but linked spatial systems for personal and extrapersonal space, resulting in improvement in attention skills and appreciation of spatial relationships on the affected side. Personal communication supplied further data and clarification of methods No differences between groups in demographic variables or initial impairment or disability including BI Outcome data for 47 of 50 stroke patients with visual neglect admitted to an SU: experimental: n = 24 (+ 1 died), control: n = 23 (+ 2 died). For the 'destination discharge' outcome, the total figure of 50 was used in this review, as deaths were entered as not going home

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	External randomisation, using random permuted block technique in groups of 10, allocated by telephone by clerical staff using computer-generated random numbers
Blinding of participants	High risk	Not possible to blind
Blinding of personnel	High risk	Not possible to blind
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Independent observer
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 lost to follow-up: 1 intervention and 2 control. All died, so low risk of bias
Selective reporting (reporting bias)	High risk	Selective reporting of multiple subtests on RPAB
Other bias	High risk	"Treatment of patients in each group was undertaken by different therapists of the unit to prevent 'crossover' of treatment techniques". Impossible to dis-



Kalra 1997 (Continued)

tinguish effect of therapy from effect of therapists. NB: recognised as preliminary study to inform design rather than to answer questions

# Karner 2019

RCT Setting: rehabilitation hospital, Germany		
Minimum age of 60 years and diagnosis of first stroke of the right hemisphere occurring within previous 3 months, with hemi-neglect of the left side, ability to sit, no major cognitive impairment Age, years (SD): intervention = 74.21 (6.53), control = 73.34 (8.13)  Sex (women/men): intervention = 10/11, control = 12/6  Hemisphere damaged: right  Time since stroke, mean (SD), days: intervention = 49.24 (29.12), control = 55.17 (22.75)		
Intervention group received treatment using a therapeutic stimulation robot. PARO is an interactive robot in the shape of a baby seal. Each treatment began with providing information to the patient. This was done verbally as well as by initial physical contact on the left upper arm: "I am now on the left side of your body, the side affected by your stroke" PARO was placed on the neglected side, so it was possible for the patient to see and grasp it. The task for the patient was focusing attention on the robot. As soon as the patient had fixed his or her attention on PARO, it was successively moved further to the neglected side		
Control group was classified as attention control, with the researcher giving physical contact to the patient on the arm with verbal information as per the intervention. A book was also given for the patient to see and grasp. The patient was then read aloud from the book		
<ul> <li>Cats cancellation test</li> <li>Line bisection</li> <li>Scores of Independence Index for Neurological and Geriatric Rehabilitation (SINGER)</li> <li>Participants were followed up for 2 weeks post intervention; therefore this does not meet our definition of 'persisting' effects of the intervention</li> </ul>		

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Unclear risk	Recruitment of study participants and assignment to study groups were carried out by the researcher
Blinding of participants	High risk	Not possible to blind
Blinding of personnel	High risk	Not possible to blind
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Attempted blinding of neuropsychologist for neglect measures and others for ADL



Karner 2019 (Continued)		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost 8 (17%), but reasons given and not markedly different between groups
Selective reporting (reporting bias)	Low risk	Outcomes reported in adequate detail
Other bias	Low risk	Nothing obvious

# **Katz 2005**

Study characteristics			
Methods	Parallel control trial Setting: rehabilitation hospital, Israel.		
Participants	19 patients with first right hemispheric stroke and persistent USN VR group = 11, control group = 8 Mean age, years: VR group = 62, control = 63 Sex (men/women): VR = 7/4, control = 5/3 Hemisphere: right Mean days between stroke and treatment: VR = 48, control = 36		
Interventions	A street crossing virtual environment was programmed via Superscape's 3D Webmaster and run on a desktop computer, with successively graded levels of difficulty that provide users with an opportunity to decide when it is safe to cross a virtual street. The level of difficulty was graded by the number and velocity of cars that approach the pedestrian cross-walk, as well as the side (right or left) from which they approach, thus increasing attentional demands on the user. In addition other destructors were included such as commercial signs, blinking lights, etc.		
	Virtual reality training protocol continued for 4 weeks, with 3 sessions per week, each of 45 minutes' duration, for a total of 9 hours. Timing of the control group computer scanning training protocol was identical. ?? Is this a control group or another active intervention?		
Outcomes	<ul> <li>Star cancellation from the Behavioral Inattention Test (BIT).</li> <li>Mesulam Symbol Cancellation test</li> <li>ADL checklist</li> <li>FIM total</li> </ul>		
	All taken immediately post intervention with no longer-term follow-up		

# Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	First 8 participants were randomly assigned to either VR training group (experimental) or computer visual scanning tasks group (control); remaining 3 participants were assigned to VR group to increase the number of participants who experienced the experimental condition
Allocation concealment (selection bias)	High risk	See above



Katz 2005 (Continued)		
Blinding of participants	High risk	No information about blinding provided
Blinding of personnel	High risk	No information about blinding provided
Blinding of outcome assessment (detection bias) All outcomes	High risk	No information about blinding provided
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Unclear risk	Unclear
Other bias	High risk	Multiple outcomes, none primary; no multiple testing adjustment. 1-tailed test not justified

# Kerkhoff 2012

Study characteristics	
Methods	RCT Setting: rehabilitation clinic, Germany
Participants	6 stroke patients with left-sided visual and auditory neglect who were "enrolled in our clinic"  Mean age, years: optokinetic stimulation (OKS) group = 62.3, SCAN group = 56.3  Inclusion criteria: single right-hemispheric lesion due to stroke (infarction or haemorrhage); evidence of left-sided visual neglect in at least 2 out of 4 screening tests, pathological rightward shift in ASMP
Interventions	Group 1 - OKS: repetitive leftward OKS stimulation with active pursuit eye movements. Participants were instructed to look at a computer screen (17") and make pursuit eye movements to the left (contralesional) side while looking at moving dot displays of 100 to 200 stimuli (mean velocity = 5° to 30°)
	Group 2 - visual scanning training: participants viewed identical visual stimuli on the same computer monitor as the OKS group, but these patterns were always static. These participants were instructed to make systematic scanning eye movements to the left side and explore visual stimuli on the screen, just as in conventional visual scanning therapy
	Both groups received 20 treatment sessions of around 50 minutes, 5 sessions per week, 1 session per workday
Outcomes	Auditory neglect: ASMP
	Visual neglect: measured by the following 3 tests: number cancellation, horizontal line bisection, and paragraph reading
	All taken immediately post intervention with no longer-term follow-up
Notes	Data presented as single subjects in graph form. This paper contains 2 studies; study 1 was excluded, as it did not report outcomes of interest
Risk of bias	
Bias	Authors' judgement Support for judgement



Kerkhoff 2012 (Continued)		
Random sequence generation (selection bias)	High risk	Drawing lots, no possibility of validation
Allocation concealment (selection bias)	High risk	"The patients were randomly allocated to either an OKS (N = 3) or a SCAN (N = 3) treatment group by having a person neither involved in the study nor associated with the clinic draw concealed papers from an envelope containing 6 sheets of paper stating either 'OKS' or 'SCAN'"
Blinding of participants	High risk	Not possible to blind
Blinding of personnel	High risk	Not possible to blind
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not stated whether outcome assessor was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	6 participants recruited; none lost
Selective reporting (reporting bias)	Low risk	No suggestion of this
Other bias	Low risk	No suggestion of this

# Kerkhoff 2014

Study characteristics	5
Methods	RCT; 2-group parallel Setting: Germany
Participants	Single right-hemisphere stroke, visual neglect in 2 screening tests (horizontal line bisection, number cancellation), and ability to execute daily neglect training for 30 minutes  Age, mean, years (SD): intervention $1 = 64$ (3), intervention $2 = 64$ (3)  Sex (men/women): intervention $1 = 7/5$ , intervention $2 = 8/4$ Hemisphere damaged: right  Time since stroke, mean (SD), days: intervention $1 = 37$ (5), intervention $2 = 30$ (4)
Interventions	Participants received visual scanning training (VST) or smooth pursuit training (SPT). During VST, patients viewed stationary displays of stimuli implemented in the same software. Stimuli were geometrical objects (circles, triangles, squares, etc.), stars, letters, or digits (see Figure 1 for an example). The number of stimuli (5 to 60) and their size (1° to 2.5°), colour, and spatial arrangement were varied (systematic vs unordered, with/without line numbering, with/without subsidiary horizontal reference lines, with/without a red vertical "anchor line" on the leftmost side of the display). Patients were trained to scan systematically from left to right and from top to bottom, naming all objects, or counting certain stimuli. The therapist kept the patient's head in a straight position for either treatment to promote eye instead of head movement. She watched continuously from the side whether the patient made smooth pursuit eye movements to the contralesional side (SPT) or saccadic eye movements (VST). If patients did not execute appropriate eye movements, instructions were repeated. If patients were tired, a short break (2 minutes) was given, adjusted to patients' individual requirements  During SPT, stimuli were random displays of 20 to 60 identically coloured and sized squares, moving
	horizontally from right to left at constant velocity, providing a coherent stimulus pattern (see Figure 1 for exemplary display). The colour, size (1° to 2.5°), and velocity (3.1° to 12.6°/s) of the stimuli were var-



# Kerkhoff 2014 (Continued)

ied from time to time. The patient was encouraged to conduct smooth pursuit eye movements, repeatedly following the stimulus pattern from right to left, without head movement

# Outcomes

- Functional neglect index (finding objects, picture search, line bisection, gaze orientation).
- Ratings of ADL by treatment-blinded caregivers
- B

Participants were followed up 2 weeks post intervention; therefore this does not meet our definition of 'persisting' effects of the intervention

# Notes

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	"Randomly allocated to SPT or VST (by a person not involved in the study who drew lots from a sealed envelope)"
Allocation concealment (selection bias)	High risk	See above. No validation possible
Blinding of participants	High risk	Not possible
Blinding of personnel	High risk	Not possible
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Attempted assessor blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	Consistent reporting
Other bias	Low risk	Nothing obvious

# Kim 2011

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St	ud	v	ch	ar	ac	te	ris	tics

Study characteristic	•
Methods	RCT Setting: rehabilitation department, South Korea
Participants	Stroke patients who were diagnosed with unilateral spatial neglect VR group = 12, control = 12  Mean age, years: VR = 62, control = 67  Sex (men/women): VR = 9/3, control = 5/7  Mean days from stroke to treatment: VR = 23, control = 26  Exclusions: patients with severe cognitive impairment or aphasia who could not understand instructions given by therapists, patients with such severely damaged sitting balance that they could not sit down on a chair with a back and armrests, patients with problems in cervical movement due to orthopaedic impairment, patients who could not recognise objects on a computer screen due to severely damaged eyesight



# Kim 2011 (Continued)

# Interventions

Physical therapy, occupational therapy, and cognitive therapy of the same intensity and time were applied to all patients. In addition, 2 occupational therapists conducted treatment for unilateral spatial neglect. One therapist conducted conventional rehabilitation programmes for the control group, such as visual tracking, reading and writing, drawing and copying, and puzzles; the other conducted virtual reality treatment on the VR group. Such treatments were applied for 30 minutes a day, once a day, 5 days a week for 3 weeks. The VR system consists of a monitor, a video camera, computer-recognising gloves, and virtual objects. The video camera recognises movements

# Outcomes

- · Star cancellation test
- · Line bisection test
- CBS
- BI

All taken immediately post intervention with no longer-term follow-up

# Notes

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details given
Allocation concealment (selection bias)	Unclear risk	No details given
Blinding of participants	High risk	Unlike other double-blind assessments, guardians knew about treatment of their patients, which means this study was not completely double-blind
Blinding of personnel	High risk	Not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	"Those tests were conducted by a therapist who was not involved in the treat- ment and did not know the state of the patients" However, CBS was filled out by guardians under supervision of the therapist
Incomplete outcome data (attrition bias) All outcomes	High risk	Only "seven subjects in the control group and three subjects in the VR group accurately performed the line bisection test and were included in the analysis"
Selective reporting (reporting bias)	Low risk	Outcomes were reported with equal detail
Other bias	High risk	9 women and 3 men in VR groups; differences not accounted for

# Kim 2013

Study characteristics	
Methods	RCT Setting: Korea, hospital
Participants	First-time cerebral stroke in the cortical or subcortical area; right cerebral ischaemic or haemorrhagic stroke. Scored > 15% deviation to the right from centre in line bisection  Age, years: intervention $1 = 68.6 \pm 14.4$ , intervention $2 = 64.1 \pm 10.3$ , control = $68.3 \pm 6.5$ Number of men: intervention $1 = 5$ , intervention $2 = 4$ , control = $6$



# Kim 2013 (Continued)

Time since stroke, days: intervention  $1 = 14.2 \pm 4.7$ , intervention  $2 = 14.3 \pm 3.6$ , control  $= 16.4 \pm 8.5$ 

### Interventions

A physiatrist performed rTMS using a Magstim Super Rapid Magnetic Stimulatora with a 70-millimeter, air-cooled coil in the shape of a figure 8. The coil was held with the handle posterior and oriented sagittally and positioned on the scalp according to the 10e20 system, which is an internationally recognised method to describe the relation between location of scalp electrodes and underlying areas of the cerebral cortex

The rTMS stimulation site corresponded with position P3, which is localised over the left PPC, and position P4, which is localised over the right PPC. Patients were seated in a comfortable chair with foam earplugs. We determined the motor threshold of the right first dorsal interossei muscle as the stimulus intensity required to produce motor-evoked potentials of more than 100 microvolt peak-to-peak amplitude in 3 of 5 consecutive trials. For low-frequency rTMS, 1-Hz stimulation at a 90% motor threshold was delivered over the left (non-lesioned) P3 in 4 trains of 5-minute duration, each separated by 1 minute. This resulted in a total stimulation period of 20 minutes and total delivery of 1200 pulses

For high-frequency rTMS, 10-Hz stimulation at a 90% motor threshold was delivered over the right (lesioned) P4 in 20 trains of 5 seconds' duration, each separated by 55 seconds. This resulted in a total stimulation period of 20 minutes and total delivery of 1000 pulses

### Outcomes

- MVPT
- CBS
- Line bisection
- Star cancellation

Measured immediately post treatment

# Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number tables
Allocation concealment (selection bias)	Unclear risk	No information
Blinding of participants	Unclear risk	Outcome group: all Use of sham but no evaluation of success nor discussion of process to ensure blinding
Blinding of personnel	High risk	Not practical to blind
Blinding of outcome as- sessment (detection bias) All outcomes	Unclear risk	"All evaluations were performed by a single experienced occupational thera- pist who was blinded to the study" No discussion of process to ensure success
Incomplete outcome data (attrition bias) All outcomes	High risk	6 participants excluded from all results due to early discharge, which may plausibly be treatment related
Selective reporting (reporting bias)	Low risk	All outcomes reported in equal detail
Other bias	Unclear risk	Unclear



# Kim 2015

Study characteristics	
Methods	RCT, parallel 2-group Setting: Korea, hospital
Participants	Patients with hemi-spatial neglect among hospitalised patients with stroke Age, years: intervention $1=62.3\pm11.2$ , intervention $2=66.7\pm6.9$ Men/women: intervention $1=10/9$ , intervention $2=5/10$ Time since stroke, months: intervention $1=19.11\pm12.39$ , intervention $2=15.73\pm12.33$
Interventions	Group 1 had low-frequency rTMS only once. rTMS was conducted a total of 1200 times for 20 minutes a the frequency of 1 Hz in the left P3 side, based on International 10–20 EEG Electrode System with 90% intensity of resting motor threshold  Group 2 had a total of 10 times of rTMS, 5 times a week, for 2 weeks. rTMS are per intervention group 1
Outcomes	<ul> <li>Line bisection test</li> <li>Letter cancellation test</li> <li>Ota's task</li> </ul> Measured immediately post treatment

Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"We randomly divided the patients into two groups"
Allocation concealment (selection bias)	Unclear risk	No mention
Blinding of participants	High risk	No indication of attempt to blind
Blinding of personnel	High risk	No indication of attempt to blind
Blinding of outcome assessment (detection bias) All outcomes	High risk	No indication of attempt to blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	No indication of attrition
Selective reporting (reporting bias)	Low risk	Outcomes reported in equal detail
Other bias	Low risk	Nothing obvious



# Kim 2018

Study characteristics	
Methods	RCT, 3-group parallel Setting: Korea, 'patients receiving rehabilitation'
Participants	Patients with left hemi-spatial neglect due to first stroke, right hemisphere stroke, no cognitive decline muscle strength > 2, no visual defect, sitting balance to perform intervention Age, years: intervention $1 = 70.3 \pm 9.6$ , intervention $2 = 66.6 \pm 12.2$ , intervention $3 = 62.5 \pm 16.5$ Men/women: intervention $1 = 5/5$ , intervention $2 = 5/5$ , intervention $3 = 5/5$ Time post stroke, days: intervention $1 = 19.2 \pm 13.4$ , intervention $2 = 24.5 \pm 22.4$ , intervention $3 = 15.3 \pm 9.8$
Interventions	Intervention 1: rTMS therapy with a coil stimulator shaped like a figure 8 at diameter of 70 mm using MagPro (MagVenture Inc., Farum, Denmark). Session included 900 stimuli applied over contralesional posterior parietal cortex at an intensity of 95% motor thresholds and a frequency of 0.9 Hz
	Intervention 2: patients in the robot group received additional treatment for hemi-spatial neglect using a rehabilitation robot (Neuro-X; Apsun Inc., Seoul, Korea) for upper limbs. During robot therapy, patients sat on the right side of the robot with the robot's monitor on their left side. Robot therapy programme was conducted through games that induced passive and active assistive range of motion of the wrist, elbow, and shoulder joints. These games consisted of 2 isometric exercises and 2 range of motion exercises. The 2 isometric exercises used wrist extension and wrist flexion, in which the default muscle strength for wrist extension and wrist flexion were measured quantitatively before the start of the game, so the game was continued only when a force exceeding a certain level of strength was applied
	Intervention 3: rTMS + upper limb robot
Outcomes	<ul> <li>Motor-Free Visual Perception Test (MVPT-3)</li> <li>Line bisection test</li> <li>Star cancellation test</li> <li>Albert's test</li> <li>Catherine Bergego Scale (CBS)</li> <li>Mini-Mental State Examination (MMSE)</li> <li>Korean version of the Modified Barthel Index (K-MBI)</li> </ul> Measured before and after intervention

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation table
Allocation concealment (selection bias)	High risk	No mention of concealment, but blocks of size 3 highly predictable
Blinding of participants	High risk	No sham for either intervention
Blinding of personnel	High risk	No sham for either intervention
Blinding of outcome assessment (detection bias) All outcomes	High risk	"Occupational therapist who did not directly participate in the treatment", but patient clearly aware



Kim 2018 (Continued)		
Incomplete outcome data (attrition bias) All outcomes	High risk	Early discharges excluded from analyses
Selective reporting (reporting bias)	Low risk	Outcomes reported in equal detail
Other bias	Low risk	Nothing obvious

# **Koch 2012**

Study characteristics	5
Methods	RCT, 2-group parallel Setting: Italy, neurorehabilitation unit
Participants	Right hemisphere subacute ischaemic stroke and affected by hemi-spatial neglect, as confirmed by radiological (CT or MRI) and clinical examination
Interventions	A MagStim Super Rapid magnetic stimulator (Magstim Company, Whitland, Wales, UK), connected with a figure-of eight coil with a diameter of 70 mm, was used to deliver cTBS. In every session; 3-pulse bursts at 50 Hz repeated every 200 msec for 40 s were delivered at 80% of the active motor threshold (AMT) over the left PPC (600 pulses). We used a neuronavigation system (Softaxic, E.M.S., Bologna, Italy) to precisely position the coil over the left PPC, using individual anatomical MRI; this technique has been described in detail previously. Individual coordinates of each stimulation site were normalised a posteriori into the Montreal Neurological Institute (MNI) coordinate system and averaged. To target the left PPC, the coil was positioned in the angular gyrus (AG) in the posterior portion of the inferior parietal lobule (IPL), close to a posterior part of the adjoining intraparietal sulcus (cIPS). The centre of the coil was positioned tangentially to the skull, with the handle pointing downward and slightly posteriorly. Sham stimulation was delivered with the coil angled at 90°, with only the edge of the coil resting on the scalp. Stimulus intensity, expressed as a percentage of maximum stimulator output, was set at 80% AMT for the FDI, inducing the same acoustic sensation as for real TBS
Outcomes	• BIT
	Assessed pre-intervention and post intervention and at 2-week follow-up
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Patients were randomly assigned to real or sham"
Allocation concealment (selection bias)	Unclear risk	"Patients were randomly assigned to real or sham"
Blinding of participants	Low risk	"Patients were unaware of their group assignment; all were only told that they had been enrolled in rehabilitation treatment for their spatial attention deficits"
Blinding of personnel	High risk	Inevitable that providers were aware



Koch 2012 (Continued)		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Therapists were also blinded in respect to the type of intervention" "Evaluation of BIT was performed by blinded raters" Unclear scope for contact between study personnel, therapists, and raters. And no discussion of effectiveness of blinding effort
Incomplete outcome data (attrition bias) All outcomes	Low risk	One post-randomisation exclusion from each group due to protocol violation. Unlikely to affect clear results
Selective reporting (reporting bias)	Low risk	Several apparently data-driven analyses, but all outcome component scores tabulated
Other bias	Low risk	Nothing obvious

# Kutlay 2018

Study characteristics			
Methods	Assessor-blinded randomised controlled clinical study.		
	Setting: inpatient reha	bilitation, Turkey	
Participants	"stroke patients with UN who were admitted for rehabilitation in the Department of Physical Medi- cine and Rehabilitation, Ankara University Medical Faculty, from February 2013 to December 2014 were screened"		
	Age, years: interventio	n = 62 (54.5 to 67), control = 63 (54 to 70.75)	
	Sex: intervention = 15/	10 (m/f), control = 17/11	
	Hemisphere damaged: right		
	Time since stroke, months: intervention = 4 (2 to 10.5), control = 3 (2 to 4.75)		
Interventions	The Kinesthetic Ability Trainer (KAT; LLC, Vista, CA, USA) is a balance and training system that provides visual feedback to control body posture on a movable platform. The KAT system works by altering the stability of a movable platform, on which an individual stands, and/or by varying the degree to which the individual alters his or her base of support by shifting weight in response to visual feedback provided by a personal computer, in addition to the therapist's guidance, encouragement, and feedback. Participants in the intervention group received a 4-week balance training programme 5 times per week with session duration of 20 to 30 minutes. Control participants received usual care		
Outcomes	1. Full BIT		
	2. FIM		
	All taken immediately post intervention with no longer-term follow-up		
Notes			
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Low risk	An independent research assistant (who was unaware of the baseline data) carried out the randomisation procedure with a block size of 4 using computer software	



Kutlay 2018 (Continued)		
Allocation concealment (selection bias)	Low risk	Sequentially numbered, opaque, sealed envelopes were used to conceal the randomisation sequence
Blinding of participants	High risk	Impossible to blind
Blinding of personnel	High risk	Impossible to blind
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The rehabilitation team evaluating patients was blinded to group assignment
Incomplete outcome data (attrition bias) All outcomes	High risk	During the study, 4 patients from the control group and 7 from the KAT group dropped out for several reasons. A final total of 28 patients in the control group and 25 in the KAT group completed the study
Selective reporting (reporting bias)	Low risk	Outcomes were reported with equal detail
Other bias	Low risk	Nothing obvious

# Learmonth 2020

Study characteristics	
Methods	Prospective randomised open blinded endpoint (PROBE) trial; feasibility study Setting: Scotland, inpatient hospital, expanded recruitment to outpatients due to low recruitment
Participants	Participants were eligible if they were aged 18 years or older; had a clinical diagnosis of stroke with brain imaging compatible with right hemisphere intracerebral haemorrhage or ischaemic stroke; had a modified Rankin score estimated as 0 to 3; and had persistent hemi-spatial neglect ≥ 4 weeks post stroke  Age, median, years: intervention 1 = 66, intervention 2 = 67, intervention 3 = 70, control = 62  Men/women: intervention 1 = 3/3, intervention 2 = 4/2, intervention 3 = 2/4, control = 4/2  Time post stroke, median, days: intervention 1 = 282, intervention 2 = 47, intervention 3 = 60, control = 268
Interventions	Intervention 1: transcranial direct current stimulation (tDCS)  Intervention 2: behavioural training. Participants were seated at a table in front of a mat measuring 14
	× 30 cm. Nine black squares labelled A through I were positioned on the left side of the mat, and were used as starting positions for each trial. Three wooden rods of different lengths (50, 75, and 100 cm - al 1.1 cm in diameter) were placed in front of the participant. At the start of each trial, participants were asked to pick up one of the rods (short, medium, or long) and place the left end of the rod at 1 of the 9 starting positions on the mat. They then were instructed to pick up the rod at its midpoint with their right hand using a pincer grip, and to assess whether the rod was balanced at its midpoint. If they felt that it was unbalanced, they were instructed to place the rod back down at its starting position and to adjust their grip (usually leftwards) until the rod was balanced. Training was intended for 15 min and involved roughly 54 trials
	Intervention 3: both tDCS and behavioural training were administered simultaneously. Behavioural training began as soon as the tDCS equipment had fully ramped up to 1 mA $$
	Control: control training was identical to behavioural training, but participants were instructed to lift up the rod at its rightmost end rather than at its midpoint. They thus performed a motor task, yet did not receive corrective proprioceptive nor visual feedback on their actions
Outcomes	• BIT



# Learmonth 2020 (Continued)

- · Line bisection
- Balloons test
- **Broken Hearts Test**
- Visual field test
- SIS
- Beck Depression Inventory

Assessed pre-intervention and post intervention and at 6-month follow-up

# Notes

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Conducted by independent trials unit (Robertson Centre)
Allocation concealment (selection bias)	Low risk	Conducted by independent trials unit (Robertson Centre)
Blinding of participants	High risk	"Participants and the Research Assistant delivering the treatment were aware of the group allocation"
Blinding of personnel	High risk	"Participants and the Research Assistant delivering the treatment were aware of the group allocation"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Allocations were concealed from outcome assessors. This concealment was maintained throughout the trial"  No further detail on or discussion of success
Incomplete outcome data (attrition bias) All outcomes	High risk	10 (42%) lost before follow-up
Selective reporting (reporting bias)	Low risk	All data reported
Other bias	Low risk	Nothing obvious

# Li 2017

Study ch	aracte	ristics
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Study characteristic	S
Methods	RCT Setting: China, rehabilitation unit
Participants	(1) People between 40 and 70 years old; (2) course of disease 2 to 4 months; (3) for the first time, brain CT or MRI confirmed that lesion was located in the right hemisphere of the brain; (4) by line bisection test, line segment marking test, bell drawing test, plane graph copying test, and other unilateral space neglect scale and clinical examination to confirm the existence of left space neglect; (5) patients' condition is stable, clear, focused, and directional, and there are no obvious memory, emotional, or intellectual barriers. Patients understand the requirements of the examination and are able to cooperate; All are right-handed, with no obvious visual impairment Age, years: intervention = $40 \text{ to } 67 (53 \pm 9)$ , control = $40 \text{ to } 69 (53 \pm 8)$ Sex (men/women): intervention = $17/3$ , control = $18/2$



Li 2017 (Continued)
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Time post stroke, months: intervention = 2 to 4 (2.9  $\pm$  0.6), control = 2 to 4 (2.9  $\pm$  0.7)

# Interventions

Acupuncture on "Xingshen Yisui Kaiqiao" acupoints

Acupoint selection: Bai Hui, Si Shen Cong, Shen Ting, Ben Shen, Shen Men, Tong Li, Tai Xi, Da Zhong, Da Ling, Nei Guan. On the basis of the 8 acupoints of Bai Hui, Si Shen Cong, Shen Ting, Ben Shen, about 10 acupoints were alternately taken from upper and lower limbs on both sides every day. All acupoints were treated with 0.30 mm × 25 mm disposable acupuncture needles. Head acupoints were applied by the oblique needle shallow acupuncture method, and the needle body was inserted straightly. The needle was retained for 30 minutes

Control group received treatment as usual

### Outcomes

- · Line bisection test
- Line cancellation test
- · Bell drawing test
- · Figure copying test

Assessed pre-intervention and post intervention

# Notes

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Prepared by statistics team
Allocation concealment (selection bias)	Low risk	Sequentially numbered, sealed opaque envelopes
Blinding of participants	High risk	No blinding
Blinding of personnel	High risk	Not practical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinded outcome assessors; no info on success of process
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	Outcomes reported in equal detail
Other bias	Low risk	Nothing obvious

# Luukkainen-Markkula 2009

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Methods RCT, single site; comparing 2 active interventions

Setting: Finland



# Luukkainen-Markkula 2009 (Continued)

### **Participants**

12 participants with left hemi-spatial neglect due to a first single right hemisphere stroke occurring a maximum of 6 months previously

Experimental 1: n = 6, experimental 2: n = 6

Number lost to follow-up: none; however data for 1 person from each group for some measures and time points were missing

There were baseline differences in the CBS OT score - arm activation group, mean 9.4 (SD 2.3) and visual scanning group, mean 13.5 (SD 7.8) - based on data from 10 participants

Age, years, mean (SD): experimental 1 = 59.5 (8.4), experimental 2 = 57.8 (11.8) Sex (male/female): experimental 1 = 3/3, experimental 2 = 2/4

Side of damage: right hemisphere stroke

Method of diagnosing stroke: CT or MRI; neurologist and radiologist

Method of diagnosing neglect:

For acute phase (< 3 months post stroke) – at least 2 of the following: score ≤ 100 on BIT conventional subtests (BIT C); ≥ 2 of the BIT subtests under the cutoff point; or CBS OT score of 10 to 30 points

For subacute phase (3 to 6 months post stroke) – at least 2 of the following: score  $\leq$  129 on BIT C subtests;  $\geq$  1 BIT C subtest under the cutoff; or CBS OT score  $\geq$  2

Time post onset, days: experimental 1 = 81.0 (64.6), experimental 2 = 95.5 (63.2)

Inclusion criteria: diagnosis of single right hemisphere stroke within 6 months, right-handed with no other co-existing disease causing cognitive decline.

Visual sensory deficit (method of assessment): experimental 1 = 1 with complete hemianopia, experimental 2 = 3 with complete hemianopia

# Interventions

Arm activation training

20 to 30 hours of left arm activation – amount determined by observation of subjective needs of individuals

Content determined by individual WMFT performance: 1 patient had constraint-induced movement therapy (intensive exercise of affected arm while unaffected arm was restrained with a sling). 5 patients without sufficient left arm mobility had modified arm activation therapy, all with left arm in left space and right arm resting on right side (50% passive arm activation FES with a glove/or for spasticity stretching by a therapist + 50% voluntary shoulder motor training in push-pull equipment in left hemi-space) vs

Visual scanning training: 10 hours traditional visual scanning training – aimed for 1 hour,  $4\times$ /week of visual scanning combined with 2 daily physiotherapy sessions + 1 hour per day of OT/group therapy achieved for 1 hour,  $5\times$ /week during 3 weeks

Content: 3 procedures (half-hour on 1, then half-hour on 2 or 3)

- Visual scanning from a wide video screen (pictures, facial expressions, words, calculations), increasing difficulty, after delay scanning cued by visual anchors and verbal cues
- · Reading and copying written material
- · Copying drawings from dot matrix model on the left to one on the right

Profession of intervention provider: arm-activation - constraint-induced movement therapist

Visual scanning - clinical psychologist

# Outcomes

Several outcomes were measured. These are given along with details (where provided) of the time point of measurement, and the profession of the person performing the measure

Beck Depression Inventory (self-completed) at baseline and at follow-up



### Luukkainen-Markkula 2009 (Continued)

- FIM (to assess general functional status) assessments at pre-rehabilitation and post rehabilitation
- BIT conventional subtests (assess visual neglect) time point unclear
- · CBS (to assess behavioural neglect) by OT
- · Modified Motor Assessment Scale (to assess motor functions) by a physiotherapist; unclear when
- Wolf Motor Function Test (to assess affected hand motor performance) scored by trained person not involved in other parts of the study
- Hand grip force of affected hand also recorded; unclear by whom or when
- Neuropsychological assessment by neuropsychologist who did not participate in rehabilitation. All but handedness were conducted at baseline, post rehabilitation, and at follow-up
- Edinburgh inventory (handedness) at baseline only
- 4 WAIS-R subtests (to assess verbal and visuospatial abilities): digit span, picture completion, similarities, and block design
- WMS-R visual reproduction, immediate and delayed recall
- List learning test (modified Rey Auditory Verbal Learning Test to assess verbal learning and recall)
- Motor learning and fluency test (3 minutes writing S and mirror image of S scored as letters and perseveration errors)

Also reported 1 person with recurrent stroke

# Notes

"Sufficient amount of active or passive left arm activation in the left half space combined with simultaneous visual tasks or while doing daily activities is likely to ameliorate visual and behavioural neglect"

Confounding factors may be due to baseline imbalance on CBS or to Beck Depression Inventory (effect on engagement in therapy) and multiple assessments

Group 1 received a lot more arm activation than Group 2 during visual scanning training. Group 2 received more OT and group therapy than group 1. Correspondence with study author states this difference is to keep total hours of therapy received by participants in each group comparable

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Personal communication with study author: "the method of randomization was carried out as follows: A clerk of the rehabilitation ward offered a pair of brown envelopes to an entering patient. One envelope included the AA group and the other envelope contained the VS group. The first patient picked one of the envelopes and the following patient entering the study was randomized automatically into the other group. This arrangement of paired randomization was necessary for the resources of the ward." Consequently allocation of the second patient would be known to researchers
Allocation concealment (selection bias)	High risk	See above
Blinding of participants	High risk	Not possible
Blinding of personnel	Unclear risk	Unclear
Blinding of outcome assessment (detection bias) All outcomes	High risk	Of the 13 assessments, a number were carried out by those who did not participate in rehabilitation. These outcome measures were visual and behavioural neglect, BIT C, and CBS. However, although assessments were carried out by someone who did not participate in rehabilitation, these people were not blinded to treatment group
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data for 1 person from each group for some measures and time points were missing



Luukkainen-Markkula 2009 (Continued)					
Selective reporting (reporting bias)	Unclear risk	Unclear			
Other bias	High risk	There were baseline differences between groups, with CBS and Beck Depression Inventory scores appearing higher and more variable for visual scanning group. There was no adjustment for baseline differences for CBS			

# Machner 2012

RCT Setting: hospital, Germany
23 patients with left spatial neglect after acute (< 14 days) right hemisphere stroke Experimental = 11, control = 10  Diagnosis of neglect: neglect if patients showed pathological performance on ≥ 2 tests of a neuropsychological test battery consisting of the following paper–pencil tests: line bisection, star cancellation, text reading, Bells cancellation, and Ogden figure copying task  Age, years, mean (SD): experimental = 69 (3), control = 39 (3)  Sex (men/women): experimental = 8/3, control = 6/4  Days between stroke and treatment, mean (SD): experimental = 3 (1), control = 5 (1)  ADL before treatment CBS, mean (SD): experimental = 17 (3), control = 18 (3)  Exclusion: previous stroke, neurodegenerative disease, inability to give informed consent
Patients in the treatment group received HEPOKS in addition to usual stroke care (physio, speech, and occupational therapy), whereas patients in the control group had usual care only. HEP was applied by spectacle frames containing non-corrective lenses for which the right half was patched with dark non-translucent tape. Participants were instructed to wear the glasses all day for 7 days and to remove them only for the OKS treatment sessions. Investigators, care providers, and patients' relatives regularly checked on correct use of the glasses. Daily OKS sessions (15 minutes each) were applied at the bedside. Seventy coloured geometric objects were coherently moving on an 18.4" notebook monitor from right to left at varying speeds (8° to 12°/s)
2 primary outcome measures: (1) mean performance (accuracy) on neuropsychological test battery, (2) neglect-related functional disability measured by Catherine Bergego Scale Secondary outcome measures were Barthel Index, modified Rankin scale, National Institutes of Health Stroke Scale Participants were assessed at 3 time points (Figure 1): baseline (Day 1), post treatment (Day 8), and follow-up (Day 30)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The principal investigator sent a fax including identification parameters of the eligible patient (no name and initials) to the IMBS. A staff member at the IMBS with no clinical involvement in the trial randomised the patient online using a computerised permuted block technique with varying block size and assigned the unique patient identification number (PID). The randomisation result and the PID were documented on the fax and sent back to the investigator
Allocation concealment (selection bias)	Low risk	See above



Machner 2012 (Continued)		
Blinding of participants	High risk	Due to the nature of a cognitive intervention trial, both investigators and patients were aware (not "blind") of the allocated arm throughout the study
Blinding of personnel	High risk	See above
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unclear if blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Low risk	Secondary outcomes are in data supplement
Other bias	Unclear risk	At baseline, study groups did not differ significantly in demographic, clinical, and neuropsychological characteristics, except for 1 paper–pencil subtest (Table). Lesion overlap analyses are provided in Figure II in the online-only Data Supplement

# Mancuso 2012

Study characteristics	
Methods	Setting: outpatient, Italy
Participants	Outpatients with left visual neglect resulting from right hemisphere vascular lesion. All patients were right-handed, had left hemiplegia or hemiparesis from ischaemic or haemorrhagic brain injury. All patients were selected in accordance with tests for neglect; those who had abnormal scores on $\geq 2$ tests were enrolled. No patient had visual field deficits, which could preclude the proper performance of tests or exercises, or severe symptoms of cognitive impairment (MMSE score $\geq 21$ of total 28, excluding tests in reading and drawing)  Age, years: intervention = 70.2 (8.8), control = 62.3 (13.1)  Sex (men/women): intervention = 7/6, control = 4/5  Hemisphere damaged: right  Mean time since stroke (SD), days: intervention = 180.153 (301.485), control = 129.00 (132.799)
Interventions	Intervention group received prism adaptation training with 5 rehabilitation sessions, lasting about 30 minutes each, from Monday to Friday for 1 week in the morning, by the same investigator, at each centre. Control group received the same treatment with neutral lenses
Outcomes	<ul> <li>Albert test</li> <li>Bells test</li> <li>Line orientation</li> <li>4 BIT-B subtest (drawing, line bisection, card dealing, object search)</li> </ul> All taken immediately post intervention with no longer-term follow-up
Notes	
Risk of bias	
Bias	Authors' judgement Support for judgement



Mancuso 2012 (Continued)		
Random sequence generation (selection bias)	Unclear risk	"After enrollment, patients were randomized by pilot center and assigned to two different groups 'A' or 'B'"
Allocation concealment (selection bias)	High risk	Randomisation done by 'pilot centre', suggesting high risk
Blinding of participants	High risk	In no case was specific information on the lens applied provided to the patient. Frames used for prismatic lenses were identical to those for neutral lenses. Nevertheless, patients likely to be able to tell that glasses are not doing anything. No assessment of success of 'blinding' attempt
Blinding of personnel	High risk	No attempt at blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessor not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	"Of the 29 patients enrolled, there were 6 dropouts caused by deterioration in health, and one outlier, that is a patient who presented very different statistical characteristics to the rest of the group." Excluding outlier without justification
Selective reporting (reporting bias)	Low risk	Similar reporting detail for all mentioned outcomes
Other bias	Low risk	No evidence of this

# Mizuno 2011

Study characteristics	5
Methods	RCT; multi-centre, double-blind Setting: rehabilitation departments, Japan
Participants	38 participants (444 screened) Experimental group (prisms): n = 20; control group: n = 18 Recruited from rehabilitation departments from 8 hospitals in Japan Age, years, mean (SD): experimental = 66.0 (11.5), control = 66.6 (7.7) Time from stroke, days, mean (SD): experimental = 67.1 (18.4), control = 64.4 (20.9) Inclusion criteria: within 3 months of first-ever right hemisphere stroke, 42 to 89 years old, neglect as assessed by BIT behavioural test Exclusion criteria: unable to sit in wheelchair, aphasia or cognitive impairment resulting in inability to understand task, inability to understand Japanese, impaired vision or hearing, impaired right upper limb, previous brain injury 34 participants completed intervention and follow-up; 4 dropouts (1 control, 3 prisms) - 2 stroke relapse, 1 refused, 1 with delirium 31 participants completed follow-up BIT
Interventions	2 daily training sessions, lasting 20 minutes, 5 days per week, for 2 weeks, for a total of 20 sessions Training - pointing at targets, whilst sitting at a table Experimental group: prisms (shifting visual field 12° to right, Fresnel lens). Pointing task - 30 times with out prisms; 90 times with; 60 times without Control group: neutral plastic glasses. Pointing task as for experimental group Routine stroke rehabilitation provided as usual
Outcomes	• BIT



# Mizuno 2011 (Continued)

- CBS
- FIM
- Stroke Impairment Assessment Set

Outcomes were recorded at baseline, after the 2-week intervention, and immediately before hospital discharge. We used immediate effects only for comparability with other studies

# Notes

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomly allocated to intervention or control group, with a computerised block randomisation scheme
Allocation concealment (selection bias)	Low risk	Computerised block randomisation, with pre-stratification according to BIT behavioural test (dichotomised to ≥ 55 or < 55) and participating hospital. All data were sent to the central office at the Department of Preventive Medicine and Public Health, School of Medicine, Keio University, before allocation assignment
Blinding of participants	High risk	Prism lenses; sham control not convincing
Blinding of personnel	High risk	See above
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Outcome assessor was masked to treatment allocation and otherwise uninvolved in the participant's treatment"; no evidence of success of this though
Incomplete outcome data (attrition bias) All outcomes	High risk	3 missing in prism group, 1 in control group
Selective reporting (reporting bias)	High risk	SIAS reported less
Other bias	Low risk	None obvious

# Nyfeller 2019

Study	char	acto	ricticc

Study Characteristics	
Methods	RCT
	Setting: Switzerland, neurorehabilitation centre
Participants	60 patients with a first, right hemispheric stroke participated in the study Age, years: sham = $70.6 \pm 11.44$ , 8cTBS = $67.8 \pm 10.13$ , $16$ cTBS = $74.3 \pm 10.23$ Sex (men/women): sham = $7/3$ , 8cTBS = $5/5$ , $16$ cTBS = $6/4$ Time post stroke, days: sham = $25.8 \pm 11.26$ , 8cTBS = $26.8 \pm 20.89$ , $16$ cTBS = $22.9 \pm 10.34$
Interventions	In brief, the cTBS protocol comprised 801 pulses, delivered in a continuous train of 267 bursts. Each burst consisted of 3 pulses at 30 Hz, repeated at 6 Hz. Duration of 1 single cTBS train was therefore 44 seconds



# Nyfeller 2019 (Continued)

In the 16cTBS group, the same daily protocol was repeated 4 times, i.e. 16 cTBS trains were applied over 4 days

In the 8cTBS group, 8 cTBS trains were applied over 2 days. Four cTBS trains were applied on Day 1 (2 cTBS trains with an interval of 15 minutes, third and fourth cTBS trains 60 and 75 minutes after the first one, respectively (Cazzoli et al, 2012), and 4 cTBS trains on Day 2 - same time intervals as for Day 1, repeated after 24 hours)

Sham stimulation was applied with the same 8cTBS protocol as described above, except for use of a sham coil

# Outcomes

- CBS
- Fluff test
- Two-Part-Picture test
- · Bird cancellation task

Assessed pre-intervention, post intervention, and 3 months post intervention

Notes

We entered this study as Nyfeller 2019 8c TBS and Nyfeller 2019 16c TBS and spilt the control group across entries

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation procedure was carried out by a blinded collaborator (TP), using a computerised block randomisation protocol to ensure equal group sizes (https://www.random.org/ integer-sets)
Allocation concealment (selection bias)	Low risk	Treatment allocation was concealed from trained observers
Blinding of participants	Low risk	"Double-blind"
Blinding of personnel	Unclear risk	Unclear
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	CBS was completed by rehabilitation nurses taking care of patients on a daily basis, who were blind with respect to the experimental protocol, and who observed patients performing different ADL. Unknown whether blinding was successful
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	3 dropped out at T2, unclear from which group though
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious

# Nyfeller 2019 16c TBS

Study	char	acte	ristics
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Methods	See Nyfeller 2019	



# Nyfeller 2019 16c TBS (Continued) Participants Interventions Outcomes Notes Risk of bias Authors! judgement Support for judgement

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation procedure was carried out by a blinded collaborator (TP), using a computerised block randomisation protocol to ensure equal group sizes (https://www.random.org/ integer-sets)
Allocation concealment (selection bias)	Low risk	Treatment allocation was concealed from trained observers
Blinding of participants	Low risk	"Double-blind"
Blinding of personnel	Unclear risk	Unclear
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	CBS was completed by rehabilitation nurses taking care of patients on a daily basis, who were blind with respect to the experimental protocol, and who observed patients performing different ADL. Unknown whether blinding was successful
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	3 dropped out at T2; unclear from which group though
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious

# Nyfeller 2019 8c TBS

Study characteristics	
Methods	See Nyfeller 2019
Participants	
Interventions	
Outcomes	
Notes	



# Nys 2008

Study characteristics		
Methods	RCT; single-blind rando Setting: stroke units, N	omised controlled design etherlands
Participants	16 participants with neglect from 3 stroke units  Experimental: n = 10, control: n = 6  Adequacy of matching at baseline? Yes  Number lost to follow-up: not clear - only those who completed were included in the report. Also excluded 1 patient with deterioration of neurological condition during treatment phase, which probably should have been a loss to follow-up rather than exclusion  Mean age, years, mean (SD): experimental = 63.6 (13.8), control = 61.5 (11.0)  Sex (men/women): experimental = 7/3, control = 3/3  Time post onset, days: experimental 1 = 8.8 (5.3), control = 11.2 (6.4)  Side of damage: right  Method of diagnosing stroke: not stated; based on referral by a stroke physician on admission to SU  Method of diagnosing neglect: ≥ 2 subtests (out of 4): BIT subtests below cutoff. The 4 tests were Star Cancellation (cutoff ≤ 51), line bisection (cutoff ≤ 7), figure copying (cutoff ≤ 2), and representational drawing (cutoff ≤ 2)  Inclusion criteria: inpatient in SU with neglect, within 4 weeks post stroke. All participants had to demonstrate an after effect of at least 3 visual degrees to the left of the landing position after the first prism adaptation; this would apply only to the active treatment group, but none were excluded for this reason  Exclusion criteria: ocular problems, disturbed consciousness or too limited attention span (participants excluded during screening)  Visual sensory deficit: 2 in the experimental group had hemianopia, diagnosed by confrontation comparing cueing and non-cueing conditions by a stroke neurologist	
Interventions	Prism adaptation: "an extended version of that used by Rosetti et al 1998". While wearing goggles with prisms inducing a rightward optical shift of 10°, participants made 100 fast pointing movements to 2 visual targets presented 10° to the left and right of the body midline. Sessions of 30 minutes were conducted 4 days in a row vs placebo - as above, but wearing goggles with no optical shift. Sessions of 30 minutes were conducted 4 days in a row  Profession of intervention provider not stated	
Outcomes	<ul> <li>Behavioural Inattention test, 1 month after treatment</li> <li>Modified BI, 1 month after treatment, but no indication what the modification was</li> <li>Schenkenberg line bisection, after every treatment session</li> <li>Letter cancellation, after every treatment session</li> <li>Gainotti Scene Copying, after every treatment session; scored retrospectively by an independent rater</li> <li>Measured up to 1 month post intervention.</li> </ul>	
Notes		of action: not clear, but stated there was a "neural basis for the therapeutic ef- because the brain is most sensitive to rehabilitative treatment early after stroke
Risk of bias	,	
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	According to a randomisation procedure in SPSS
Allocation concealment (selection bias)	Unclear risk	Insufficient details "according to a randomisation procedure in SPSS"
Blinding of participants	High risk	Nature of prism glasses, no details given



Nys 2008 (Continued)		
Blinding of personnel	High risk	Nature of prism glasses, no details given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Only 1 measure, scene copying, appears to have been scored retrospectively by an independent rater. Not stated whether outcome assessor was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious

# Pandian 2014

Study characteristics		
Methods	Prospective, open, blinded endpoint (PROBE design) RCT Setting: hospital, India	
Participants	48 stroke patients with thalamic and parietal lobe lesions within 48 hours of stroke onset who had upper limb weakness  Treatment = 27, control = 21  Diagnosis of neglect: star cancellation = 51 or fewer stars cancelled by the patient  LBT: cutoff score for unilateral visual neglect was an error > 1.4 cm left or right  Age, mean (SD), years: treatment = 63 (11), control = 64 (12)  Sex (men/women): treatment = 14/13, control = 14/7  Hemisphere damaged (right/left): treatment = 21/6, control = 16/5  Exclusion criteria: Glasgow Coma Scale score < 7	
Interventions	During the MT, patients sat near a table on which a mirror box (35 × 3 × 35 cm) was placed vertically. The affected hand was hidden behind the mirror, and the unaffected hand was placed in front of the mirror. Patients were asked to see only the unaffected hand in the mirror. Patients were instructed to perform flexion and extension movements of the non-paretic wrist and fingers while looking into the mirror. Thus, they were seeing the reflection of the unaffected hand as movement of the affected hand in the mirror. During the session, while they were moving the non-paretic hand, patients were asked to do the same movements in the paretic hand	
	Control group carried out similar exercises for the same time period but used the non-reflecting side of the mirror. The paretic hand was hidden from their sight. Control therapy was given by the same physiotherapist. Both treatment and control groups received limb activation	
Outcomes	Primary outcomes  Star cancellation test (SCT)  Line bisection test (LBT)  Picture identification task (PIT)  Secondary outcomes	
	<ul> <li>Functional independence measure (FIM)</li> <li>Modified Rankin Scale (mRS) (good outcome: mRS ≤ 2)</li> <li>Measured up to 6 months post intervention</li> </ul>	



# Pandian 2014 (Continued)

Notes

Study authors did not give SDs for neglect outcomes. We imputed the SD for baseline at outcome. We attempted to impute mean from change scores that were provided; however the presented change scores require further explanation, as they imply perfection at follow-up (a score of 53 on star cancellation, on which the maximum is 52), and because the magnitude of difference given the SD appears extreme. We are yet to receive a response from study authors

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	All eligible participants were randomised to the MT group or the control group (sham MT). A random allocation sequence was made using random digits generated by RALOC (random allocation) software and was conveyed to investigators by sealed numbered envelope
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants	High risk	Not possible to blind
Blinding of personnel	High risk	Not possible to blind
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Physiotherapist who was unaware of group assignments assessed outcomes at 1, 3, and 6 months. No evidence suggests that this assumption was tested
Incomplete outcome data (attrition bias) All outcomes	Low risk	Very little attrition - 1 each group
Selective reporting (reporting bias)	Unclear risk	3 primary outcomes
Other bias	High risk	There was some imbalance in stroke lesions, manual dexterity, and stage of motor recovery between randomised groups Use of LOCF ("missing values on outcomes were imputed using last observation carried forward method")

# Park 2015

Study characteristics	
Methods	RCT Setting: South Korea
Participants	Inclusion criteria for participation were as follows: (1) left hemiparesis with onset duration > 6 months; (2) patient with unilateral neglect (> 6.3 mm deviation of the true centre of the line in the line bisection test); (3) cognition (> 23 points on the Korean version of Mini-Mental Status Examination); (4) no hemi-anopsia or apraxia; and (5) imagination ability (average score < 3 in the Vividness of Movement Imagery Questionnaire)  Age, years, mean (SD): intervention = 61.5 (5.1), control = 63.6 (6.0)  Sex (men/women): intervention = 8/7, control = 6/9  Hemisphere damaged: right  Time since stroke, months: intervention = 6.8 (0.9), control = 6.9 (1.0)



# Park 2015 (Continued)

### Interventions

Participants received a mental practice intervention or usual care. During mental practice, experimental group (EG) participants mentally practised positioning and movement of the left upper limb as intensively as possible in a repetitive fashion. EG participants sat comfortably and leaned back against the back rest with feet on the floor and imagined the scene while listening to the voice of the researcher for 10 minutes with eyes closed. Contents of mental practice were to pick up a baseball, a pencil, and a coin at the centre of a body using the left hand, respectively, then move them into a basket lying on the left side. Verbal feedback provided by participants assured correct execution of imagery tasks. Each task was repeated up to 10 times per session. At the beginning of each task, break time was given to patients to induce relaxation and concentration internally on the left arm. EG participants received mental practice for additional 10 minutes (5 days a week for 4 weeks)

### Outcomes

- · Line bisection
- · Star cancellation

All taken immediately post intervention with no longer-term follow-up

### Notes

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Based on a computer-generated randomisation programme by a research assistant under the blind condition
Allocation concealment (selection bias)	Unclear risk	No detail given
Blinding of participants	High risk	No detail given
Blinding of personnel	High risk	No detail given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	All clinical measures were administered by the blinded assessor, but no detail was given
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data apparent
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious

# Park 2015b

Study characte	ristics
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Methods	Setting: rehabilitation centre, South Korea
Participants	Inclusion criteria for participation were (1) onset duration > 6 months, (2) right hemisphere stroke with UN, (3) Mini Mental State Examination score > 24, (4) ability to imagine (average score on Vividness of Movement Imagery Questionnaire < 3), and (5) active wrist muscle strength > 2 on Medical Research Council (MRC) Scale



### Park 2015b (Continued)

Exclusion criteria were (1) an implanted cardiac pacemaker, (2) skin lesion on affected side or hypersensitivity at the electrode site, (3) history of seizure or epilepsy, and (4) unstable medical conditions

Age, years: intervention =  $67.5 \pm 10.3$ , control =  $62.2 \pm 10.2$ Sex (men/women): intervention = 10/6, control = 8/9

Hemisphere damaged: right

Time since stroke, months: intervention =  $3.3 \pm 1.3$ , control =  $3.5 \pm 1.6$ 

### Interventions

Experimental group (n = 16) received MP-EMG ES in addition to conventional rehabilitation therapy (CRT: physical therapy and occupational therapy), whereas control group (n = 17) received cyclical ES in addition to the same CRT. Mentamove (Mentamove Deutschland GmbH, Munich, Germany) was used to apply MP-EMG ES in the experimental group. Surface electrodes were attached to the wrist extensor muscle, and a reference electrode was attached at the lateral side of the forearm. The site of electrode placement was marked using a permanent marker throughout the intervention. During motor imagery training, electrical potentials were generated in the affected arm and were recorded using EMG. When potentials reached a pre-set threshold, the induced electrical stimulation would contract the targeted muscle. The Mentamove process consisted of 3 stages: (1) motor imagery (approximately 12 seconds), (2) electrical stimulation (approximately 6 seconds), and (3) relaxation (approximately 12 seconds). Motor imagery used in this study was vigorous waving of the affected whole arm. This imagery was selected because the EMG was not able to detect electrical stimulation induced by motor imagery of simple extension of the wrist or elbow. The EMG pick-up threshold was set afresh for each patient in every session. If the patient repeatedly reached the threshold during MP-EMGES, the threshold was automatically increased slightly. Instructions were as follows: first, relax in a comfortable position. Imagine that your left arm moves rapidly and intensely when you see "motor imagery" in the tool window. If your performance is successful, you will experience an electrical stimulation in your forearm. If your performance fails, maintain the relaxed state. Cyclical ES (Mendel GmbH, Germany) without the EMG function was used to apply electrical stimulation in the control group. Electrodes also were attached to the wrist extensor muscle. With either instrument, biphasic pulses with frequency of 35 Hz and pulse width of 200 μS were applied for 12 seconds. Stimulation intensity led to a clear extension of the wrist (average 20 to 30 mA)

### Outcomes

- · Line bisection
- Star cancellation
- CBS

All taken immediately post intervention with no longer-term follow-up

# Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear
Allocation concealment (selection bias)	Low risk	Randomly allocated to the 2 groups by block randomisation using opaque envelopes containing a code specifying the group
Blinding of participants	High risk	No details given
Blinding of personnel	High risk	No details given
Blinding of outcome assessment (detection bias) All outcomes	High risk	No details given
Incomplete outcome data (attrition bias) All outcomes	Low risk	None incomplete



<b>Park 2015b</b>	(Continued)
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Selective reporting (reporting bias)

Low risk Outcomes reported in equal detail

Other bias Low risk No evidence of this

# Polanowska 2009

Study	cha	racto	rictics
Stuav	cna	racte	ristics

Methods

RCT, single site and double-blinded Setting: Poland

**Participants** 

40 participants with first-ever stroke and hemi-neglect

Experimental: n = 20, control: n = 20

Adequacy of matching at baseline? No, although age, sex, BI, and MMSE are well balanced at baseline, accuracy on neglect tests seems lower in experimental vs control group

Number lost to follow-up: study authors confirm no losses to follow-up

Mean age, years, mean (SD): experimental = 61.6 (8.3), control = 58.3 (12.9)

Sex (men/women): experimental = 11/9, control = 14/6

Side of damage: right

Method of diagnosing stroke: confirmed by neuroimaging and neurological exam (CT)

Method of diagnosing neglect: confirmed by neuropsychological exam as fulfilling 2 of 3 criteria: ≥ 4 omissions of left-sided targets in subtest A of Balloons test; marked rightward bias (cutoff score of 7) on line bisection; spontaneous behaviours specific to neglect (e.g. ipsilesional deviation of head, eyes, trunk); attending to ipsilesional side; neglect dyslexia and dysgraphia with tendency to initiate search on right of stimulus sheet

Time post onset, days: experimental = 44.4 (27.3), control = 46.6 (26.2)

Inclusion criteria: first right hemisphere stroke, left visuospatial neglect, recruited from single rehabilitation unit, 2 to 12 weeks post stroke, right-handedness, 25 to 75 years of age, informed consent obtained

Reasons for exclusion: if electrical stimulation contraindicated, history of dementia, neurological or psychiatric disorders; if communication or other problems meant unable to co-operate Visual sensory deficit: 'visual sensory deficit': experimental = 13/20, control = 13/20; and 'hemianopia': experimental = 6/20, control = 9/20, as assessed by "standard neurological assessment"

# Interventions

Electrical somatosensory stimulation of the left hand combined with conventional visual scanning training, 1 month duration of 20 session of 45 minutes duration each, 5 days per week. This stimulation lasted for the first 30 of the 45 minutes. Electrical stimulation was provided by 2 electrodes on the hand, giving a maximum intensity of 15 mA. Visual scanning used 2 programmes from RehaCom computerised system to get active purposeful exploration of visual field (1 - saccadic training - seek stimuli within detailed background; 2 - attention and concentration - detect and identify stimuli, then seek their counterpart on the opposite side within a detailed background). Visual scanning also used some paper-and-pencil tasks to improve scanning when reading and writing; drawing and copying; and analysing form and content of complex visual stimuli. Verbal and visual cues and instructions given, as was feedback on achievements and errors vs visual scanning training as above, with placebo stimulation when electrodes were applied to the hand but without "current intensity"

Visuospatial scanning training was conducted by a neuropsychologist, and electrostimulation was supervised by a neurologist

# Outcomes

- Line-crossing cancellation subtest (from BIT)
- Star cancellation subtest (from BIT)
- Reading aloud (48 letters)
- BI
- MMSE
- Auditory verbal learning test



# Polanowska 2009 (Continued)

Also measured after only 1 day of stimulation but excluded those results in favour of the more meaningful 1 month results, which are immediate post rehabilitation – so no maintenance/follow-up outcomes were measured

### Notes

Postulated mechanism of action: visual scanning training aims to remind and motivate participants to scan to the left to build the habit of voluntarily scanning their neglected space. Requires awareness by the participant, which is not always present, hence use of passive (non-volitional) physiological approaches such as sensory stimulation. Assumes manipulated sensory inputs are linked to auto levels of orientation behaviour. But effects seem transitory, so this study attempts to combine active training of visual scanning with passive stimulation to enhance activation of right hemisphere attention system and to improve visual exploration of extra-personal space

All participants received visual scanning training - the only difference was electrical stimulation

Study authors state in the paper that 11 participants reported a tingling sensation during a trial electrostimulation period. During the study itself, however, only 1 participant noted such a sensation; afterwards, it was noted this person was in the sham group

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Blocked randomisation was performed by 1 person unblinded to group allocations and was based on random number tables. For each 10 subjects, numbers 1-5 meant that patients would be in group E, the numbers 6-10 meant that patients would be in Group C with the constraint that in each block of 10 there would be 5 in group E and 5 in group C"
Allocation concealment (selection bias)	Low risk	"Allocations were stored in sealed, numbered envelopes that were opened only at the time of recruitment and the author has confirmed all envelopes were prepared before recruitment began by someone other than the recruiter"
Blinding of participants	Low risk	"Simulated stimulation was used for the controls"
Blinding of personnel	Low risk	"Both the psychologist who conducted the assessment and the person who supervised rehabilitation and evaluated therapy outcome were blinded to each patient's group assignment. A third person who knew patient allocation controlled the generation of current during stimulation and ensured that the patients and other researchers remained blinded to the level of current delivered"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	States outcome assessor blinded, but not evidenced
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study authors advise that all randomised participants were followed up on all variables, and there were no post-randomisation exclusions
Selective reporting (reporting bias)	Unclear risk	Unclear
Other bias	High risk	Control group had significantly better scanning accuracy at baseline. No adjustment was made for differences in scanning accuracy



# Raghavan 2017

Study characteristics			
Methods	RCT Setting: UK, community hospital		
Participants	Inclusion criteria: (1) spatial and/or object neglect as identified by asymmetry scores on the Hearts Cancellation test of the Oxford Cognitive Screen (OCS); (2) neglect diagnosis confirmed by multi-disciplinary team (MDT); (3) between 1 week and within 6 months of the stroke event; (4) medically fit; (5) able to comprehend instructions and provide informed consent as per the opinion of the MDT; (6) ability to concentrate for 20 to 30 minutes as judged by the MDT; (7) no co-morbid psychological or neurological disorders (e.g. depression, dementia) as judged by the MDT; (8) no contraindications for rTMS administration upon administration of a screening questionnaire  Age, years, mean: intervention = 75. 2, SD = 8.5; control = 80.08, SD = 7.1  Sex: intervention 3 women, control 1 woman  Time post stroke, days: screening was done on average 19 days (SD = 9 days) after stroke for Intervention group, and 27 days (SD = 21 days) after stroke for control group		
Interventions	a figure of 8 coil was us sity of stimulation requ interosseous muscle, in "hotspot" in each patie then provided at 90% of	magnetic stimulator (Magstim Company, Whitland, Wales, UK) connected to sed to deliver rTMS. The resting motor threshold was defined as lowest intensired to elicit 5 visible motor twitches in the relaxed right hand's first dorsal in response to 10 consecutive stimuli. To identify this threshold, the optimal int's motor cortex was identified and stimulated (Rossini et al, 2015). rTMS was of this identified resting motor threshold. Intervention group received 20 minutes rulses) to the left inferior parietal lobe (P3) of the intact hemisphere	
Outcomes	<ul> <li>OCS Hearts Cancellation</li> <li>Line bisection</li> <li>Neglect-Specific Activities of Daily Living (ADL) tasks (non-specific test used)</li> <li>Follow-up testing on the same cognitive test battery as at baseline was conducted both in the short term, i.e. less than 1 month post rTMS, and in the long term, i.e. at 6 or more months post rTMS</li> </ul>		
Notes	Data are from Chapter 5 of thesis		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	"Based on computerized randomization" only detail	
Allocation concealment (selection bias)	Unclear risk	No details	
Blinding of participants	Unclear risk	No details	
Blinding of personnel	High risk	Different placement of probe suggests not possible	
Blinding of outcome assessment (detection bias) All outcomes	High risk	No details	
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 dropped out of intervention group, 1 from control group	



Raghavan 2017 (Continued)		
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious. Multiple testing adjustments made

# Robertson 1990

Study characteristics	
Methods	RCT Setting: hospital, UK
Participants	30 (see Notes) inpatients of Edinburgh hospitals who showed left visual field neglect on BIT Experimental: n = 17, control: n = 13 (The following data describe the 36 initial participants: see Notes) Mean age, years (SD): experimental = 64.2 (12.6), control = 63.1 (9.6) Sex (men/women): experimental = 9/11, control = 10/6 Onset of neglect, weeks (SD): experimental = 19.2 (21.1), control = 10.8 (6.3) Inclusion: presence of neglect (failure on at least 3/9 behavioural tests), oriented for time and place, ability to consent, ability to concentrate sufficiently to sit at computer-based task for at least 15 minutes
Interventions	15½ hours (14 sessions of 75 minutes each, 2×/week for 7 weeks) computerised scanning and attention training (intensive briefing about nature of participant's problems, feedback on left and right latencies, trainer reinforcement and encouragement) vs 11.4 hours recreational computing (to minimise scanning and timed attention tasks, without any potential neuropsychological mechanism to improve cognitive function, but exposed to computer activities such as games, quizzes, and simple logical games)
Outcomes	<ul> <li>Study collected several types of outcomes</li> <li>BIT</li> <li>WAIS-R subtests (picture completion and block design)</li> <li>Neale Reading test</li> <li>Letter cancellation</li> <li>Observer's report of neglect</li> <li>Rey CFT (copy only)</li> <li>The BIT was the principal outcome measure. (Although not explicitly stated, it is assumed from the description on page 664 and the low scores in Table 2 that only the BIT behavioural subtests were given.)</li> <li>Outcomes were given immediately after training and after 6 months. Study also collected data on several other tests, including the GHQ and the FAI, to ensure matching of groups (see Notes). These were collected at each time point. This review used the BIT, immediately and after 6 months</li> </ul>
Notes	This review entered n = 30 of initial 36 (33 with CVA, 2 with HI, 1 had surgery for excision of meningioma). 3/36 not followed up immediately, and 9/36 not seen at 6 months, but no information on which group these were from, so data entered into this review subtracted 3 and 9 from each group at first (n = 30) and second assessments, respectively. Information on allocation concealment provided by personal communication. 6 months' follow-up Exclusion: participants with BIT score > 70 Cancellation data reported as errors rather than correct performance Review could not include FAI data as these were not reported
Risk of bias	
Bias	Authors' judgement Support for judgement



Robertson 1990 (Continued)		
Random sequence generation (selection bias)	High risk	Randomisation restricted in blocks of patients with severe or mild neglect; therefore stratified by severity
Allocation concealment (selection bias)	Low risk	External randomisation. Randomisation restricted in blocks of patients with severe or mild neglect; therefore stratified by severity. Randomisation was carried out by a third party
Blinding of participants	High risk	No information given
Blinding of personnel	High risk	No information given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinded outcome assessor stated but not evidenced
Incomplete outcome data (attrition bias) All outcomes	High risk	3/36 not followed up immediately and 9/36 not seen at 6 months, but no information on which group these participants were assigned to
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Slight difference in letter cancellation errors and Wisconsin at baseline. Adjustment not necessary

# **Robertson 2002**

Study characteristics	•
Methods	RCT Setting: UK
Participants	40 randomised but 36 seen for immediate outcome assessment (see Notes); recruited from London hospital and community rehabilitation teams; had left visual neglect on cancellation or bisection tests (The following data describe the initial 40 participants: see Notes)  Experimental: n = 19, control: n = 21  Mean age, years (SD): experimental = 69.3 (9), control = 67 (9.4)  Sex (male/female): experimental = 13/6, control = 16/5  Onset of neglect, days (SD): experimental = 152.8 (142.4), control = 152.1 (117.9)  Inclusion: right hemisphere stroke, younger than 80 years, right-handedness, no history of major psychiatric/disease/disability that would prevent participation or contaminate results
Interventions	LAT wearing (on the wrist/leg/shoulder) an active limb activation device during perceptual training. The device emitted an auditory tone if no left-sided movement was made; vs perceptual training wearing an inactive (no tone) limb activation device  Both groups received training at their residence (usually own home) for 12 weeks for approximately 4: minutes per week  Perceptual training for both groups involved working on visuoperceptual puzzles and reading tasks that implicitly but not explicitly involved advice to scan to the left
Outcomes	Outcomes:  BI/Nottingham EADL Bergego Rating Scale of Neglect (informant rated) BIT Behavourial subtest



# Robertson 2002 (Continued)

 Motricity Index (total left body side) at 4 time points: immediately post training; at 3 months, 6 months, and 18 to 24 months. In addition, the Comb and Razor Personal Neglect test and the Modified Landmark test were given at the first 3 time points

For comparability with other studies, this review used only the following time points: immediate and 6 months

# Notes

Attrition: 36/40 followed up immediately (experimental = 17, control = 19); 32 at 6 months, 26 at 18 to 24 months

Groups appeared appropriately matched for demographic and clinical baseline variables No information on number per group at 6 months. Known that 4 were lost, but not whether all were from a single group, so assumed worst case and subtracted 4 per group, i.e. conservative sample estimate of 28 not 32

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No detail given
Allocation concealment (selection bias)	Low risk	Robertson 2002 confirmed that recruiters were unaware of and were unable to predict allocation concealment. Study authors confirmed randomisation but did not specify the method used. Concealment was highly likely to have been achieved, although this could not be guaranteed
Blinding of participants	High risk	Nature of intervention
Blinding of personnel	High risk	No detail given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinded outcome assessor; no more detail given
Incomplete outcome data (attrition bias) All outcomes	Low risk	4 (2 from each group) dropped out during treatment. 36 participants were followed up at 3 months, and 32 at 6 months. Of the 4 who dropped out at 6-month follow-up, 2 had a further CVA, 1 died, and 1 refused. Low risk; loss to follow-up unlikely to affect outcomes
Selective reporting (reporting bias)	Low risk	'Selected variables' chosen for table, but no evidence of bias
Other bias	Low risk	Nothing obvious

# **Rode 2015**

Study characteristic	s
Methods	Double-blind RCT Setting: rehabilitation unit, France
Participants	20 single-stroke patients with left SN at least 1 month following ischaemic event (aged 18 to 90)  Prism = 10, control = 10  Definition neglect: LBT, balloon, copy of a drawing, dictation, and reading of a text  Age, years, mean (SD): prism = 56 (12), control = 62 (13)  Sex (men/women): prism = 5/4, control = 5/4  Days, mean (SD), between stroke and treatment: prism = 77 (38), control = 70 (38)



Rode 2015 (Continued)

Exclusion: existence of multiple brain lesions; temporospatial disorientation; psychiatric disorders; associated, non-stabilised pathology

### Interventions

In the 'prism' group, PA was carried out by wearing a pair of glasses producing a 108 rightward optical deviation of the visual field. Prismatic lenses were composed of 2 superimposed, curved, point-topoint lenses fitted with a "glacier" frame containing lateral leather protectors designed to avoid access to non-shifted vision. Prisms covered a total visual field of 105% in which each monocular field represented 75 degrees, and the central visual binocular field represented 45 degrees. During prism exposure, the patient had to execute 80 rapid pointing movements towards visual targets located 10 degrees to the left or to the right of the middle of her/his body, with targets made to pseudo-randomly alternate. In spite of repeated instructions to carry out rapid movements, movements produced in brain damaged patients generally remain too slow as to allow visual retroaction, and errors committed by our patients did not necessarily reflect the amplitude of optical deviation or the phase of adaptation. However, their degree of rapidity remained compatible with the development of actual sensory-motor adaptation by reducing the strategic components of compensation. Pointing movements were performed with a pause of 30 seconds after each series of 20, thereby favouring an increased number of errors at the start of the following series. During exposure, the patient did not see the initial position of her/his hand, which entered the visual field only once the movement was approximately 30% to 50% complete, in such a way as to favour proprioceptive-visual coding of the movement. All in all, prism exposure lasted from 6 to 10 minutes

Although 'control' group patients carried out this visuomotor task under the same conditions, they were wearing a pair of placebo glasses fitted out with neutral lenses of the same weight consisting of two 5-degree prismatic lenses set up so as not to produce any optical deviation

Each patient carried out the exposure task (with prismatic glasses or neutral lenses) 4 times: at D0 (Expo1), at D + 7 (Expo2), at D + 14 (Expo3), and at D + 21 (Expo4)

All exposure sessions took place under the same conditions and with the same operators

# Outcomes

Primary outcome measure of the study was functional improvement in daily life activities following rehabilitation, assessed by the Functional Independence Measure (FIM)

Secondary outcome measure was total score on the Behavioural Inattention Test (BIT)

Measurement with regard to the primary endpoint was carried out 4 times: in pre-tests and in post-tests at 1 (M1), 3 (M3), and 6 (M6) months after the initial PA session. BIT evaluations were performed twice: in pre-test, and then in post-test at 6 months

# Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisation and drawing by lots of the patients into 'prism' or 'control' groups were carried out by Denis Pelisson, director of the ImpAct team, in the Lyon Neuroscience Research Centre. Randomisation was produced at 2 levels, first by selection of patients for the 'prism' or 'control' group; second, by selection of patients according to severity of the initial SN assessed by BIT score, with the objective that the ratio of patients with severe neglect and patients with moderate neglect is comparable in the 2 groups
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants	Low risk	Double-blind; justified in text
Blinding of personnel	Low risk	See above
Blinding of outcome assessment (detection bias)	Low risk	Examiners carrying out the evaluation (GR, SL, EM) did not know whether a given patient had undergone PA. They were distinct from examiners perform-



Rode 2015 (Continued) All outcomes		ing the task of exposure to prismatic or neutral glasses (YR, SJC, LP). The double-blind procedure was facilitated by the fact that SN patients were not aware of the disturbance induced by prism deviation and did not present the vegetative reactions expected during the appearance of motor errors when prisms were worn for the first time. Consequently, they could be assigned without their knowledge to the 'prism' and 'control' groups. This also entailed that examiners performing the assessment did not receive information from patients. All of this might have compromised the double-blind trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition of only 1 in each group
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious

# Rossit 2019

Study characteristics	
Methods	Controlled prospective study using a single-blind design Setting: hospital, UK
Participants	Inclusion criteria: stroke lesions as identified by brain imaging report, hemi-spatial neglect symptoms (in line bisection, BIT, or balloons test), ability to follow instructions, and medical fitness to participate
	Exclusion criteria were previous or concomitant neurological (e.g. brain tumour, dementia), visual (e.g. cataract), or motor (e.g. arthritis) disease unrelated to the current stroke Age, mean, years (SD): intervention = 65.6 (2.8), control = 64.9 (2.5)  Sex (men/women): intervention = 3/7, control = 8/2  Hemisphere damaged: right  Time since stroke, months (SD): intervention = 3.1 (0.9), control = 3.2 (0.5)
Interventions	Visuomotor feedback training (VFT) is a neglect rehabilitation technique that involves simple, inexpensive, and feasible training of grasping to lift rods at the centre. Patients in the intervention group were asked to reach for and grasp the rod with a pincer grip (using the forefinger and the thumb) and to try to lift it up at its centre, so it would be balanced. If they felt that it was not balanced after lifting it, they could repeat the trial until satisfied. Feedback was provided only from the tilting rod; the experimenter did not comment on performance. Patients in the control group were instructed to simply reach for and grasp the rod with a pincer grip (using the forefinger and the thumb) by its non-neglected end (usually the right) and to lift it up from the mat on that side and place it back down again. Training was delivered for 2 sessions by an experimenter; then patients self-administered it for 10 sessions over 2 weeks
Outcomes	<ul> <li>BIT-C</li> <li>Line bisection</li> <li>Subtest B of the Balloons test</li> <li>Landmark task</li> <li>Room description task</li> <li>Straight ahead pointing task</li> <li>Stroke Impact Scale</li> </ul>



# Rossit 2019 (Continued)

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear
Allocation concealment (selection bias)	High risk	Patients randomly assigned to intervention or control group as determined in the order of a list (complete/unrestricted randomisation); order of the list not hidden
Blinding of participants	Low risk	"Patients, carers and scorers of our outcome measures remained blind to group assignment throughout the trial, except for the Stroke Impact Scale"
Blinding of personnel	High risk	It seems instructions for the 2 arms are different; therefore it is impossible for the staff not to know which people belong to which group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"The outcome assessment was performed by the experimenter (except the SIS) who also delivered the treatment. However, all measures were scored by a treatment-blinded researcher"
		However (see above), it seems unlikely that these could be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition equal in each group
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Nothing obvious

# Rusconi 2002

C4d	-6	
Stuav	cnarac	teristics

Study characteristics		
Methods	RCT Setting: Italy	
Participants	24 randomised (see Notes), but outcome data collected on 20 (The following data describe the 20 participants)  Experimental: n = 12, control: n = 8 (experimental is Type 1 and control is Type 2: see Interventions)  Mean age, years: experimental = 69.8, control = 65.1  Sex (men/women): experimental = 5/7, control = 3/5  Mean weeks post stroke: experimental = 6.92, control = 8.38  Inclusion: unilateral right hemisphere stroke assessed by CT scan, right-handedness, symptoms of unilateral neglect, admission to hospital for rehabilitation 5 weeks post stroke  Exclusion: dementia	
Interventions	Study compared more than 2 interventions. First, there is a comparison of 2 types of cognitive training: Type 1 vs Type 2. Each 'type' is then subdivided into whether or not TENS is added (see Notes) Type 1 vs Type 2: both consist of 5 × 1-hour sessions per week for 2 consecutive months (40 sessions) using 4 procedures requiring participants to actively scan the visual field (reading sentences and stories, doing line drawing on a dot matrix, assembling 3D cubes, matching cards containing the name and visual image of an object). Types 1 and 2 differed in that only Type 1 involved verbal and visuospatial	



Rusconi 2002 (Continued)	cueing and verbal feedback. Although Type 2 used the same 4 procedures, it did not involve cueing or feedback, i.e. aspects of the training designed to improve awareness and encourage compensation
Outcomes	Assessments were classified as 'functional and neurological' (i.e. BI, standard clinical neurological examination) or 'neuropsychological' (i.e. line cancellation, letter cancellation, line bisection, sentence reading, o'clock test, judgement of drawings, anosognosia, RCPM, facial recognition, position deficit). These were taken at 4 time points: on admission for neurorehabilitation at least 5 weeks post stroke (T0); 1 month later (T1), after which eligibility was determined and participants were randomised; after 1 month of intervention (T2); and after 2 months of intervention (T3)  For comparability with other studies, this review used only T3 letter cancellation and BI. As intervention continued for 2 months, T3 is coded in this review as immediate effects
Notes	Study author provided clarification and raw data by personal communication 24 people were randomised: 12 to Type 1 and 12 to Type 2. Study authors excluded 4 from the final evaluation because of "clinical worsening that prevented the conclusion of the treatment". These 4 were allocated to Type 2  Cancellation scores were for the numbers correctly cancelled. Separate scores were given for left and right space, but this review used total score. Line bisection data were for mean deviation in millimetres left (negative) or right (positive) of the midpoint. Line cancellation data could not be used, as the experimental group's SD was 0

# Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear
Allocation concealment (selection bias)	High risk	Paper states "randomly assigned"; no details provided Subsequent information states allocations stored in sequentially numbered, sealed, opaque envelopes. Concealment of allocation is unlikely
Blinding of participants	High risk	No detail given
Blinding of personnel	High risk	No detail given
Blinding of outcome assessment (detection bias) All outcomes	High risk	No detail given
Incomplete outcome data (attrition bias) All outcomes	High risk	None reported in paper, but study authors reported 24 people were randomised: 12 to Type 1 and 12 to Type 2. Study authors excluded 4 from final evaluation because of "clinical worsening that prevented the conclusion of the treatment". These 4 were allocated to Type 2. No intention-to-treat analysis
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious

# Schroder 2008

Study characteristics		
Methods	RCT, 3-arm study Setting: Germany	



# Schroder 2008 (Continued)

# **Participants**

30 right-handed participants with right brain damage, moderate left neglect

Experimental 1: n = 10, experimental 2: n = 10, control: n = 10

Number lost to follow-up: none

Adequacy of matching at baseline? Yes, no significant differences at baseline

Mean age, years, mean (SD): experimental 1 = 68.4, experimental 2 = 60.6, control = 67.3

Sex (men/women): experimental 1 = 7/3, experimental 2 = 5/5, control = 6/4

Time post onset, days, mean (SD): experimental 1 = 43.8 (23.6), experimental 2 = 24.6 (9.6), control = 36.2 (24.2)

Side of damage: right

Method of diagnosing stroke: not stated

Method of diagnosing neglect

- NET (Neglect test, Fels & Geissner, 1996) using subtests line cancellation, star cancellation, line bisection, figure copy and freehand drawing
- Neglect subtest from 'Testbatterie zur Aufmerksamkeitsprufung' (TAP)
- Reading test A from the electronic reading and exploration apparatus (ELEX) manual and writing a
  dictated sentence ('Heute ist ein schöner Tag')

No details of cutoffs provided

Inclusion criteria: right-handedness, less than 90 days post stroke, left brain damage, at least moderate neglect

Exclusion criteria: not stated Visual sensory deficit: not stated

### Interventions

Visual exploration and TENS: 20 therapy sessions, each lasting 25 to 40 minutes over 4 weeks (TENS: 100 Hz, over left trapezius, applied throughout exploration training) vs visual exploration and OKS 20 therapy sessions, each lasting 25 to 40 minutes over 4 weeks (OKS: small randomly spaced squares moving slowly to the left across a screen, 2 × 10-minute periods of OKS separated by 10 to 20 minutes of exploration training) vs visual exploration (control) using the ELEX apparatus (stimuli patterns were presented on a screen that subtended 53° vertically and 40° horizontally: after initial fixation, participants had to shift fixation to a yellow stimulus)

Profession of the intervention provider not stated

# Outcomes

- NET subtests: line cancellation, star cancellation, line bisection, figure copy, freehand drawing
- TAP: neglect subtest (composite values given)
- · Reading test
- Writing dictated sentence (composite values given)

Measured up to 1 week post intervention

# Notes

TENS: "a non-specific activation of the right hemisphere or a directional effect on the egocentric coordinates of extrapersonal space"

OKS "activates multiple cortical (temporoparietal and vestibular cortex, the insula) and subcortical structures (basal ganglia) involved in multisensory integration"

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Randomly assigned"; no other details
Allocation concealment (selection bias)	Unclear risk	Unclear
Blinding of participants	High risk	No details given



Schroder 2008 (Continued)				
Blinding of personnel	High risk	No details given		
Blinding of outcome assessment (detection bias) All outcomes	High risk	No details given		
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	None reported		
Selective reporting (reporting bias)	Unclear risk	Unclear		
Other bias	Low risk	For the few variables given, groups appear comparable at baseline		

# Seniow 2016

Study characteristics	
Methods	Setting: rehabilitation unit, Poland
Participants	29 right-handed Polish-speaking patients with left-sided hemi-spatial neglect, who were admitted to the Neurorehabilitation Unit during a 3-year period, were enrolled in the study Inclusion criteria were as follows: (1) adults 75 years of age, to avoid enrolling patients who would have difficulty actively participating in daily therapy and/or patients with age-related cognitive decline; (2) first-ever right hemisphere ischaemic stroke; (3) clear signs of hemi-spatial neglect in the visual modality, as confirmed through a neuropsychological assessment; (4) time since stroke: 3 weeks to 6 months; (5) good general condition, to actively participate in rehabilitation programme; (6) provided written informed consent Exclusion criteria were as follows: (1) previous brain damage and non-stroke neurological and psychiatric diseases that influence cognitive—behavioural functioning (e.g. dementia, addiction, depression); (2) impaired primary visual perception; (3) using medications that affect cortical excitability (e.g. antiepileptics, benzodiazepines); (4) contraindications to electrostimulation Age, years, mean (SD): intervention = 63.4 (7.7), control = 60.2 (9)  Sex (men/women): intervention = 7/7, control = 8/7  Hemisphere damaged: right  Time since stroke, days (range): intervention = 40.5 (25 to 140), control = 34.5 (27 to 45)
Interventions	Intervention group patients received a therapeutic programme combining conventional visual scanning training with TENS applied by a mesh glove on the left hand. Control participants received the same treatment with sham TENS
	The 3-week hemi-spatial neglect rehabilitation programme comprised 15 consecutive individual therapeutic sessions (5/week) with active or sham electrostimulation applied during the first 30 minutes of the 45 minutes of visual scanning training
Outcomes	BIT subtests (line crossing, letter cancellation, star cancellation, figure and shape copying, line bisection, representational drawing)
	All taken immediately post intervention with no longer-term follow-up
Notes	
Risk of bias	
Bias	Authors' judgement Support for judgement



Seniow 2016 (Continued)		
Random sequence generation (selection bias)	Unclear risk	No detail given
Allocation concealment (selection bias)	Unclear risk	No detail given
Blinding of participants	Low risk	Member of the research team blinded to groups applied the same montage of electrodes to the left (contralesional) hand of each patient during each therapeutic session
Blinding of personnel	Unclear risk	No detail given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Hemi-spatial neglect severity was assessed twice by the same experienced clinical neuropsychologist (KP), blinded to group, on the day preceding the rehabilitation programme (baseline measurement) and on the day after its completion (post treatment)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No detail given
Selective reporting (reporting bias)	Low risk	Nothing obvious
Other bias	Low risk	Nothing obvious

# Sesh 2018

Study characteristics			
Methods	RCT		
Participants	Patients within 2 weeks following acute right MCA territory ischaemic stroke with clinical features suggestive of visual and/or sensory neglect Fully conscious, oriented without any significant aphasia (should have normal/useful level of comprehension and communicative capabilities) Age > 18 and < 80 years Age, years: intervention group = $56 \pm 12.03$ , control group = $61 \pm 6.6$ Sex (men): intervention = 3, control = 6 Time post stroke: not reported, although < 2 weeks in inclusion criteria		
Interventions	Stimulate patients with hemi-neglect using visual stimuli (optokinetic drum), cutaneous sensory stimuli (alarm bell), and auditory stimuli (using music played from a mobile phone)		
	Control group: usual care		
Outcomes	<ul> <li>Star cancellation</li> <li>Line bisection</li> <li>Picture identification</li> <li>Clock drawing</li> <li>mRS</li> <li>NIHSS</li> </ul>		
	Assessed pre-intervention, post intervention, and 3 months post intervention		



### Sesh 2018 (Continued)

Notes

Study author reported median scores only for mRS assessments. We imputed the median for the mean and calculated SD to match t-tests given in the paper

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Full details given
Allocation concealment (selection bias)	High risk	Open label
Blinding of participants	High risk	No details
Blinding of personnel	High risk	No details
Blinding of outcome assessment (detection bias) All outcomes	High risk	No details
Incomplete outcome data (attrition bias) All outcomes	High risk	2 dropped out of treatment group, 0 dropped out of control group
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	High risk	Baseline imbalance in NIHSS not accounted for in methods

### **Song 2009**

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Study characteristics	
Methods	Pilot RCT Setting: China, rehabilitation hospital
Participants	Inclusion criteria: patients with right brain haemorrhage or cerebral infarction confirmed by computerised tomography (CT) or magnetic resonance imaging (MRI) and with VSN according to line cancellation and line bisection tests
	Exclusion criteria: recurrent stroke, epilepsy, serious heart disease, serious physical disease, in vivo metal implants such as cardiac pacemakers, increased intracranial pressure, obvious aphasia and understanding obstacles, use of tricyclic antidepressants or tranquilisers, pregnancy, younger than 18 years of age  Age, years, mean: intervention = 56.14 (SD 8.9), control = 64.43 (SD 12.57)  Sex (men/women): intervention = 2/5, control = 6/1
	Time post stroke, days: intervention = mean 38.43 (SD 15.20), control = mean 31.57 (SD 11.47)
Interventions	Repetitive, low-frequency stimuli were delivered with the patient lying on his or her back and the coil oriented with the handle pointing upwards. Stimulus intensity was set to 90% of the individual motor threshold and frequency was set to 0.5 Hz. The site of stimulation was the contralateral posterior parietal cortex corresponding to P3 with regard to electroencephalogram (EEG) 10–20. Each treatment session was 15 minutes long, and treatments were performed twice a day for 2 consecutive weeks. Control group received usual care



### Song 2009 (Continued)

Outcomes

- · Line bisection
- Line cancellation

Study duration was 6 weeks. All participants performed line bisection and cancellation tests every 2  $\,$ weeks, providing a total of 4 time points of evaluation

Notes

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details given
Allocation concealment (selection bias)	Unclear risk	No details given
Blinding of participants	High risk	Control notably different from intervention
Blinding of personnel	High risk	No details given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Evaluation at clinical testing was blinded"; no further detail
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts
Selective reporting (reporting bias)	Low risk	Outcomes reported in equal detail
Other bias	High risk	Gender differences between groups

## Ten-Brink 2017

Study characteristic	s
Methods	RCT Setting: rehabilitation centre, Netherlands
Participants	Stroke patients with clinically diagnosed symptomatic stroke (first or recurrent, ischaemic, or intracerebral haemorrhagic lesion) admitted consecutively. Patients had to be aged between 18 and 85 years and had to have sufficient comprehension and communication skills. Patients were not included in cases of interfering psychiatric disorders or substance abuse, when they were physically or mentally unable to participate, or when expected discharge was < 3 weeks  Age, median, years (IQR): intervention = 59.31 (14.45), control = 61.48 (13.37)  Sex (men): intervention = 74%, control = 69%  Hemisphere damaged: lesion side, %: intervention = left 21, right 77, bilateral 3; control = left 21, right 73, bilateral 6  Time since stroke, median days: intervention = 41.50 (39.00), control = 37.00 (37.00)
Interventions	Prism adaptation or plain lenses. PA procedure was adapted from Rossetti et al. Patients wore a pair of goggles fitted with wide-field point-to-point prismatic lenses, inducing an ipsilesional optical shift of $10^\circ$ (PA) or goggles with plain lenses (SA). Exposure consisted of $\pm 100$ fast-pointing movements to 3



#### Ten-Brink 2017 (Continued)

stimuli (red, yellow, blue) presented on a horizontal axis at a distance of  $\pm 65$  cm. Left and right stimuli were located  $10^\circ$  away from the body midline. The investigator indicated which stimulus was the target. A board was held under the chin to prevent viewing of the hand at its starting position but allowing an unobstructed view of targets and terminal errors. The co-ordinates of the touch responses were recorded

#### Outcomes

- CBS
- Dynamic navigation task
- Static cancellation task

All taken immediately post intervention with no longer-term follow-up

#### Notes

### Risk of bias

Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	"Before the start of the study, the investigator put 70 printed cards with the treatment condition (35 PA and 35 SA) in envelopes. After completion of the baseline assessment, the investigator opened an envelope and allocated the patient based on the treatment written on the card." Insufficient detail on randomisation and allocation	
Allocation concealment (selection bias)	Unclear risk	See above	
Blinding of participants	Low risk	Patients could not be (completely) blinded to treatment because they had to wear the goggles. However, patients were not explicitly told which treatment they had received, and none of them expressed any awareness of assigned condition (after informal enquiry)	
Blinding of personnel	High risk	Nurses, physical therapists, and occupational therapists who filled in the CBS were blinded to treatment conditions (low risk of bias)  The investigator (AFTB) who treated and tested patients regarding secondary outcomes was not blinded to treatment because she had to put on the goggles (high risk of bias)	
Blinding of outcome assessment (detection bias) All outcomes	High risk	As above	
Incomplete outcome data (attrition bias) All outcomes	High risk	All 4 dropouts in intervention arm	
Selective reporting (reporting bias)	Low risk	Outcomes reported equally	
Other bias	Low risk	Nothing obvious	

### **Tsang 2009**

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Methods	RCT



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#### Setting: rehabilitation hospital, Hong Kong

#### **Participants**

35 participants (1 dropout during the trial)

Experimental: n = 17, control: n = 17 Adequacy of matching at baseline? Yes

Number lost to follow-up: 1; no details as to which group - no data included in analyses

Mean age, years, mean (SD): experimental = 70.47 (9.30), control = 71.82 (5.26)

Sex (men/women): experimental = 12/5, control = 9/8

Time post onset, days, mean, (SD): experimental = 22.18 (15.87), control = 21.50 (21.67)

Side of damage: right (experimental right 11, basal ganglia 0, other 6; control right 11, basal ganglia 2,

other 4)

Method of diagnosing stroke: CT or MRI

Method of diagnosing neglect: BIT conventional subtest < 129

Inclusion criteria: subacute inpatients with right hemisphere stroke, undergoing rehabilitation, left visual field inattention, right-handedness, within 8 weeks after onset of stroke, Glasgow coma scale of 15 Exclusion criteria: severe dysphasia, TIA, or reversible neurological deficit; significant impairment in visual acuity caused by cataracts, diabetic retinopathy, and glaucoma; history of other neurological disease, psychiatric disorder, or alcoholism

Visual sensory deficit: visual acuity screened for; no other method of assessing visual fields, etc., noted

#### Interventions

Right half-field eye-patching glasses: 4 weeks of conventional OT with right half-field eye-patching during OT session (conventional OT = 30 minutes ADL training and 30 minutes upper limb training using neurodevelopmental therapy - this seems to be the standard procedure, rather than a record of what participants actually got; there was no mention of deviation from this amount). Other standard care received was 5 physiotherapy sessions of 60 minutes/week, speech and language therapy, and psychological counselling as indicated; skilled nursing care; daily medical round vs control (4 weeks of conventional OT as described above, without patching). Other standard care received was 5 physiotherapy sessions of 60 minutes/week, speech and language therapy, and psychological counselling as indicated, skilled nursing care, daily medical round

Profession of intervention provider: OT

#### Outcomes

- BIT conventional subtest
- FIM

All taken immediately post intervention with no longer-term follow-up

# Notes

"Concentrates the patients' attention on the contralesional space by blocking the ipsilesional visual field, and hence lessens the disinhibition of the orienting mechanism of the ipsilesional side resulting from interhemispheric imbalance"

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Patients were randomly assigned, by a designated person using consecutively numbered sealed envelopes for each group (according to random permuted blocks of four that were derived from the block of 4 randomisation table)"
Allocation concealment (selection bias)	Low risk	The designated person was the case therapist, and envelopes were prepared by a different person - an OT
Blinding of participants	Unclear risk	States 'single-blind' study but gives no details
Blinding of personnel	High risk	As stated single-blind, safe to assume personnel were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Correspondence with study author states, "An occupational therapist, who was the blinded assessor and did not know the group allocation, was responsi-



Tsang 2009 (Continued)		ble for all the outcome measures, both pre and posttests", but assumption was not tested
Incomplete outcome data (attrition bias) All outcomes	High risk	1 participant dropped out but was not included in the analysis. Both base- line and outcome assessments include only the 34 who completed the study. Therefore no intention-to-treat analysis was performed
Selective reporting (reporting bias)	Unclear risk	Unclear
Other bias	Low risk	Study is free from systematic differences

### Turton 2010

Study characteristics	s
Methods	RCT, single-blind, pilot, 2 sites Setting: hospital, UK
Participants	37 participants consented following screening; 1 person excluded post recruitment but pre-randomisation for failing to complete assessments, so 36 randomised Experimental: n = 17, control: n = 19  Adequacy of matching at baseline? Yes, although large variation in severity of neglect Number lost to follow-up: overall 34 of the 36 randomised remained at 4 days and 28 at 8 weeks Mean age, years, mean (SD): experimental = 72 (14), control = 71 (14)  Sex (men/women): experimental = 8/8, control = 11/7  Time post onset, days, mean (SD): experimental 1 = 45 (23), control = 47 (39)  Side of damage: right  Method of diagnosing stroke: not specified  Method of diagnosing neglect: star cancellation task and/or line bisection test of BIT Inclusion criteria: right hemisphere stroke, at least 20 days before entry to study; self-care problems due to neglect identified by OT (from consecutive hospital admissions); ability to sit and point with the unaffected hand; ability to understand and follow instructions; medical fitness to participate Exclusion criteria: neglect prior to this stroke  Visual sensory deficit: sensory score at baseline given Hemianopia: experimental = 3/16, control = 4/18  Assessed by Nottingham Sensory Assessment and confrontation
Interventions	Prism adaptation training (repeated pointing movements to targets using the right 'unaffected' hand while wearing prism glasses; prism power of 10 diopters that shifted the field of view 6° to the right; training once per day, each working day for 2 weeks) vs sham treatment (same pointing procedure wearing plain glasses)  Once a day for each working day for 2 weeks  Profession of intervention provider: OT
Outcomes	<ul> <li>Conventional BIT subtests at 4 days and at 8 weeks, completed by OT</li> <li>CBS at 8 weeks</li> <li>"Motor and sensory deficits and general independence in ADL" using motoricity index (contralesional limbs), adapted Nottingham Sensory Assessment, visual field loss using confrontation, BI by participant's OT (so presumably, this 1 measure was unblinded)</li> </ul>
Notes	Conflict between proprioception and vision occurs when pointing wearing prisms and they mis-point to the right, and there is subsequent adaptation. "Treatment triggers a realignment of the egocentric coordinate system that is responsible for the localisation of the body in space and of object position in relation to the body"



#### Turton 2010 (Continued)

Therapy and control were well tolerated, with only 1% and 3%, respectively, of sessions missed by participants due to illness

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A secretary who was located outside of the stroke services administered the randomisation procedure
Allocation concealment (selection bias)	Low risk	"A minimisation method using a 4:1 element of chance was implemented and automated using Microsoft Excel for pseudo-random allocation to groups"  The participant's group was revealed, via telephone, to the occupational therapist who delivered the intervention
Blinding of participants	High risk	Prism lenses; sham not convincing
Blinding of personnel	High risk	See above
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Outcome assessments were carried out with assessors blind to group allocation" but not evidenced
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts accounted for
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious

#### Van Wyk 2014

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Methods	RCT Setting: rehabilitation centre, South Africa
Participants	<ul> <li>Age 19 to 74</li> <li>Within 1 and 3 weeks post stroke</li> </ul>
	Exclusions
	• < 7 on the Mini Mental State Evamination and presenting with Glasgow coma scale score < 14

- < 7 on the Mini Mental State Examination and presenting with Glasgow coma scale score < 14
- History of an organic disorder or major psychiatric problems
- Included in other pharmacological or rehabilitation intervention studies
- Another comorbid condition musculoskeletal or neuromuscular disability such as cancer or amputation that would have prevented participation over a period of 4 weeks

Age: not reported Sex: not reported

Hemisphere damaged: not reported Time since stroke: not reported

Interventions

Group 1 received saccadic eye movement training with visual scanning exercises



### Van Wyk 2014 (Continued)

integrated with task-specific activities; group 2 received task-specific activities only. Only the guideline of the interventions is given because principles were adapted to each participant's functional ability. VSEs integrated with task-specific activities consisted of dual-task activities, which require the ability to allocate information-processing resources between 2 tasks, and to maintain sufficient attention on visual scanning task during dual-task performance

#### Outcomes

- King-Devick test
- Star cancellation
- BI

All taken immediately post intervention with no longer-term follow-up

#### Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Participants were matched and allocated on the basis of their scores on the SAS to ensure that participants in the 2 groups were comparable with regard to their level of functional activity. The first participant who was eligible for participation in the study was allocated to group 1 (experimental group). Participants who matched a previous participant's score on the SAS were automatically placed in the second group (control group). If a participant had a score that did not match another participant's SAS score, the participant was randomly allocated to either group 1 or group 2 using a formula on a Microsoft Excel programme to randomly allocate participants. The allocation process was repeated until 12 participants had been allocated to each group
Allocation concealment (selection bias)	High risk	As above
Blinding of participants	Low risk	Participants from group 1 and group 2 were blinded to the group they were assigned to. Participants in groups 1 and 2 were treated in separate venues to control blinding of participants throughout the study
Blinding of personnel	Unclear risk	Unclear
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	To ensure reliability of research data, a skilled assessor who was blinded to groups conducted all assessments of participants in the trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	If a participant dropped out of the study for any reason, another participant was recruited to replace him or her during the 4 weeks of the study
Selective reporting (reporting bias)	Low risk	All 3 outcomes results reported in detail. No primary?
Other bias	Low risk	No statistical difference was noted between groups at baseline (P = 0.24). Based on interpretation of the SAS, the motor function of participants from group 1 and group 2 was similar at the beginning of the intervention period. It can be concluded that the 2 groups were comparable to each other regarding motor function and level of functional activity prior to intervention



### Varalta 2019

Methods	Single-center, pilot RCT Setting: Italy
Participants	Inclusion criteria: age > 18 years; presence of ischaemic or haemorrhagic stroke (as documented by computerised tomography or magnetic resonance imaging scan) that had occurred at least 6 months earlier; presence of hemi-spatial neglect (Star Cancellation Test score < 50); ability to actively rotate th head toward the left in a closed-eyes condition (absence of musculoskeletal disorders)
	Exclusion criteria: participation in other trials; dementia (Mini Mental State Examination correct score 23.80); presence of severe comprehension deficits, psychiatric disorders, deficits of somatic sensation involving the cervical dermatome map (C3–C5), or visual field deficits as assessed by neurological examination; other neurological or orthopaedic conditions involving the neck and visual ability Age, years, mean (SD): intervention = 65.5 (10.2), control = 67.0 (11.5)  Sex (men/women): intervention = 2/5, control = 4/1  Hemisphere damaged: not reported  Time since stroke, mean months (SD): intervention = 19.7 (27.7), control = 28.0 (40.6)
Interventions	Neck taping or sham neck taping. For the intervention group, tape was placed according to Kenzo Kase's Kinesio Taping Method by an experienced physiotherapist. The tape strip was applied from the mastoid bone to the clavicle (rostrocaudal direction) with the sternocleidomastoid kept in a position of maximum stretching. Two I-strips were applied: the first placed on the medial (sternal) head, and the second on the lateral (clavicular) head, of the sternocleidomastoid muscle, with 15% to 25% tension (paper-off tension)
	For the control group, smaller I-strips were used. To eliminate the specific therapeutic elements of elastic taping (i.e. longitudinal stretch, start and ending points of tape application), the strips were applied All patients wore the tape for 30 days
Outcomes	<ul> <li>Star cancellation</li> <li>Active range of motion in neck - left rotation</li> <li>Letter cancellation</li> <li>Comb and razor test</li> <li>Active range of motion of the neck</li> <li>Cervical Joint Position Error Test</li> </ul> All taken immediately post intervention with no longer-term follow-up

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Balanced (restricted) randomisation scheme"; only detail
Allocation concealment (selection bias)	Low risk	We used an allocation concealment mechanism (sequentially sealed numbered containers). Another investigator checked for correct patient allocation according to the randomisation list. After unmasking at the end of the study, we checked that no allocation errors had been made
Blinding of participants	Unclear risk	All participants were taped by the same investigator, who was not involved in the outcome assessment
Blinding of personnel	Unclear risk	Unclear



Varalta 2019 (Continued)		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All patients were evaluated by the same investigator, who was blinded to group allocation. The success of blinding was tested by asking the assessor to make an educated guess
Incomplete outcome data (attrition bias) All outcomes	Low risk	None
Selective reporting (reporting bias)	Low risk	Outcomes reported with equal detail
Other bias	Low risk	Nothing obvious

# Vatanparasti 2019

tion (selection bias)

Study characteristics		
Methods	RCT, pilot Setting: Iran, stroke unit	
Participants	Stroke patients with neglect, diagnosis of whom was verified by magnetic resonance imaging and clinical examination, right-handed Age, years: intervention 1 PA = $65.5 \pm 10.2$ , intervention 2 PA + cTBS = $67.5 \pm 8.4$ Sex (men/women) no. (%): intervention 1 PA = 5 (70), 2 (30); intervention 2 PA + cTBS = 5 (70), 2 (30) Time since stroke onset, no unit of measurement specified: subacute no. (%): intervention 1 PA = 3 (42.9), intervention 2 PA + cTBS = 3 (42.9) Time since stroke onset, no unit of measurement specified: chronic no. (%): intervention 1 PA = 4 (57.1), intervention 2 PA + cTBS = 4 (57.1)	
Interventions	Prism adaptation + cTBS  Intervention 1: all patients were asked to wear a pair of prism glasses with a rightward prismatic shift of 10° when patients were asked to actively move their intact hand in front of a vertical mirror box for 20 minutes. Sham TMS followed the same protocol except the coil was positioned at a 90° angle to the skull, and a small part of the coil was resting on the skull  Intervention 2: in addition to prisma adaptation, 1 group of patients received 10 sessions of TMS over the intact left posterior parietal cortex	
Outcomes	<ul> <li>Star cancellation task</li> <li>Line bisection task</li> <li>Figure copying test</li> <li>Clock drawing</li> <li>Modified Rankin scale (MRS)</li> </ul> Assessed pre-intervention and post intervention	
Notes		
Risk of bias		
Bias	Authors' judgement Support for judgement	
Random sequence genera-	Unclear risk No details	



Vatanparasti 2019 (Continued)		
Allocation concealment (selection bias)	Unclear risk	No details
Blinding of participants	Low risk	"Patients were unaware of the group assignments; they were informed that they are going to undergo the treatment for their visuospatial neglect of left side of their body"
Blinding of personnel	High risk	However, therapist was aware about patients' group allocation
Blinding of outcome assessment (detection bias) All outcomes	High risk	No details given
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No details given
Selective reporting (reporting bias)	Unclear risk	Unclear
Other bias	Low risk	Nothing obvious

### Volkening 2016

Study characteristics	S .
Methods	Double-blind RCT Setting: clinic, Germany
Participants	29 first-ever right hemispheric, right-handed stroke patients with signs of left-sided spatial neglect (age 18+) Cathode left = 8, cathode right = 8, sham = 8 Neglect test: according to a cutoff score criterion of ≤ 135 for mild neglect or suspicion of neglect on the Neglect test (NET, adapted German version of the BIT) Age, mean (range): cathode left = 71 (55 to 80), right = 73 (61 to 83), sham = 70 (45 to 82) Sex (men/women): cathode left = 2/6, right = 4/4, sham = 4/4 Days between stroke and treatment, mean (range): cathode left = 1.9 (1.1 to 3.9), right = 1.3 (0.4 to 2.2), sham = 1.0 (0.7 to 1.5) Exclusion: any metal implants; brain tumour, previous epileptic seizure, craniotomy, degenerative or psychiatric disorder, unable to perform the NET
Interventions	As standardised therapy, all patients received smooth pursuit eye movement training (SPT) and visual scanning training (VST). Both training programmes were presented on a 14.1-inch laptop monitor (60 Hz refresh rate). For SPT, computer-generated random displays of 350 dots (blue on a white background) moving coherently towards the left hemi-space (speed: 6.9°/s) were presented. Patients were instructed to look at the displays and to make smooth pursuit eye movements towards the direction of motion and return to the rightward side of the screen whenever they had reached the leftward border of the screen. For VST, different training exercises from the therapy programme Cogpack were used to facilitate exploration of the left hemi-space. VST programmes and their difficulty levels were adjusted individually depending on each patient's capabilities. In each session, patients first received 2 to 4 runs of SPT, followed by VST
	Simultaneously, patients received GVS or sham stimulation. Bilateral bipolar GVS was delivered by a battery-driven, direct current stimulator (neuroConn Ilmenau, Germany). Two electrodes (anode and cathode) were inserted into natrium-chloride-soaked sponges (30 cm² each) and placed over both mastoids. Polarity placements were changed for each of the 3 stimulation conditions: for CL-G VS, the cathode was placed on the left and the anode on the right mastoid. This electrode setup was reversed for



#### Volkening 2016 (Continued)

CRGVS. For CL- and CR-GVS, the current was ramped up (in steps of 0.1 mA/s) to 1.5 mA, kept there for 20 minutes, and ramped down again (in steps of 0.1 mA/s). Conforming to established safety limits, patients were stimulated for only 20 minutes with a current intensity of 1.5 mA. Apart from the intervention, patients received occupational therapy and physiotherapy but no other specific neglect training

### Outcomes

Primary outcome measures

- "Neglect test" battery (NET)
- · German adaptation of the Behavioural Inattention Test
- Subtests: cancellation (lines, letters, and stars; egocentric), copying of symmetrical figures (star, flower, diamond; object-centred)
- Short text in form of a postal address (object-centred)
- · Line bisection

Secondary outcome measures: subjective visual (SVV) and haptic vertical (SHV) were used to assess verticality perception. All taken immediately post intervention with no longer-term follow-up

#### Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	17 out of 24 patients were randomly allocated to treatment groups by the research co-ordinator, who drew cards from a sealed envelope. Since patients with more severe spatial neglect might respond differently to interventions than those with milder impairments, we allocated 7 patients using minimisation (see Scott, McPherson, Ramsay, & Campbell, 2002, for further details). Minimisation was based on NET scores. The NET score range for inclusion was subdivided into 3 strata: 0 to 45, 46 to 90, 91 to 135. Minimisation was performed by a post-doctoral researcher otherwise not involved in the study
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants	Low risk	Patients were also blinded to the allocated add-on intervention (GVS)
Blinding of personnel	High risk	Not possible
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Outcome measures were assessed by trained neuropsychologists, masked to treatment allocation and not otherwise involved in patients' treatment." Assumption of unawareness was not tested
Incomplete outcome data (attrition bias) All outcomes	High risk	For SVV and SHV, there were more missing data points because some patients were not able to perform tasks at baseline (in total, SVV = 9; SHV = 5) due to impaired comprehension. Baseline measurements were therefore substituted with the group mean. Except for 1 case, all patients were able to perform the tasks after the intervention. Accordingly, LOCF was applied for missing data for the following time points
Selective reporting (reporting bias)	Unclear risk	Several primary outcomes
Other bias	High risk	Use of LOCF



# Welfringer 2011

Study characteristics	
Methods	RCT, designed as a feasibility study Setting: Germany
Participants	30 participants with right hemisphere stroke, less than 6 months previously Inclusion criteria: diagnosis of right hemispheric stroke dated less than 6 months earlier; no history of major psychiatric problems and no other coexisting disease/disability; showed unilateral left visuospatial neglect symptoms as defined by a score ≤ 54 on the Letter Cancellation Test; no diagnosis of hemianopia; sufficient sensory, physical, and cognitive capacities to follow instructions for more than 30 minutes and no additional verbal-memory deficits as defined by a percentage rank > 16 in the story recall subtest of the Wechsler Memory Scale-Revised (WMS-R); aged between 20 and 75 years; right-handed; provided informed consent Experimental: n = 15; mean age = 56.3 years (SD 11.2); mean time since stroke = 3.2 months (SD 1.5) Control: n = 15; mean age = 57.3 years (SD 11.3); mean time since stroke = 3.4 months (SD 2.8)
Interventions	Visuomotor-imagery therapy (2 daily half-hour sessions of visuomotor-imagery therapy as add-on treatment over a period of 3 weeks; participants mentally practised positions and movements of the contralesional upper limb in a repetitive fashion and as vividly and intensively as possible; over the course of the 3-week intervention period, they participated in 28 to 30 training sessions; a total of 4 positions and 6 sequences (simple and complex movements) were imagined, with 1 exercise repeated up to 10 times per session) vs no supplementary intervention
	All participants received standardised rehabilitation therapies including 45 minutes of exploration training 4 times per week
Outcomes	<ul> <li>Neglect tests: Bells Cancellation test; drawing tasks; text-reading task</li> <li>Representation tests: test of mental representation of left side of body</li> <li>Arm function texts: sensation of left arm; Action Research Arm Test</li> <li>Measured immediately post treatment</li> </ul>
	For analyses within this review, we used neglect - Bells Cancellation test
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Allocation sequences have been generated by study personnel prior to beginning the trial using a web-based randomisation generator (http://www.randomization.com)
Allocation concealment (selection bias)	Low risk	Blocked randomisation, in blocks of 10; computer-generated sequence, delivered by person independent of intervention
Blinding of participants	High risk	Impossible to blind
Blinding of personnel	High risk	Impossible to blind
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	States: "outcome measures were assessed by a blinded tester." although no detail given
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up



Welfringer 2011 (Continued)		
Selective reporting (reporting bias)	Low risk	All reported with equal detail
Other bias	Low risk	Nothing obvious

### **Wiart 1997**

Study characteristics	
Methods	RCT Setting: hospital, France
Participants	22 people within 3 months of onset of stroke and severe left unilateral neglect, hospitalised in 2 neurorehabilitation hospitals, positive for neglect on 3 tests (see Outcomes)  Experimental: n = 11, control: n = 11  Mean age, years: experimental = 66, control = 72  Sex (men/women): experimental = 6/5, control = 6/5  Time post onset, mean days: experimental = 35, control = 30  Exclusions: history of stroke, alteration of general status, cognitive difficulties incompatible with rehabilitation
Interventions	1 hour per day for 20 days of experimental treatment followed by traditional rehabilitation (1 to 2 hours physiotherapy and 1 hour OT); experimental treatment is Bon Saint Come method: participant wears a thoracolumbar vest with attached metal pointer above the head; participant points to target on mobile wooden panel; audible and luminous signals provide biofeedback effect when targets are touched; initially conducted when sitting, this progresses to standing; the therapist participates actively during the session, stimulating, guiding, and correcting vs 3 to 4 hours of traditional rehabilitation per day
Outcomes	Study collected 2 types of outcomes
	<ul> <li>Quantitative assessment of neglect (line bisection, line cancellation, bell cancellation)</li> <li>Autonomy (FIM)</li> </ul>
	These assessments were conducted 3 times: Day 0, Day 30 (after therapy), and Day 60 This review used only data from line bisection and FIM. Both 30-day (immediate) and 60-day (persisting) data were used in this review
Notes	The paper consists of 2 studies. These data refer to Study 1 only The experimental group was younger and had a higher initial FIM score (66) than the control group (54) Cancellation data were reported as errors rather than correct performance. Only 1 set of cancellation data (lines not bells) were entered in this review to avoid entering the same group of participants twice into the meta-analysis Line bisection scores are % deviation to the right Control group had more, but not significantly so, omissions on line cancellation (control 16, experimen tal 14) and right deviations on line bisection (control 53%, experimental 50%) at baseline compared with experimental group

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	They were randomly divided into 2 groups (using a randomisation table)
Allocation concealment (selection bias)	High risk	Information on allocation concealment unclear; random number tables



Wiart 1997 (Continued)		
Blinding of participants	High risk	No detail given; participants unlikely to be blinded due to nature of intervention
Blinding of personnel	Unclear risk	No detail given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated. Assessment done by 'one of us (LW)'; different from person delivering therapy
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	High risk	Control group older and more disabled – no correction made

### Wilkinson 2014

Study characteristics		
Methods	RCT Setting: rehabilitation units, UK	
Participants	Inclusion criteria	
	<ul> <li>&lt; 129 on BIT</li> <li>Right unilateral stroke</li> <li>≥ 6 weeks post stroke</li> <li>≥ 18 years of age</li> <li>Score ≤ 2 on the 6-item screen for dementia</li> <li>≤ 29 on BDI</li> </ul>	
	<ul> <li>Exclusion criteria</li> <li>Evidence of moderate to severe aphasia</li> <li>Prior significant neurological or vestibular illness</li> <li>Electronic implants</li> </ul>	
	Age, years, mean (SD): group $1 = 66.9$ (10.6), group $2 = 66.0$ (9.37), group $3 = 65.7$ (8.72) Sex (women/men): group $1 = 3/12$ , group $2 = 6/12$ , group $3 = 3/13$ Hemisphere damaged: right Time since stroke, days (median IQR): group $1 = 68$ (39 to 229), group $2 = 75$ (41 to 479), group $3 = 94$ (39 to 534)	
Interventions	Repeated sessions of galvanic vestibular stimulation. Participants received 1, 5, or 10 sessions, each lasting 25 minutes, of subsensory, left-anodal right-cathodal noisy direct current (mean amplitude = 1 mA)	
Outcomes	BIT-C BI	
	Taken up to 1 month post intervention	



### Wilkinson 2014 (Continued)

Notes

Risk (	of bias
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Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was conducted using a secure, remote randomisation facility independent of the research team
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants	Low risk	Treatment allocation was double-blind; since GVS was subsensory, participants did not know their allocation, and a stimulation protocol (active or sham) pre-determined by the randomisation officer was naively administered by the experimenter by typing a 4-digit code (which changed every time) into the stimulation device. Participants' in-patient neglect treatment (typically visual scanning therapy but sometimes limited to informal reminders given by occupational therapy staff to look left during functional activities) was suspended while they remained on-study
Blinding of personnel	Low risk	See above
Blinding of outcome assessment (detection bias) All outcomes	Low risk	BIT and BI were administered by the experimenter
Incomplete outcome data (attrition bias) All outcomes	Low risk	2, 1, 0 dropouts in each arm
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	No evidence of this

# Wu 2013

Study	charac	taristics

Study Characteristic	
Methods	Single-blinded, randomised pre-test and post-test control group design Setting: rehabilitation clinics and medical centres, Taiwan
Participants	27 patients with right side cerebral stroke and neglect CIT + EP = 9, CIT = 9, control = 9  Neglect definition: results on 2 or more of 4 tests (double simultaneous stimulation test, line bisection test, random shape cancellation test, random Chinese word cancellation test)  Age, years, mean (SD): CIT + EP = 56.1 (14.5), CIT = 65.5 (9.8), control = 61.3 (11.2)  Sex (men/women): CIT + EP = 5/2, CIT = 5/3, control = 7/2  Time between stroke and treatment, months, mean (SD): CIT + EP = 13.0 (13.9), CIT = 10.1 (10.4), control = 13.7 (14.1)  Exclusion: no excessive spasticity in the affected arm, including shoulder, elbow, wrist, and fingers; no severe cognitive impairment by showing awareness and ability to respond to oral instructions; no severe impairment of visual acuity after rectification; no participation in any experimental rehabilitation or drug studies during the study period



Wu 2013 (Continued)

#### Interventions

All participants received 2 hours of therapy, 5 days/week for 3 weeks, with 1-to-1 supervision. Interventions were provided at participating hospitals by occupational therapists who were trained in administration of the 3 protocols by investigators and who completed a written competency test before they administered treatment. Treating therapists were not blinded to group allocation. All other routine rehabilitation, such as physical therapy or speech therapy, proceeded as usual

Constraint-induced therapy (CIT) + eye-patching (EP) group. Participants in this group received CIT + EP. CIT addressed forced use of the affected UE and restricted the unaffected UE during training. Shaping skills were delivered while participants were forced to use their affected UE in the mass practice of functional tasks such as drinking water and opening a jar. Participants wore a mitt on their unaffected hand and wrist for 6 hours/d during the 3-week training and reported their compliance in a daily log. Home skill activities were assigned to promote this training in daily life, and problems were discussed to aid participants in overcoming barriers they encountered. Participants were also asked to wear glasses with a patch on the right lens to block the visual stimuli from the right side and to force them to receive stimuli from the left visual field.

CIT group. The intervention in the CIT group resembled the intervention in the CIT + EP group, except participants did not wear the EP glasses

Control group. The control group received traditional occupational therapy matched in intensity and duration with that of the other groups. The training programme for the affected UE included stretching and weight bearing, improving range of motion, muscle strengthening, and practising tasks used for functional training that might involve the unaffected UE assisting the affected UE, for example, stabilising a bottle while opening its lid or moving pegs into holes on a board

Control group received usual care

#### Outcomes

- · Catherine Bergego Scale (CBS)
- Eye movement analysis and eye movement variables
- · Kinematic analysis and kinematic variables

All taken immediately post intervention with no longer-term follow-up

Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Eligible participants were randomly assigned to CIT + EP, CIT, or conventional intervention in accordance with a random number table. When a new participant was enrolled, the study co-ordinator gave a sealed opaque envelope identifying the participant's group to therapists, and they were informed of group allocation and delivered therapy accordingly
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants	High risk	Single-blinded
Blinding of personnel	High risk	Treating therapists were not blinded to group allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Three certified occupational therapists blind to group allocation were trained to provide the evaluations before and after a 3-wk intervention. The same rater administered all the study measurements to each participant at baseline and after the 3-wk intervention." Not enough detail to evidence lack of communication between team members
Incomplete outcome data (attrition bias)	Low risk	2 dropped out of one group, 1 from another



# Wu 2013 (Continued)

All outcomes

Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious

# **Yang 2015**

Study characteristics	
Methods	Pilot RCT Setting: Taiwan, patients receiving routine rehabilitation
Participants	Inclusion criteria: patients between 18 and 80 years of age; (2) first-stroke patients (cerebral infarction or haemorrhage) confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) and in recovery time within 60 to 180 days; (3) USN confirmed by line bisection test, star cancellation test, or clinical examination; (4) patients without serious heart, lung, and kidney disease or epilepsy; (5) patients without metallic implant of diamagnetic substance  Age, years: intervention $1 = 46.72 \pm 13.11$ , intervention $2 = 48.01 \pm 12.25$ , intervention $3 = 49.45 \pm 10.78$ , control = $47.70 \pm 11.81$ Sex (number of men): intervention $1 = 6$ , intervention $2 = 4$ , intervention $3 = 5$ , control = $7$ Time since stroke: within 60 to 180 days
Interventions	rTMS Intervention 1: stimulation parameter in the 1-Hz group was 1 Hz, and stimulus duration for each sequence was 8 seconds; repeated 82 sequences with a total of 656 pulse number Intervention 2: stimulation frequency in the 10-Hz group was 10 Hz, with a total pulse number of 1000 and stimulation interval of 55 seconds Intervention 3: continuous TBS group parameter was 801 pulses, in bursts of 3 pulses at 30 Hz, repeated every 100 milliseconds (5 Hz, $\theta$ rhythm) Control: sham stimulation
Outcomes	<ul> <li>Line bisection</li> <li>Star cancellation</li> <li>2 weeks before treatment (designated as time point 1), beginning of treatment (time point 2), end of treatment (time point 3), 1 month after treatment (time point 4)</li> </ul>

### Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No detail given
Allocation concealment (selection bias)	Unclear risk	No detail given
Blinding of participants	Unclear risk	No detail given
Blinding of personnel	High risk	No detail given



Yang 2015 (Continued)		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Mentions assessor was blinded, although unclear if blinding achieved
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts
Selective reporting (reporting bias)	Low risk	Although tables for 2 out of 3 outcomes are presented (the significant 2), unsure if this constitutes high bias
Other bias	Low risk	No evidence of this

### Yang 2015 10Hz

14119	
Study characteristics	
Methods	See Yang 2015
Participants	
Interventions	
Outcomes	
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No detail given
Allocation concealment (selection bias)	Unclear risk	No detail given
Blinding of participants	Unclear risk	No detail given
Blinding of personnel	High risk	No detail given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Mentions assessor was blinded, although unclear if blinding achieved
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropout
Selective reporting (reporting bias)	Low risk	Although tables for 2 out of 3 outcomes are presented (the significant 2), unsure if this constitutes high bias
Other bias	Low risk	No evidence of this



Yang 2015 1Hz

Study characteristics	
Methods	See Yang 2015
Participants	
Interventions	
Outcomes	
Notes	

### Yang 2015 cTBS

Study characteristics	
Methods	See Yang 2015
Participants	
Interventions	
Outcomes	
Notes	

## **Yang 2017**

Study characteristics	
Methods	RCT Setting: China, rehabilitation ward
Participants	Inclusion criteria: (1) diagnosis of right hemispheric stroke through neurological examination and CT or MRI scans; (2) duration since onset longer than 1 week; (3) presenting with unilateral neglect confirmed by conventional subtests of the Behavioural Inattention Test with cutoff score of 129; (4) unilateral neglect as a result of recent acute stroke; (5) aged 18 or over; (6) Mini Mental State Examination score > 17.1  Age, years, mean: all participants = $58.0 \pm 12.3$ Sex (men/women): intervention $1 = 14/6$ , intervention $2 = 12/8$ , control = $17/3$ Time post stroke, days: intervention $1 = 36.6 \pm 33.2$ , intervention $2 = 37.5 \pm 26$ , control = $42.5 \pm 30.6$
Interventions	Intervention 1: rTMS and sensory cueing groups were exposed to low-frequency repetitive magnetic pulses generated by the TMS stimulator for 2 weeks. Patients were asked to wear the sensory cueing device on their left wrist for 3 hours a day, 5 times a week, over the 2 weeks. The cue was given every 5 minutes in the form of vibration (196 Hz, similar to the vibration of a cell phone) generated from the device; participants were required to press the acknowledgement button on the device to stop the cueing each time it was emitted Intervention 2: rTMS only Control: usual care



### Yang 2017 (Continued)

### Outcomes

- BIT C
- CBS
- Fugl-Meyer Assessment
- Action Research Arm Test
- Modified Barthel index

Measured up to 1 month post intervention

### Notes

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation table according to random permuted blocks of 4
Allocation concealment (selection bias)	Unclear risk	Allocation-to-treatment sequences were concealed from all investigators responsible for carrying out the training or from patients involved
Blinding of participants	High risk	No detail given
Blinding of personnel	High risk	No detail given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Investigators were blinded from all assessments carried out; unknown how this worked in practice
Incomplete outcome data (attrition bias) All outcomes	Low risk	1, 1, and 2 lost in each group
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious

# Yi 2016

Study characteristics	
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Study Characteristics	
Methods	RCT Setting: South Korea, hospital
Participants	30 participants with left visuospatial neglect diagnosed as right cerebral ischaemic or haemorrhagic stroke 10 anodal, 10 cathodal, 10 sham Mean age, years: anodal = 63, cathodal = 62, sham = 62 Sex (men/women): anodal = 7/3, cathodal = 8/2, sham = 6/4 Cause of neglect (haemorrhagic/ischaemic): anodal = 1/9, cathodal = 1/9, sham = 2/8 Neglect defined as > 6.33 mm average deviation from the centre line on the line bisection test (LBT) Exclusions: severe cognitive dysfunction or aphasia, contraindications for tDCS, systemic disease, on going neoplasia



<b>Yi 2016</b> (Continued)	Υi	20	16	(Continued)
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Interventions Transcranial direct current stimulation (tDCS) applied over posterior parietal cortex: anodal, cathodal,

or sham

15 sessions of tDCS. Sessions were 5 times per week for 3 weeks. A direct current was delivered by 2 sets of battery-powered devices using 2 pairs of saline-soaked sponge electrodes(5 cm  $\times$  5 cm). Stimulation was delivered while the patient was receiving conventional occupational therapy

All patients received conventional physical therapy throughout the duration of the 3-week tDCS proto-

col

Outcomes

- Motor-free visual perception test (MVPT)
- LB<sup>7</sup>
- Star cancellation test (SCT)
- Catherine Bergego Scale (CBS)

Assessed pre-treatment and post treatment

Notes

We entered this study into meta-analysis as 2 studies: Yi (2016) anodal, and Yi (2016) cathodal

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Patients were identified by a number assigned by a centralized computer-generated randomization code"
Allocation concealment (selection bias)	Unclear risk	Insufficient detail to confirm
Blinding of participants	Low risk	"Sham stimulation was performed in the same way as active stimulation, but the stimulator was turned off after 30 seconds. This ensured that subjects could feel the initial itching sensation at the beginning of tDCS and allowed for a successful blinding of the subjects to their stimulation condition"
Blinding of personnel	High risk	"Sham stimulation was performed in the same way as active stimulation, but the stimulator was turned off after 30 seconds"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropout seemingly
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious

#### Yi 2016 anodal

Methods See Yi 2016

**Participants** 



Notes

Yi 2016 anodal (Continued)		
Interventions		
Outcomes		
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Patients were identified by a number assigned by a centralized computer-generated randomization code"
Allocation concealment (selection bias)	Unclear risk	Insufficient detail to confirm
Blinding of participants	Low risk	"Sham stimulation was performed in the same way as active stimulation, but the stimulator was turned off after 30 seconds. This ensured that subjects could feel the initial itching sensation at the beginning of tDCS and allowed for a successful blinding of the subjects to their stimulation condition"
Blinding of personnel	High risk	"Sham stimulation was performed in the same way as active stimulation, but the stimulator was turned off after 30 seconds"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropout seemingly
Selective reporting (reporting bias)	Low risk	Outcomes reported equally
Other bias	Low risk	Nothing obvious
Yi 2016 cathodal		
Study characteristics		
Methods	See Yi 2016	
Participants		
Interventions		
Outcomes		



### Zeloni 2002

Study characteristics	
Methods	RCT Setting: Italy
Participants	8 randomised (see Notes)  Experimental: n = 4, control: n = 4  Mean age, years: experimental = 68.8, control = 76.3  Sex (men/women): experimental = 4/0, control = 2/2  Mean months post stroke: experimental = 11.25, control = 4.5  Inclusion: "post-acute" patients with right hemisphere vascular lesions and neglect, admitted to hospital, right-handed, left hemiplegic  Exclusions: normally wore glasses
Interventions	Wearing plastic goggles for 1 week, removing them only to go to sleep (the right side of each lens was blinded) vs no goggles All 8 participants were involved in the hospital's daily activities including usual treatment for neglect, tasks to train compensation for faulty scanning
Outcomes	Participants were assessed on 3 occasions: at recruitment, after the experimental group had received 1 week of hemi-blinding goggles, and again 1 week after goggle treatment ended. Controls were assessed at the same time points but never wore the hemi-blinding goggles. Testing was performed without goggles. Outcomes used were line, letter, and bell cancellation, copy drawing, line bisection For this version of the review, we used single letter cancellation outcome data only. We used data from the third time point; as this was only 1 week after intervention; it is coded in this review as 'immediate' effects
Notes	Personal communication from study authors confirmed the methods used and provided data. The 8 randomised participants are numbers 1 to 4 in treatment and control groups as listed in the study authors' Table 1, page 196. The original study recruited 11 participants. The first 8 were randomised as de scribed above. The other 3 were non-randomly added to the groups (1 to treatment and 2 to control). This review used only the 8 randomised participants  Cancellation tests were scored as number correct. Line bisection was scored as % correct, decreasing for rightward deviation. Study authors provided raw data (%) for the 8 participants on line bisection. Mean (SD) values were as follows: experimental = 62.5 (35.2), control = 73.8 (22.2). These data were used in the 2006 version of this review, but for this version, the number of neglect outcomes was reduced and the line bisection data removed

Bias	Authors' judgement	Support for judgement
	- Tuttiers Juagement	
Random sequence generation (selection bias)	High risk	See below
Allocation concealment (selection bias)	High risk	For the first 8 participants, group allocation was performed by randomly selecting a label from a pre-printed set of 8 (see Notes). Label preparation was performed by a member of the trial team, but selection was performed by a student who had no previous or later involvement in the trial. Although allocation was done externally, the method used did not permit verification
Blinding of participants	High risk	Blinding not possible
Blinding of personnel	High risk	Blinding not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	No details



Zel	loni	2002	(Continued)

Incomplete outcome data

(attrition bias)

Low risk

No missing outcomes

Selective reporting (re-

porting bias)

All outcomes

Low risk

Outcomes reported equally

Other bias

Unclear risk

No baseline adjustments made - controls seem somewhat older, although sample was very small

ADL: activities of daily living.

ASMP: auditory subjective median plane.

BI: Barthel Index.

BIT: Behavioural Inattention Test.

CBS: Catherine Bergego Scale occupational therapist's evaluation score.

cm: centimetre.

CT: computerised tomography. CVA: cerebrovascular accident.

FA: functional approach. FAI: Frenchay Activities Index.

FIM: Functional Independence Measure.

FT: feedback training.

GHQ: General Health Questionnaire. GVS: Galvanic Vestibular Stimulation. HFVS: Harrington Flocks Visual Screener.

HHA: homonymous hemianopia.

HI: head injury.

IQR: interquartile range. LAT: limb activation training. LBT: line bisection test.

mm: millimetre.

MMSE: Mini Mental Status Exam.

MVPT: Motor-Free Visual Perception Test.

N/A: not applicable.

Nottingham EADL: extended ADL index.

OKS: optokinetic stimulation. OT: occupational therapy/therapist.

RBD: right brain damage.

RCPM: Raven's Coloured Progressive Matrices.

RCT: randomised controlled trial.

Rey CFT: Rey Osterreith Complex Figure Test.

RH: right hemisphere.

RMA: Rivermead Motor Assessment.

RPAB: Rivermead Perceptual Assessment Battery. rTMS: repetitive transcranial magnetic stimulation.

SCT: star cancellation test. SD: standard deviation.

SEM: standard error of the mean.

SIAS: Social Interaction Anxiety Scale.

SIS: Stroke Impact Scale.

SU: stroke unit.

tDCS: transcranial direct current stimulation.

TENS: transcutaneous electrical nerve stimulation.

TIA: transient ischaemic attack.

ToT: transfer of training. VN: visual neglect.

WAIS-R: Revised Weschler Adult Intelligence Scale.

WMFT: Wolf Motor Function Test. WRAT: Wide Range Achievement Test.



# **Characteristics of excluded studies** [ordered by study ID]

Study	Reason for exclusion		
Akinwuntan 2010	Study does not include a neglect population. It is a study of 3 types of attention problems (selective attention, divided attention, speed of processing) that would affect driving ability. Refers to visual problems, but these are not neglect. No neglect measures are used		
Al Mahasneh 1991	Extreme difficulties with recruitment and participant attrition. 14 participants with neglect consented. These were unevenly assigned to experimental (9) and control (5) groups. Only 5 participants completed 3 weeks of treatment. Review authors did not feel the data were adequate for meta-analysis, e.g. missing data, no SDs		
Angeli 2004	Not an RCT		
Bar-Haim 2011	The method of allocation was not fully randomised. Clarification from study author stated, "the first individual was assigned randomly to 1 of the 3 groups (by assigning numbers to the groups, 1-3, and drawing a number for that patient). From that point on, each new participant was assigne to the next group consecutively"		
Beis 1999	Controlled trial but not RCT: allocation by fixed order of presentation of participants, i.e. first to group 1, second to group 2, etc. Outcome assessors were blinded to allocation. Personal communication provided FIM data, confirmed allocation method, and revealed that assessments were carried out by 2 blinded researchers		
Butter 1992	Clarification of randomisation sought but not obtained. Appropriate results (means and SDs) not reported. Review authors were not sure that the trial was actually evaluating a treatment for spatial neglect		
Carter 1980	Clarification of randomisation sought but not obtained. Separate data for stroke patients also requested but not obtained. Appropriate data (means, SDs) not reported		
Chen 2014	Clarification of randomisation sought; study author confirmed allocation not randomised		
Cubelli 1993	Identified as a potential RCT of spatial neglect for the 2006 version. As further information could not be obtained, this was added to studies awaiting classification. As further details have still not been obtained, it has been moved to Excluded studies. We will re-consider this study for inclusion further information becomes available		
Diller 1974	Reported data inadequate for review. No reply to our letter of 9 February 1999, asking for difficult-to-extract data		
EEG-NF 2009	Not a cognitive rehabilitation approach		
Facchin 2019	Cross-over		
Frassinetti 2002	Controlled clinical trial: non-random allocation (n = 13). Controls at different hospital. Assessment of outcomes not clear (probably non-blind)		
Gordon 1985	Controlled trial: quasi-randomisation based on rehabilitation service to which participant was assigned. Experimental and control conditions alternated every 6 months between the 2 services. Not randomised		
Harvey 2003	Controlled trial: non-randomised, initial recruits allocated by date of admission to hospital ward, later recruits allocated by attempting to match groups on their scores on pre-intervention neglect assessments. Study author provided clarification and unpublished data by personal communication		



Study	Reason for exclusion
Harvey 2010	Not an RCT
Jacquin-Courtois 2010	Did not collect outcomes of relevance to this review
Kang 2009	Not specific to neglect
Keller 2006	Although the English abstract states that participants were "randomly assigned", the full German paper does not state random allocation, and it appears that this study is not a randomised study
Keller 2009	Cross-over
Kerkhoff 2005	Not randomised. States that participants were "consecutively collected and matched for clinical and demographic variables as well as neglect severity" and "all subjects were treated in a single-subject baseline design"
Kerkhoff 2012b	The intervention involved a single treatment session (i.e. this was not a rehabilitation programme)
Klos 2005	Personal communication from an expert in the field reported that Klos had completed an unpublished RCT of prism adaptation therapy for neglect. Excluded from review, as no reply to request for clarification of methods and data. Will reconsider for inclusion in next update if further information becomes available
Ladavas 2013	Not randomised
Lesniak 2013	Not neglect
Lincoln 1985	RCT of patients with general perceptual problems. Problems are likely to have included neglect, but this subgroup could not be separately identified
Loverro 1988	Controlled trial: reported as randomly assigned but allocation based on bed availability; outcome assessors blinded to purpose of the study
Nakamura 2015	Cross-over
Niemeier 1998	Controlled trial: not randomised, selected in order of consecutive admissions and on documented left or right neglect. No information on concealment
Osawa 2010	No mention of randomisation and appears that group allocation was based on whether or not they happened to have family
Paolucci 1996	Controlled trial: abstract states randomly assigned but allocated on the basis of bed number (odd or even); bed number had been assigned by Hospital Administration; odd numbers got immediate training, even numbers got training after 2 months (delayed training); neglect screening assessment done after allocation by psychologist unaware of purpose of study; outcome assessor blinded to purpose of the study; after 8 weeks, the delayed group received training and the immediate group received control treatment (broad cognitive stimulation)
Patole 2015	No comparison group, pre-post study
Pizzamiglio 2004	Non-random controlled trial (n = 22): alternate allocation. Blind assessment of outcome on BI (functional outcome). Not clear if outcome assessed blind on impairment measures
Rossetti 1998	Controlled trial: further data from study author confirm it was not randomised. First 6 consecutive cases were allocated to experimental group and next 6 to control. Outcome assessors were not blinded. The trial is the second of 2 experiments reported in the paper



Study	Reason for exclusion
Rossetti 2005	Ongoing pharmacological study
Rossi 1990	Less than 50% of participants had neglect
Schindler 2002	Non-randomised cross-over controlled trial. First 10 participants were randomised to 1 of 2 groups, but the data on these 10 were not available at the time of this version of this review. It would be considered for inclusion at the next update if study authors could provide randomised data
Schmidt 2013	Cross-over
Serino 2006	Not randomised
Serino 2009	Non-randomised controlled trial. After the first 5 participants, allocation is by alternation in blocks of 4
Svaerke 2019	Cross-over
Tham 1997	Non-random controlled trial. First 7 participants assigned to novel treatment group, second 7 participants to conventional treatment group
Toglia 2009	RCT of assessment methods - dynamic vs static
Trudell 2003	Published abstract suggested this may be an eligible study. Excluded from review, as no information with which to confirm methods. No further information has become available
Turgut 2018	Cross-over
Vaes 2016	Communication with study author confirmed study not randomised: "We did not look at the nature of neglect for assigning patients to the experimental or control group. Because the time post-stroke could be a factor that influences treatment results, we took the number of days post-stroke into account and tried to match this between the groups. However we did not use a tool or statistical method"
Van Kessel 2013	Cross-over
Van Os 1991	Not randomised (confirmed by native Dutch speaker)
Van Puymbroeck 2014	Not specific to neglect, not an RCT
Webster 2001	Controlled clinical trial: 40 assigned, 1 excluded, and matched participant excluded, n = 38. 20 controls were from a previous study, not simultaneous. Non-blind assessment of outcomes. Wheelchair navigation (functional measure) as outcome; no impairment measures
Weinberg 1977	Patients did not necessarily have neglect
Weinberg 1979	Clarification of randomisation procedure sought but not obtained, and unlikely to be, given the age of this article. The time scale of publication (and a statement in the results) suggests that participants in this study were not in the Weinberg 1977 study; however, this has not been confirmed by study authors. On the other hand, the 1979 paper does not explicitly mention 'neglect' and may instead be a trial of visual perception. Given the amount of uncertainty about this study's fit to the inclusion criteria, inability to obtain confirmation and clarification about this old study and lack of detail on randomisation, we decided to exclude the 1979 article
Weinberg 1982	Confirmation regarding randomisation sought from trialist but not obtained. No SD reported



Study	Reason for exclusion
Young 1983	Controlled trial: not randomised. Divided into 3 groups matched for age, education, time since onset, and degree of deficit: no further information provided other than assessor blinded to group's membership

BI: Barthel Index.

FIM: Functional Independence Measure. RCT: randomised controlled trial.

SD: standard deviation.

# **Characteristics of studies awaiting classification** [ordered by study ID]

### Cazzoli 2015

Methods	RCT
Participants	Left-sided, hemi-spatial neglect after subacute right hemispheric stroke
Interventions	cTBS was applied at 100% of patients' individual resting motor threshold of the right small hand muscles. Sham stimulation was applied according to the same protocol, with the exception that a sham coil was connected to output from the stimulator
Outcomes	<ul><li>Balloons test</li><li>Cancellation tests</li></ul>
Notes	Report analyses data from 13 patients. Five were "randomly allocated" (no further detail) to active or sham intervention. Remaining 3 received first sham, and then, within 5 days, active. Absence of statistically significant differences between data for these 3 and allocated groups was misinterpreted by study authors as "comparable in all these respects". All analyses are done as if allocated groups were each n = 8

### Chan 2013

Methods	Before-and-after trial
Participants	40 patients with stroke and associated unilateral neglect
Interventions	12-session visual scanning programme for 4 weeks, whereas patients in the control group received standard rehabilitation services only
Outcomes	Modified BI, MMSE, and 2 neglect-related measures, namely, Behavioural Inattention Test - Conventional subtests, and Catherine Bergego Scale
Notes	We will include in future updates if deemed eligible

# **Chan 2017**

Methods	Randomised double-blind controlled trial
Participants	Inclusion criteria: first or second stroke (haemorrhagic or ischaemic) confirmed by computer axial tomography scan or magnetic resonance imaging



### Chan 2017 (Continued)

Neurological representation compatible with unilateral right lesion involvement (i.e. left hemiplegic); exhibited left visual field inattention or neglect by following any of the following criteria: obtaining a total score of star cancellation subtest in the conventional battery of the Behavioural Inattention Test < 51 (out of 54), obtaining a total score of line bisection subtest in the conventional battery of the Behavioural Inattention Test < 7 (out of 9), score on Catherine Bergego Scale  $\geq$  1, right-handed, less than 6 months since onset of stroke at study entry, able to follow simple command

Exclusion criteria: patients with severe dysphasia (either expressive or comprehensive) that restricts communication; history of other neurological disease, psychiatric disorder, or alcoholism; significant impairment in visual acuity caused by cataracts, diabetic retinopathy, glaucoma, or hemianopia; any additional medical or psychological condition that would affect ability to comply with the study protocol

Ages eligible: child, adult, and senior

Sexes eligible: all

Interventions	Experimental: TMS and trunk rotation Sham comparator: sham TMS and trunk rotation	
Outcomes	Primary: BIT - Chinese version Secondary: Catherine Bergego Scale, FTHUE-HK, UE-Fugl Meyer, FIM, SA-SIP 30	
Notes	End date: 1 June 2019; unable to obtain further information	

#### Hauer 2007

Methods	3-arm trial
Participants	18 participants with visuospatial neglect
Interventions	Prism adaptation. Group 1 had 1 daily treatment, Group 2 had 2 daily treatments, and Group 3 had none
Outcomes	Symptoms of neglect
Notes	Unsure if fully random allocation - awaiting translation

### Iwata 2017

Methods	
Participants	Inclusion criteria: (1) scoring less than cutoff value in the line cancellation task, (2) no severe cognitive impairment (MMSE > 15)  Exclusion criteria: (1) inability to understand the task because of aphasia or other cognitive impairment, (2) inability to sit on a wheelchair, (3) inability to recognise objects on a screen due to severely damaged eyesight, (4) inability to reach with upper limb extremity because of restricted range of motion, (5) inability to give informed consent form  Age minimum: 20 years old  Age maximum: 85 years old  Gender: men and women
Interventions	Patients were attached to a head-mounted display (HMD) and presented 3-dimensional virtual reality space where multiple objects were installed. First, they answer aloud the objects' name of far space in 3-dimensional virtual reality space with HMD. Second, they touch the objects of near space with 1 hand that is synchronised in 3-dimensional virtual reality space with HMD. At this time, they are promoted attentional disengagement from the ipsilesional stimuli by blocking visual stimuli to



#### Iwata 2017 (Continued)

direct attention and attentional movement from the ipsilesional to the contralesional side by expanding the visible area to the contralesional side. This took about 6 minutes

Patients were seated at a desk. They conducted visual scanning training on the desk. The task of patients is to answer the objects' name that is pointed by the therapist. Objects were installed on the desk. This took about 6 minutes

Patients were seated at a desk. They conducted visual scanning training on the screen. The screen is installed in front of the patient. The task of patients is to answer the name of the object that is pointed to by the therapist. Objects were installed on the screen. This took about 6 minutes Patients were attached to a head-mounted display (HMD) and presented 3-dimensional virtual reality space, where multiple objects were installed. They answer aloud the name of objects of far space in 3-dimensional virtual reality space with HMD. At this time, patients' attention is inducted to neglect side of an object. This took about 13 minutes

Outcomes	Primary: line cancellation, line bisection, star cancellation, letter cancellation task Secondary: not stated
Notes	Status - not yet recruiting Status seems unusual given the start date; we have been unable to gain further information

#### Lim 2017

Methods	Single-blind RCT
Participants	Inclusion criteria: presence of hemi-spatial neglect as defined by Behavioral Inattention Test score of 129 or worse (maximum score 146) Exclusion criteria: presence of aphasia at time of testing, recent seizures, major psychiatric illness, prior unrelated neurological disease
Interventions	1/2 patients receive visual stimulation with rehabilitation glasses. 1/2 patients receive control stimulation with rehabilitation glasses
Outcomes	Primary: BIT Secondary: none stated
Notes	Status: completed; we have been unable to gain further information

### Marandola 2020

Methods	RCT
Participants	30 patients with ischaemic stroke and diagnosis of hemi-neglect
Interventions	Modified constraint-induced movement therapy (mCIMT) or conventional therapy
Outcomes	Catherine Bergego Scale (CBS) for assessment hemi-neglect; Fugl-Meyer tests for the motor function of lower and upper limb, and BI and modified Rankin scale for the rest of objectives
Notes	We will include this study in future updates if eligible



Mueller-Planitz 2017  Methods RCT					
Methous	RCI				
Participants	Inclusion criteria: 18 years old or older; demonstrated visual/spatial neglect, as demonstrated by NIH Stroke Scale (NIHSS), and deficits in assessing tactile extinction and visuospatial neglect done on admission  Exclusion criteria: severe pain or skin disease at the posterior neck, severe atherosclerosis of carotid arteries by an ultrasonic evaluation  Ages eligible: 18 years of age and older  Sexes eligible: all				
Interventions	Experimental: vibration to upper posterior neck muscles. Treatment will be performed by occupational therapist practitioners prior to regular occupational therapy session using a vibration tool Active comparator: standard of care Regular occupational therapy session				
Outcomes	Primary: BIT Secondary: Catherine Bergego Scale (CBS, Activity Measure for Post-Acute Care (AM-PAC))				
Notes	End date: 12 April 2018 Study terminated early due to poor enrolment				

### Park 2021

Methods	RCT
Participants	Inclusion criteria
	Gender: both
	Age limit: minimum 65 years, maximum 85 years
	<ul> <li>Right hemisphere stroke confirmed by computed tomography scan or magnetic resonance imaging; first-ever ischaemic or haemorrhagic stroke; intact global cognitive function confirmed by Korean version of Mini-Mental State Examination score ≥ 24; time since stroke onset ≥ 6 months; presence of hemi-spatial neglect diagnosed by performance on the Line Bisection Test</li> </ul>
Interventions	Robot-assisted hand training Type: experimental Classification: behavioural Descriptions: exercises were carried out as follows: (1) grasp and release training (digital joint flex-
	ion/extension exercise from the thumb to the fifth finger) for 15 minutes; (2) count training (count a number sequence from 1 to 5) for 15 minutes
Outcomes	Outcome name: Line Bisection Test
	Metric/method of measurement: hemi-spatial neglect Time point: before and after the 20 sessions
	Outcome name: Albert's test
	Metric/method of measurement: hemi-spatial neglect
	Time point: before and after the 20 sessions
	Outcome name: Catherine Bergego Scale
	Metric/method of measurement: hemi-spatial neglect
	Time point: before and after the 20 sessions
Notes	We will include this study in future updates if eligible



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Methods Setting: rehabilitation hospital and community, Germany			
Participants	Main inclusion criteria: right hemisphere injury, intact left hemisphere, intact cerebellum, overall stable health condition, significantly impaired performance on more than 3 of 9 neuropsychological neglect tests  Age: ages reported individually  Sex (women/men): 5/7  Hemisphere damaged: right  Time since stroke: time since stroke reported individually		
Interventions	Participants received either neck vibration (NV) or neck vibration plus prism adaptation (NVPA)		
	NV was applied for 20 minutes on the left posterior neck muscle of the patient. The location at the neck was found by asking patients to monitor a small green light 2 metres in front of them. While the apparatus was adjusted, patients were asked openly if they noticed any changes in their perception of the light. If a patient reported an alteration (e.g. the light point moving to the right side at the time of stimulation and to the left side when the NV module is removed), the NV module was applied at that exact location. The NV module was glued with medical tape to patients' neck muscles. Both groups of patients underwent NV while seated in front of an adaptation box. The NVPA group underwent PA treatment simultaneously to the NV. Patients in this group were asked to perform rapid pointing movements approximately 4 times per minute while wearing 10° right-shifted prism glasses. Participants were able to see their pointing only for the last 1 to 2 cm before their finger reached the dots of the adaptation box. Pointing errors reduced with repeated pointing until the landing point was aligned with the dots		
Outcomes			
Notes We are awaiting details on randomisation to check eligibility and will include the study future updates			

### Seo 2017

Methods Double-blind RCT			
Participants	Inclusion criteria: (1) first-ever stroke on the right hemisphere, (2) right-handedness, (3) left hemi spatial neglect (Line Bisection Test = 15% to right side), (4) patients over 18 years old who gave informed consent, (5) stroke onset within the last 6 months  Exclusion criteria: (1) medically unstable patients, (2) general contraindication of tDCS (pacemaker, implantable cardioverter-defibrillator, metal implants in brain), (3) pregnancy, (4) history of seizure or brain surgery, (5) severe skin lesion on stimulation sites, (6) severe cognitive impairment (MMSE < 10)  Age minimum: 18 years  Age maximum: no limit  Gender: both		
Interventions	Experimental group receives 2.0 mA cathodal tDCS 5 times a week for 2 weeks (10 times). Each treatment takes 20 minutes. Control group receives sham tDCS		
Outcomes	Primary: line bisection test		
Notes Status: not yet recruiting, unable to obtain further information			



Toglia 2020	
Methods	Randomised controlled proof-of-concept pilot
Participants	40 patients with left-sided neglect after right brain stroke were included
Interventions	Multi-context treatment approach using a protocol of spatial exploration strategy training in 1 brief session (20 to 30 minutes)
Outcomes	Spatial Neglect Assessment Battery
Notes	We will include this study in future updates if eligible

### Vilimovsky 2021

Methods	RCT		
Participants	34 stroke patients receiving inpatient rehabilitation		
Interventions	Prism adaptation training		
Outcomes	<ul> <li>CBS using the KF-NAP process</li> <li>Cancellation</li> <li>Line bisection</li> </ul>		
Notes	We will include this study in future updates if deemed eligible		

### Zigiotto 2020

Methods	Pilot study		
Participants	20 USN stroke patients		
Interventions	2-week treatment (20 sessions, twice per day) of intensive audiovisual multi-sensory stimulation compared with prismatic adaptation		
Outcomes	Neuropsychological clinical tests (target cancellation, line bisection, sentence reading, personal neglect, complex drawing) and the Catherine Bergego Scale for functional disability		
Notes	We will include this study in future updates if eligible		

BI: Bathel Index.

BIT: Behavioural Inattention Test.

HADS: Hospital Anxiety and Depression Scale.

MMSE: Mini Mental State Examination. RCT: randomised controlled trial.

TUG: timed up and go,

# **Characteristics of ongoing studies** [ordered by study ID]

### Elshout 2018

Study name



Εl	sho	ut 2	018	(Continued)
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Methods	RCT					
Participants	Inclusion criteria					
	<ul> <li>Clinically diagnosed symptomatic stroke (ischaemic or intracerebral haemorrhagic lesion), first or recurrent, if possible verified by magnetic resonance imaging (MRI) and/or computed tomography (CT) data</li> </ul>					
	<ul> <li>Signs of neglect: asymmetry between left and right sides of the stimulus field in number of missed items of at least 2 on a shape cancellation task and/or bias towards the left or right side of space on a line bisection task and/or Catherine Bergego Scale score higher than 6</li> </ul>					
	<ul> <li>18 to 85 years of age</li> <li>Sufficient ability to comprehend and to communicate, as observed during neuropsychological assessment and/or neglect screening</li> </ul>					
	<ul> <li>Sufficient motivation to participate in a daily rehabilitation treatment programme for 2 weeks</li> <li>Written informed consent</li> </ul>					
	Exclusion criteria: patients who recovered from neglect between inclusion and start of training (i.e. no signs of neglect anymore on all baseline measurements) will be excluded					
Interventions	15 neglect patients will receive visual scanning therapy 15 neglect patients will receive visual scanning training combined with congruent hand move-					
	ments Outcome measures for each training group will be compared to 15 stroke patients without neglect and 15 age-matched healthy controls					
Outcomes	Primary outcomes					
	Shape cancellation task (T0, T1)					
	• Line bisection task (T0, T1)					
	Visual discrimination task (T0, T1)					
	Catherine Bergego Scale (T0, T1)					
	Secondary outcomes					
	<ul> <li>Visual exploration task (T0, T1)</li> </ul>					
	Virtual supermarket (T0, T1)					
	Eye movement behaviour					
Starting date						
Contact information						
Notes	End date: 31/05/19. Study author confirms in write-up phase					
ICDCTN002072C0						
Study name	A feasibility study for attention loss after stroke (SPATIAL)					
Methods	Feasibility RCT					
Participants	Participant inclusion criteria (current participant inclusion criteria as of 10/02/2020)					
i articipants	i articipant inclusion criteria (current participant inclusion criteria as or 10/02/2020)					

• Confirmed stroke (ischaemic or haemorrhagic)

Patient participantsOver 18 years old



### ISRCTN88395268 (Continued)

- · Positive for spatial inattention at routine screening
- Spatial inattention impacting on functional task performance
- At least 1 week post stroke onset
- Eligible for standard occupational therapy (for at least 1 session)
- Ability to provide informed consent (or availability of personal/professional consultee)
- Ability to sit with support and perform brief research intervention (e.g. has sufficient vision, physical mobility, and cognition to be able to participate)

### Carer participants

- Informal carer of a patient in the trial
- · Aged 18 or over
- · Ability to provide informed consent

### Staff participants

- A member of the NHS occupational therapy team (occupational therapist, occupational therapy assistant, rehabilitation assistant)
- · Trained in study processes
- Has treated a minimum of 1 patient participant from the intervention arm

#### Interventions

Trialists are testing how sensible and practical it is to use PAT as part of an occupational therapy session to inform a larger trial. This will be done in multiple hospitals. Patients will be split into 2 groups at random: 1 will receive PAT in addition to normal occupational therapy, the other will receive just normal occupational therapy. The entire study will be evaluated to find out what it was like for everyone who was involved. The study will also test whether PAT helps people participate in occupational therapy. The study has been designed in collaboration with stroke service users

For participants in the intervention group, prism adaptation training (PAT) will be offered at the start of a standardised session of OT for up to 3 weeks, 5 days a week. PAT takes no more than 5 minutes plus setup time (seating participants and fitting glasses). To perform PAT, participants will be seated at a table in front of a training box that has open ends.

Participants will be fitted with 12.5° prism glasses, and the occupational therapist will hold up targets at the opposite end of the box and will ask participants to reach to the target; this will be repeated a maximum of 90 times, or for a maximum of 5 minutes, whichever is shorter When prism glasses have been removed, the session will continue with standardised OT. The effect of prism adaptation training is strongest in the hours soon after treatment; reducing the spatial inattention for long enough to take part in usual OT that aims to increase independence in activities of daily living. OT staff will record the time that PAT took place, the number of repetitions of pointing, and length and type of therapy intervention

### Outcomes

### Primary outcome measure

Functional ability measured using EADL at 12 weeks

### Secondary outcome measures

- Inattention measured using star cancellation, Oxford Cognitive Screen, reading test, and KF-NAP at baseline and at 3 and 12 weeks
- Impact of cognitive problems measured using PRECiS at 12 weeks
- Health status measured using EQ-5D-5L at 12 weeks
- Impact on carers measured with the Carer Experience Scale, the modified Carer Strain Index, and self-reported informal carer costs at 12 weeks

# Starting date 1 July 2018 Contact information Prof Audrey Bowen SPATIALstroke@manchester.ac.uk



### ISRCTN88395268 (Continued)

Notes End date: 30 June 2020

### **Luvizutto 2017**

Study name	A clinical study of non-invasive brain stimulation in unilateral spatial neglect after stroke
Methods	Randomised double-blind placebo-controlled trial; parallel, with 2 arms
Participants	Inclusion criteria: diagnosis of stroke of either sex, 18 to 85 years of age, ischaemia or bleeding in the right parietal lobe, confirmed by computed tomography or magnetic resonance imaging, objective diagnosis of unilateral spatial neglect Exclusion criteria: metal into cranial cavity, injuries in the area of electrode placement, clinical instability, severe cognitive impairment, global aphasia, previous visual disturbances, other neurological disease
Interventions	Transcranial direct-current stimulation (tDCS): applied through current stimulator battery powered using sponge pair of surface electrodes (5 cm × 5 cm) soaked in saline solution. A constant current of 2 mA of intensity will be applied for 20 minutes based on security guidelines in the right posterior parietal lobe. For stimulation of the posterior parietal lobe, will be placed on the anode P4 point (international electroencephalogram system) and the cathode in the left supraorbital area after cleaning the areas with alcohol. After stimulation, areas of electrode placement will be checked Control group (sham): patient is placed in the same room and position of tDCS group with the same device programming for 20 minutes, and the current will be delivered by first 10 seconds and off by 19 minutes and 50 seconds Each group will consist of 20 participants, and the tDCS will be performed for 15 sessions, 3 times a week, for 5 weeks
Outcomes	Primary: Catherine Bergego Scale Secondary: Barthel Index, modified Rankin Scale, European (5D) Quality of Life Scale
Starting date	1 July 2016
Contact information	Gustavo Luvizutto Av. Prof. Montenegro, Distrito de Rubião Junior, sem número 18.618-97 Botucatu Brazil gluvizutto@gmail.com Affiliation: Hospital das Clínicas da Faculdade de Medicina de Botucatu
Notes	End date: 31 January 2020

Study name	Prism adaptation therapy for spatial neglect
Methods	Randomised double-blind controlled trial
Participants	<ul> <li>Inclusion criteria: participants</li> <li>18 to 100 years of age, inclusive</li> <li>Stroke on the right side of the brain</li> <li>Ability to give Informed consent</li> <li>Spatial neglect (if known)</li> <li>Ability and willingness to comply with the study protocol, including availability for all scheduled clinic visits</li> </ul>



Exclusion criteria: participant has or had a serious brain condition other than stroke
Experimental: prism adaptation treatment: 2 weeks of prism adaptation treatment followed by 4 weekly assessments and long-term follow-ups at 3rd and 6th months
No Intervention: control: standard rehabilitation care: participants will continue with their standard inpatient rehabilitation care. They will be assessed with cognitive and functional scales for tracking their recovery
Primary: improvement in spatial neglect (method not stated) Secondary: not stated
October 2012
Anna M Barrett, MD Kessler Institute for Rehabilitation, West Orange, New Jersey, United States, 07052
End date: October 2020

Study name	
Methods	Randomised double-blind controlled trial
Participants	Inclusion criteria
	<ul> <li>Right-handed</li> <li>All participants must be between the ages of 18 and 80</li> <li>Patients with unilateral negligence consecutive to a right hemispheric stroke</li> <li>Hospitalised in the Department of Physical Medicine and Rehabilitation (day or week) or with external monitoring</li> <li>Ischaemic or haemorrhagic stroke with right hemispheric topography - evidenced by a radiological report</li> <li>Diagnosis of negligence evidenced by Behavioural Inattention Test (BIT): score ≤ 129</li> <li>Stroke &gt; 1 month before study enrolment</li> </ul>
	<ul> <li>Exclusion criteria</li> <li>Degenerative neurological complaint</li> <li>Uncontrolled epilepsy</li> <li>Temporospatial disorientation</li> <li>Language disorders or psychiatric disorders preventing understanding instructions</li> <li>History of prior stroke, multiple stroke</li> <li>Medical condition not stabilised</li> <li>Pregnancy</li> <li>Implanted material (pacemaker, defibrillator, cochlear implant, surgical clips, metal object)</li> <li>Intracranial material</li> <li>Unweaned alcoholism</li> </ul>
Interventions	Transcranial direct current stimulation (tDCS) vs placebo stimulation
Outcomes	Primary: Behavioural Inattention Test (BIT)



NCT02213640 (Continued)	Secondary: Negligence Battery Test (BTN), Functional Independence Scale (FIM), Catherine Bergego Scale (CBS), Jamar
Starting date	
Contact information	
Notes	Confirmed ongoing by study author in analysis
NCT02680171	
Study name	Feasibility and effectiveness study of implementing prism adaptation as a treatment for spatial neglect after stroke
Methods	Randomised double-blind controlled trial
Participants	Inclusion criteria
	<ul> <li>Experience mild to severe symptoms of neglect (as measured by Sunnybrook Neglect Assessment Procedure and/or as determined based on clinical judgement of treating team)</li> <li>Willingness to participate</li> <li>Ability to consent to participate</li> <li>Medically stable</li> <li>Normal or corrected to normal vision</li> <li>Ability to point to targets presented on a computer screen</li> <li>Exclusion criteria</li> <li>Other neurological disease (e.g. multiple sclerosis, Parkinson's disease)</li> <li>Dementia</li> </ul>
Interventions	Experimental: prism goggles with 10-degree rightward deviating prism lenses will be used to implement prism adaptation treatment, in addition to standard care Sham comparator: non-shifting goggles (sham) will be worn by patients in the control condition. These goggles do not shift patients' visual field
Outcomes	Primary: Sunnybrook Neglect Assessment Procedure (SNAP) Secondary: Johnny Shirt Visual Scanning Task, Behavioural Inattention Test - Behaviour subtests (BIT-B), Catherine Bergego Scale (CBS), Halifax Neglect Severity Scale, Functional Independence Measure (FIM), Frenchay Activities Index, length of inpatient stay at the Rehabilitation Centre, discharge destination, proprioceptive and visuo-motor pointing midline tasks
Starting date	Feburary 2016
Contact information	Gail A Eskes, PhD gail.eskes@dal.ca
Notes	Champod AS, Taylor K, Eskes GA. Development of a new computerized prism adaptation procedure for visuo-spatial neglect. Journal of Neuroscience Methods 2014;30;235:65-75. doi: 10.1016/j.jneumeth.2014.05.023. Epub 2014 Jun 19
	End date: 30 June 2019. PI confirms study is ongoing



NCT03168360	
Study name	Effect of intensive cognitive rehabilitation in subacute stroke patient
Methods	RCT
Participants	Inclusion criteria
	<ul> <li>Acute first-ever stroke</li> <li>Korean Mini-Mental State Examination: 11~24 at 7 days after stroke onset</li> </ul> Exclusion criteria
	Transient ischaemic stroke
Interventions	Intensive cognitive rehabilitation by cognitive therapist for 1 hour on every working day during subacute stroke phase
Outcomes	Primary outcome measure  • Korean-Montreal Cognitive Assessment (K-MoCA) [Time Frame: Change of K-MoCa after intensive cognitive rehabilitation for 4 weeks]
Starting date	1 November 2016
Contact information	Contact: Won Hyuk Chang, MD, PhD02-3410-2818; wh.chang@samsung.com
Notes	End date: 31 December 2021

Study name	Improving measurement and treatment of post-stroke neglect
Methods	Participants will receive both conditions (active and sham transcranial direct current stimulation paired with arm rehabilitation training (repetitive task-specific practice)) in this cross-over design study. Individuals will be randomised to determine which condition they receive first, and the participant and the treatment therapist and assessor will be blinded to the order that the interventions are delivered. The PI will oversee randomisation, so that each patient is randomised and is assigned a unique 5-digit code. When this code is entered on the tDCS device, the device will automatically assign the patient to receive either real or sham stimulation. Because sham stimulation provides a ramp up/ramp down stimulation for 15 seconds at the start and end of the session, the participant may perceive the sham stimulation as active stimulation
Participants	<ul> <li>Right ischaemic or haemorrhagic subcortical stroke 3 months post stroke</li> <li>Fugl-Meyer Upper Extremity (FMA-Upper Extremity) score between 20 and 56/60</li> <li>Inducible motor evoked potential (MEP) of the abductor pollicis brevis (APB) on paretic stimulation (TMS)</li> <li>Demonstrated presence of unilateral neglect (Virtual Reality Lateralized Attention Test score &lt; 18)</li> </ul>
Interventions	Single session of bilateral active parietal cortex tDCS (2.0 mA for 30 minutes) paired with repetitive task-specific practice (RTP)
Outcomes	Primary outcome measures  Excitability of fronto-parietal connectivity measured by paired pulse twin coil transcranial magnetic stimulation (TMS) test. In each session, the difference in excitability of fronto-parietal connectivi-
	ty between pre-stimulation and post stimulation will be measured



### NCT03317860 (Continued)

• Change in excitability of fronto-parietal connectivity [Time Frame: Participants will be assessed at baseline and 30 minutes later]

Secondary outcome measures

Kinematic assessment will be conducted to assess changes in motor impairment

Neglect assessment (conventional subtests) will be conducted to assess changes in attentional impairment. Total scores range from 0 to 146, with lower scores indicating greater impairment

- Change in upper extremity kinematics [Time Frame: Participants will be assessed at baseline and 30 minutes later]
- Change on Behavioral Inattention Test [Time Frame: Participants will be assessed at baseline and 1.5 hours later (immediately following experimental condition)]

### Other outcome measures

This neglect assessment will be administered to examine the impact of neglect on performance of daily activities. Total scores range from 0 to 30, with higher scores indicating greater impairment

This neglect assessment (behavioural subtests) will be administered to examine the impact of neglect on performance of daily activities. Total scores range from 0 to 81, with lower scores indicating greater impairment

This neglect assessment will be administered to examine the impact of neglect on performance of daily activities. Each item has a score of 0 to 6, with lower scores indicating greater impairment. The Lateralized Attention Score (LAS) is difference between contralateral and ipsilateral proportions of items. Higher LAS scores indicate greater impairment

- Catherine Bergego Scale [Time Frame: Participants in the cross-sectional study will be assessed at baseline]
- Behavioral Inattention Test [Time Frame: Participants in the cross-sectional study will be assessed at baseline]
- Naturalistic Action Test [Time Frame: Participants in the cross-sectional study will be assessed at baseline]

Starting date	2 July 2018
Contact information	grattan@musc.edu
Notes	End date: 3 July 2023

Study name	Family-clinician collaboration to Improve neglect and rehabilitation outcome after stroke
Methods	RCT
Participants	Inclusion criteria
	<ul> <li>Latest stroke occurred within last 60 days</li> <li>Functionally independent before latest stroke</li> <li>Presence of spatial neglect (moderate to severe, will be confirmed by medical records)</li> <li>Ability to follow instructions and to understand verbal or written English</li> <li>Exclusion criteria</li> <li>History of progressive neurological disorder</li> </ul>



NCT03402906 (Continued)	History of significant psychiatric disorder
Interventions	Experimental group will be performing the Family-Clinician Collaboration Programme. Family members will work closely with the clinician to understand the status and goals of the stroke survivor, and family members will integrate family-mediated treatment procedures into their time spent with the patient Intervention: behavioural - family-clinician collaboration programme; behavioural - standard care at KIR Family-mediated treatment activities and collaboration between clinician and family members Other name: FCC Participants will receive standard care provided at Kessler Institute for Rehabilitation Arm Intervention/treatment Experimental: family-clinician collaboration programme; behavioural: standard care at KIR
Outcomes	Primary outcome measures: assessment of overall functional independence  • Functional Independence Measure (FIM) [Time Frame: within 72 hours before IRF discharge]
Starting date	30 September 2017
Contact information	Peii Chen, PhD, Kessler Foundation
Notes	Active, no longer recruiting End date: 29 September 2020

Study name	Optokinetic stimulation for the treatment of hemi-spatial neglect - safety and efficacy studies
Methods	Cross-over
Participants	Inclusion criteria
	<ul> <li>Patients with right hemispheric lesions resulting in hemi-spatial neglect as confirmed by Behavioral Inattention Test or Center of Cancellation Test</li> </ul>
	Exclusion criteria
	Reduced vision
	Documented vestibular disorder
Interventions	Optokinetic stimulation will be displayed on a see-through liquid crystal display lens placed in front of participants
Outcomes	Primary outcome measures: performance on Center of Cancellation Test, performance on Behavioural Inattention Test, visual acuity, reading speed
	Change in hemi-spatial neglect scores [Time Frame: after 1 hour of OKS]
	<ul> <li>Change in hemi-spatial neglect scores [Time Frame: after 1 hour of OKS]</li> </ul>
	Effect of OKS on vision [Time Frame: after 1 hour of OKS]
	Effect of OKS on vision [Time Frame: after 1 hour of OKS]
	Secondary outcome measures: line bisection score, grip strength, extinction score, gait assessment, balance assessments
	<ul> <li>Changes in secondary hemi-spatial neglect scores [Time Frame: after 1 hour of OKS]</li> <li>Changes in secondary hemi-spatial neglect scores [Time Frame: after 1 hour of OKS]</li> </ul>



NCT03451708 (Continued)

NC103431106 (Continued)	<ul> <li>Changes in secondary hemi-spatial neglect scores [Time Frame: after 1 hour of OKS]</li> <li>Effect of OKS on gait [Time Frame: after 1 hour of OKS]</li> <li>Effect of OKS on gait [Time Frame: after 1 hour of OKS]</li> </ul>
Starting date	1 May 2018
Contact information	Principal investigator: Chun Lim, MD, Beth Israel Deaconess Medical Center
Notes	End date: 31 August 2022
NCT03458611	
Study name	Virtual Reality Attention Training in stroke patients (VRAT)
Methods	Study design is a mix of within-subject manipulation of placebo and active intervention conditions and between-subject manipulation of the order of these 2 within-subject conditions. To clarify, a placebo and an active version of VR game-based attention training will be administered to each patient. The order of these 2 within-subject conditions is counterbalanced between subjects to account for differences in order between the 2 treatment conditions
Participants	Inclusion criteria
	<ul> <li>Above 18 years of age</li> <li>Have had a stroke</li> <li>Expected discharge of patients is not in a period shorter than 7 weeks</li> </ul> Exclusion criteria
	They or their legal representatives are unable to provide informed consent
	<ul> <li>They have a severe comorbid psychiatric (e.g. psychotic symptoms) disorder</li> <li>They have a pre-morbid neurodegenerative disease (e.g. Alzheimer's dementia, vascular dementia)</li> </ul>
	They have severe spoken language comprehension deficits
	<ul> <li>They have a medical implant, such as a cochlear implant or a pacemaker</li> <li>They have a severe visual or auditory impairment that cannot be corrected for by wearing glasses or a hearing aid</li> </ul>
	They are unable to concentrate on a task for longer than 15 minutes
	<ul> <li>They have a history of epileptic seizures</li> <li>They do not show signs of hemi-spatial neglect on a battery of screening tasks</li> </ul>
Interventions	An audiovisual expanding (looming) stimulus is presented repeatedly to patients during the intervention. During the game, a disk is presented to the player. This disk expands and contracts in size. Presentation of the disk coincides with presentation of a sound that matches in frequency. The disk predicts the location where the next target will be presented. The player must discriminate between 2 types of target stimuli that are presented at the centre of the disk. To discriminate between the 2 targets, the player receives a limited time window. The locations of the disk and target
	algorithm is to present multi-sensory looming stimuli more frequently in the contralesional field than in the ipsilesional field
Outcomes	Primary outcome measure: the measure of spatial asymmetry will be the difference in accuracy for target detection between left and right visual fields (visual L-R score)  • Change in visual L-R score [Time Frame: this primary outcome variable is measured repeatedly on Days 2. 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, and 25 and at 1 follow-up assessment for Group B on Day 35]
Outcomes	stimuli are adjusted in real time as a function of the player's performance. The primary go algorithm is to present multi-sensory looming stimuli more frequently in the contralesion than in the ipsilesional field  Primary outcome measure: the measure of spatial asymmetry will be the difference in accordance detection between left and right visual fields (visual L-R score)



### NCT03458611 (Continued)

### Secondary outcome measures

While patients play the VR game, their head orientation is logged at a fixed rate. The cumulative time a patient's head is oriented towards the left or right side during moments in the VR intervention that there are no target stimuli presented will be calculated. The difference between time with the head oriented towards the left vs the right will be used as an index of spatial asymmetry in the VR environment (VR L-R score)

Difference between percentage of cumulative fixation duration for left and right visual fields as measured with an eye tracker during a visual computer task

Difference between percentages of the direction of the first saccade in each trial of the task as measured with an eye tracker during a visual computer task

Accuracy for auditory signals presented to the left and right ear is measured with a computerised task. Accuracy difference for left and right signals will be calculated

Hemi-spatial neglect symptoms in daily life are measured with the Catherina Bergego Scale (Azouvi et al, 2003). This scale has 10 items of behaviour that are observed and are given a score from 0 (= no signs of neglect) to 3 (= patient always shows signs of neglect or does not correct for it). The sum of individual scores is the outcome index

- Change in VR L-R score [Time Frame: this secondary outcome variable will be measured on each day of the clinical trial (Day 6 to Day 26)]
- Change in the fixation L-R score [Time Frame: this outcome variable is measured repeatedly on Days 2, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, and 25 and at 1 follow-up assessment for Group B on Day 35]
- Change in the first saccade L-R score [Time Frame: this outcome variable is measured repeatedly on Days: 2, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, and 25 and at 1 follow-up assessment for Group B on Day 35]
- Change in auditory L-R score [Time Frame: this outcome variable is measured repeatedly on Days 2, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, and 25 and at 1 follow-up assessment for Group B on Day 35]
- Change in Catherina Bergego Scale (CBS) score [Time Frame: this outcome variable is measured at 4 time points with 2 weeks in between each measurement. Thus the CBS is scored on Days 5, 15, and 25, and for Group B also on Day 35 of the clinical trial]

Starting date	1 September 2018		
Contact information	celine.gillebert@kuleuven.be		
Notes	End date: February 2020		

Study name	Effect of mirror therapy on unilateral neglect for patients after stroke			
Methods	Single-blinded randomised controlled trial to investigate effects of mirror therapy, with reference to sham mirror (a glass wall) and control (a covered mirror), in reducing unilateral neglect for patients with stroke			
Participants	Inclusion criteria			
	<ul> <li>Ischaemic or haemorrhagic stroke, confirmed by medical diagnoses compatible with unilateral right lesion involvement (i.e. left hemiplegic), exhibited left visual field inattention or unilateral neglect by obtaining a total score of star cancellation subtest in the conventional battery of the Behavioural Inattention Test ≤ 51 (out of 54)</li> </ul>			
	<ul> <li>Stroke with onset of neurological condition ≤ 6 months previously</li> </ul>			
	<ul> <li>Normal or corrected-to-normal visual acuity better than 20/60 (6/18) in the better eye</li> </ul>			



NCT03854487 (Continued)			
	<ul> <li>Hemiplegic upper extremity functional levels 3 to 7 as rated by Functional Test for the Hemiplegic Upper Extremity and able to move against gravity</li> </ul>		
	• Ability to understand and follow simple verbal instructions, with Mini Mental State Examination ≥ 21		
	Ability to participate in a therapy session lasting at least 30 minutes		
	Consent to participant in the study		
Interventions	Mirror therapy		
Outcomes	Behavioural Inattention Test		
	Gap Detection Test		
	Catherine Bergego Scale		
	Fugl-Meyer Assessment		
Starting date	July 2016		
Contact information			

Study author confirmed ended and in write-up stages

### NCT03887962

Notes

Study name	Virtual Environment Rehabilitation for Patients With Motor Neglect Trial (VERMONT)
Methods	RCT
Participants	Inclusion criteria
	<ul> <li>Diagnosis of stroke (of any cause), traumatic brain injury, or chronic pain condition of more than 3 months' duration (e.g. back and referred leg pain; complex regional pain syndrome; fibromyalgia) who are undergoing an inpatient or outpatient rehabilitation programme</li> </ul>
	<ul> <li>Motor neglect as assessed by standard clinical examination by a physiotherapist trained to detect such motor neglect (EV). This is defined as weakness and functional impairment without loss of strength, reflexes, or sensation</li> </ul>
	Exclusion criteria
	<ul> <li>Active serious medical problems that might affect ability to participate in the exercise protocol (e.g. ongoing sepsis; recent myocardial infarction)</li> </ul>
	<ul> <li>Inability to use treadmill safely as judged by the screening physiotherapist (EV)</li> </ul>
	<ul> <li>Inability to give informed consent through issues related to competency or to language</li> </ul>
	<ul> <li>Significant previous experience of virtual reality rehabilitation</li> </ul>
Interventions	Participants will be instructed to walk on a treadmill, moving at a constant speed, following a "virtual path" displayed on a flat screen in front of them. In this group, the gait task may involve avoiding virtual obstacles on the screen in the path or stepping on targets as determined by the therapist
Outcomes	Primary outcome measures
	<ul> <li>Distance walked in 5 minutes at Week 2 compared to baseline (% change)</li> <li>Self-reported 20-question Functional Activity Questionnaire with minimal clinically important difference of 9 (range 0 to 80). Each question scored 0 to 4. Low scores indicate less function</li> </ul>



### NCT03887962 (Continued)

- Self-reported 20-question Functional Activity Questionnaire with minimal clinically important difference of 9 (range 0 to 80). Each question scored 0 to 4. Low scores indicate less function
  - \* Distance walked (machine-reported) [Time Frame: Week 2]
  - \* Lower Extremity Functional Index [Time Frame: Week 2]
  - \* Lower Extremity Functional Index [Time Frame: Week 24]

### Secondary outcome measures

- Self-reported questionnaire mean score (11-point analogue scale). High scores indicate more pain. % change from baseline will be calculated
- Self-reported questionnaire (0 to 94 points). Low scores indicate loss of function
- Self-reported questionnaire (0 to 21 on each dimension of Anxiety and Depression). High scores indicate high anxiety or depression
- Self-reported questionnaire (1 to 6). High scores indicate more neglect-like symptoms
- Self-reported questionnaire (0 to 5). High scores indicate high satisfaction
- Average stride length (cm)
- Number of steps (whole number)
- Asymmetry (left-right split presented in numerical form)
- Timing (proportion of gait with planted foot and raised foot measured as %)
  - \* Brief Pain Inventory [Time Frame: Weeks 2, 12, 24]
  - \* Human Activity Profile [Time Frame: Weeks 2, 12, 24]
  - \* Hospital Anxiety and Depression Scale [Time Frame: Weeks 2, 12, 24]
  - \* Neglect Like Symptom Questionnaire [Time Frame: Weeks 2, 12, 24]
  - \* Satisfaction questionnaire [Time Frame: Weeks 2, 24]
  - \* Machine-reported average stride length [Time Frame: Week 2]
  - \* Machine-reported number of steps [Time Frame: Week 2]
  - \* Machine-reported gait symmetry [Time Frame: Week 2]
  - \* Machine-reported gait timing [Time Frame: Week 2]

Starting date	1 May 2017		
Contact information	Principal Investigator: Nicholas GN Shenker, MD, Cambridge University Hospitals, NHS Foundation Trust		
Notes	End date: 1 November 2020		

Study name	Repetitive transcranial magnetic stimulation in spatial attention after stroke (r-TMS)			
Methods	RCT			
Participants	Ages eligible for study: 18 years to 80 years (adult, older adult) Sexes eligible for study: all Accepts healthy volunteers: no Inclusion criteria			
	<ul> <li>Diagnosis of ischaemic stroke in the right middle cerebral artery or right intracerebral haemor-rhagic stroke, confirmed by brain CT and/or brain MRI</li> <li>Diagnosis of LHSN with specific test (asymmetry score on Bells cancellation test &gt; 3)</li> <li>Intrahospital rehabilitation setting (ordinary hospitalisation or DH) or outpatient setting</li> <li>Age between 18 and 80 years</li> <li>Time between stroke onset and study recruitment 3 weeks to 3 months</li> </ul>			



#### NCT04080999 (Continued)

• Availability to provide informed consent to participate

### Exclusion criteria

- Clinical instability at recruitment (e.g. fever, acute internist conditions)
- History of epilepsy and/or occurrence in the acute phase of at least 1 seizure crisis
- Presence of intracranial metallic implants
- Presence of devices that could be altered by r-TMS, such as pacemakers, ventricular-peritoneal derivations, Baclofen pump
- Absence of a bone operculum following neurosurgical operation of decompressive craniotomy
- Presence of behavioural disturbances with inversion of the sleep-wake rhythm
- Monolateral or bilateral occipital lesions documented on CT and/or history of cortical blindness or visual agnosia
- · Concomitant psychiatric disorder and/or history of substance abuse
- · State of pregnancy
- Inability to execute the following simple order: "take the pen instead of the key and put it on the sheet"
- Severe acoustic deficit not corrected by use of a hearing aid
- · Severe reduction in the visus despite use of eyeglasses
- · Positive anamnesis of previous cognitive decline

### Interventions

### Device: r-TMS

Interventions have a total administration time of 75 minutes per day. For TMS stimulation, the coil will be positioned tangentially on the target area. Each r-TMS session will last 15 minutes and will be administered every other day (e.g. Monday-Wednesday-Friday, Monday-Wednesday-Friday, Monday). Visual scanning treatment involves the presence of a therapist, who administers various visual scanning tasks, used to increase patient's awareness and to teach strategies to improve spatial exploration abilities (Pizzamiglio et al, 1992). Trainings include 3 increasing levels of difficulty (9 possible combinations). Each level of difficulty will be exercised until the patient reaches a level of accuracy of 75%. The CCT will be carried out in 50-minute sessions for 5 days a week within 15 days (11 sessions in total). On the days when r-TMS is also administered, administration of the CCT will immediately follow brain stimulation

### Outcomes

Primary outcome measures: battery for assessment of cognitive and behavioural symptoms in LHSN

 Change from baseline: Behavioural Inattention Test (BIT) [Time Frame: up to 21 days post baseline and up to 90 days' follow-up]

Secondary outcome measures: battery for assessment of LHSN symptoms in activity of daily living. Two subtests will be executed - "alertness" and "visual field/neglect" - to assess attentive functions. The motor subscale will be executed to assess motor independence. A test will assess motor impairment in stroke patients. A test to assess ability to control the trunk after stroke. Psychophysiological index of inter-hemispheric transmission. Psychophysiological index of inter-hemispheric imbalance in a visual-spatial attention task

- Change from baseline: Catherine Bergegò Scale (CBS) [Time Frame: up to 21 days post baseline and up to 90 days' follow-up]
- Change from baseline: Test of Attention Performance (TAP/TEA) [Time Frame: up to 21 days post baseline and up to 90 days' follow-up]
- Change from baseline: Functional Independence Measure (FIM) [Time Frame: up to 21 days post baseline and up to 90 days' follow-up]
- Change from baseline: Motricity Index (MI) [Time Frame: up to 21 days post baseline and up to 90 days' follow-up]
- Change from baseline: Trunk Control Test (TCT) [Time Frame: up to 21 days post baseline and up to 90 days' follow-up]
- Change from baseline: Inter-Hemispheric Transmission Time (IHTT) [Time Frame: up to 21 days post baseline and up to 90 days' follow-up]



NCT04080999 (Continued)	<ul> <li>Change from baseline: Visual-Attention Bias Index (vABI) [Time Frame: up to 21 days post baseline and up to 90 days' follow-up]</li> <li>5 December 2018</li> </ul>			
Starting date				
Contact information	Contact: Emanuela Casanova, MD, 3398999147; e.casanova@ausl.bologna.it Contact: Francesco Di Gregorio, PhD, 3290762585; francesco.digregorio@ku.de			
Notes	End date: 1 March 2021			
NCT04227132				
Study name	Evaluation of an adaptive computerized training for rehabilitation of spatial neglect in stroke survivors (MULTITASK)			
Methods	Randomised cross-over. Both experimental and control trainings will be administered consecutively to all patients. Each type of training will be delivered for 10 sessions, with order of training randomised across participants			
Participants	Inclusion criteria			
	<ul> <li>First-stroke patients with right brain damage</li> <li>Right-handedness</li> <li>Preserved Italian language comprehension to provide informed consensus</li> <li>Clinical signs of spatial neglect (diagnosis by BIT)</li> </ul>			
	Exclusion criteria			
	<ul><li>Prior history of psychiatric or neurological disease</li><li>Substance abuse</li></ul>			
	Inability to sustain experimental trainings			
Interventions	Patients will receive at first the Labyrinth training for 10 sessions of 45 minutes, delivered 4 days per week. Then, they will undergo standard training for 10 sessions of 45 minutes, for around 4 days per week. Before and after each training, patients will be tested for primary and secondary outcomes with standardised tests			
	Patients sit in front of a computer monitor and play the adaptive video game with a joystick. The game requires to orient and move inside a maze, and it includes phases that engage multi-tasking abilities. The level and speed of the game are adapted online to patients' performance			
	Experimental: Labyrinth training, then standard training device: adaptive computer game training			
Outcomes	Primary outcome measures			
	Diagnostic test for spatial neglect, composed of different subtests of spatial attention			
	Test for everyday functional outcome			
	<ul> <li>Changes on Behavioral Inattention Test (BIT) [Time Frame: baseline; immediately after first training; immediately after second training; finally after 3 weeks from completion of second training]</li> <li>Changes on KF-NAP Scale [Time Frame: baseline; immediately after first training; immediately after second training; finally after 3 weeks from completion of second training]</li> </ul>			
	Secondary outcome measures			
	Computerised test on spatial monitoring and multi-tasking abilities			
	Test for allocentric and egocentric spatial neglect			



NCT04227132 (Continued)	<ul> <li>Changes on Load Test [Time Frame: baseline; immediately after first training; immediately second training; finally after 3 weeks from completion of second training;</li> <li>Changes on Apple Test [Time Frame: baseline; immediately after first training; immediately second training; finally after 3 weeks from completion of second training]</li> </ul>			
Starting date	16 December 2019			
Contact information	Contact: Francesca Meneghello, MD, 0412207183 ext 0039; francesca.meneghello@ospedalesan-camillo.net			
Notes	End date: 31 December 2021			
NCT04273620				
Study name	Combined optokinetic stimulation and cueing-based reading therapy to treat hemi-spatial neglect following stroke (OKS-READ)			
Methods	This study will be a monocentric, randomised, controlled clinical trial. Using a cross-over design with 2 arms, patients will receive the intervention therapy first, then the control treatment, or twill start in the control arm and will then switch to the intervention arm			
Participants	<ul> <li>First-time stroke in the right hemisphere (confirmed by cranial CT or MRI) within the last 6 months</li> <li>Left-sided hemi-spatial neglect (as detected on at least 1 subtest of the neuropsychological test battery at screening)</li> <li>Ability to read and understand German language</li> <li>Ability to give informed consent</li> <li>Exclusion criteria</li> <li>Dementia</li> <li>Other structural brain lesions besides unilateral stroke (e.g. multiple or bilateral stroke lesions, hydrocephalus, inflammatory lesions)</li> <li>Low vision (corrected &lt; 0.7) due to ophthalmological disease</li> </ul>			
Interventions	Behavioural: optokinetic stimulation and cueing-based reading therapy (OKS-READ)  Each intervention session starts with optokinetic stimulation (OKS) of at least 15 minutes' duration. A pattern of squares, dots, triangles, and stars will coherently and continuously move to the left on a computer screen in front of patients. Patients are instructed to choose 1 stimulus and follow it with the eyes until it has reached the left side of the screen, then jump to the right edge of the screen and start again  The second part of each intervention session is the cueing-based reading therapy (READ), which will also last at least 15 minutes. The task of patients is to read out loud words or a text presented on a paper in front of them. We will use exogenous (e.g. the therapist highlights words when they are omitted) and endogenous cues (verbal instructions that require intrinsic action by patients) to facilitate attentional shifts to the left. The intensity of cueing will be matched to the actual severity of neglect (adaptive therapy)  Behavioural: general neuropsychological treatment  As a control treatment, patients will receive neuropsychological treatment without targeting visuospatial attention. Examples for components implemented are supporting conversations, diagnostic assessments (e.g. memory diagnostics), and training of memory and executive functions			
Outcomes	Primary outcome measures			



#### NCT04273620 (Continued)

Composite score of different established computerised tests assessing spatial neglect (minimum 0%, maximum 100%; higher score means better outcomes)

Clinical score of neglect-related functional disability (Catherine Bergego Scale, CBS; minimum 0, maximum 30; higher score means worse outcomes)

- Neglect symptom severity (neuropsychological test performance) [Time Frame: intraindividual difference of the outcome's change during 3 weeks' intervention phase vs 3 weeks' control phase, i.e. (T3 on Day 21 T2 on Day 1) (T5 on Day 42 T4 on Day 22)]
- Neglect-related functional disability [Time Frame: intraindividual differences in outcome change during 3 weeks' Intervention phase vs 3 weeks' control phase, i.e. (T3 on Day 21 - T2 on Day 1) -(T5 on Day 42 - T4 on Day 22)]

#### Secondary outcome measures

Performance in the Menu reading task of the Behavioural Inattention Test battery (minimum 0 correct words (worst outcome), maximum 24 correct words (best outcome))

Bias of the Center of Cancellation (CoC) during the Bells test (values between -1 (strongest leftward bias), 0 (no bias), and +1 (strongest rightward bias))

Bias of the Center of Fixation (CoF) during free viewing of naturalistic photographs as measured with an infrared remote eye tracker (values between -1 (strongest leftward bias), 0 (no bias), and +1 (strongest rightward bias))

Differences between investigator-assessed CBS score and patients' self-assessed CBS score

Barthel Index (minimum 0, maximum 100; higher score means better outcomes)

Functional Independence Measure (18-item scale with scores between 0 and 7 points; higher scores mean better outcomes)

- Neglect dyslexia [Time Frame: intraindividual differences in outcome change during 3 weeks' intervention phase vs 3 weeks' control phase, i.e. (T3 on Day 21 T2 on Day 1) (T5 on Day 42 T4 on Day 22)]
- Attention bias during visuomotor cancellation task [Time Frame: intraindividual difference in outcome change during 3 weeks' intervention phase vs 3 weeks' control phase, i.e. (T3 on Day 21 T2 on Day 1) (T5 on Day 42 T4 on Day 22)]
- Oculomotor bias during visual exploration [Time Frame: intraindividual difference in outcome's change during 3 weeks' intervention phase vs 3 weeks' control phase, i.e. (T3 on Day 21 - T2 on Day 1) - (T5 on Day 42 - T4 on Day 22)]
- Anosognosia [Time Frame: intraindividual difference in outcome change during 3 weeks' intervention phase vs 3 weeks' control phase, i.e. (T3 on Day 21 T2 on Day 1) (T5 on Day 42 T4 on Day 22)]
- Non-neglect-specific functional outcome (Barthel) [Time Frame: intraindividual difference in outcome change during 3 weeks' intervention phase vs 3 weeks' control phase, i.e. (T3 on Day 21 T2 on Day 1) (T5 on Day 42 T4 on Day 22)]
- Functional Independence (FIM) [Time Frame: intraindividual difference in outcome change during 3 weeks' intervention phase vs 3 weeks' control phase, i.e. (T3 on Day 21 T2 on Day 1) (T5 on Day 42 T4 on Day 22)]

Starting date	22 January 2020		
Contact information	bjoern.machner@neuro.uni-luebeck.de		
Notes	End date: 21 February 2022		



Modulating connectivity with non-invasive brain stimulation during spatial neglect rehabilitation		
RCT		
<ul> <li>30 to 80 years of age</li> <li>Subacute stroke (stroke occurred more than 2 weeks and less than 6 months ago; first or recurrent, ischaemic or intracerebral haemorrhagic lesion)</li> <li>Diagnosed visuospatial neglect and/or spatial neglect symptoms (left sided or right sided) on the basis of clinical judgement (i.e. by the cooperating clinical (neuro)psychologist)</li> <li>Sufficient comprehension and communication skills to benefit from training (based on clinical judgement)</li> </ul>		
We will combine evidence-based visual scanning training with 40 minutes of (active or sham) dual-site tACS at theta (6 Hz) and gamma (80 Hz) frequencies. The intervention is administered 5 times a week for a duration of 2 weeks		
Primary outcome: performance on digitalised Star Cancellation Test  Secondary outcomes  Performance on Computerised Visual Detection Task Performance on Line Bisection Task Performance on Baking Tray Task		
9 October 2019		
olof.vanderwerf@maastrichtuniversity.nl		
End date: 1 June 2022		

### **Olson 2020**

Chudunama	Calaria vastitudar atiravlatian fartusatus ont of unilatoral mada et
Study name	Caloric vestibular stimulation for treatment of unilateral neglect
Methods	Unknown
Participants	Unknown
Interventions	Unknown
Outcomes	Unknown
Starting date	Unknown
Contact information	catrina.olson@und.edu
Notes	

RCT: randomised controlled trial.

### DATA AND ANALYSES

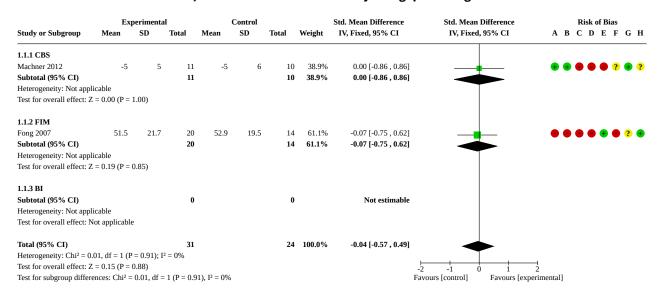


### Comparison 1. Visual interventions versus any control

Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
1.1 Activities of daily liv- ing: persisting effects	2	55	Std. Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.57, 0.49]
1.1.1 CBS	1	21	Std. Mean Difference (IV, Fixed, 95% CI)	0.00 [-0.86, 0.86]
1.1.2 FIM	1	34	Std. Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.75, 0.62]
1.1.3 BI	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.2 Activities of daily liv- ing: immediate effects	3	75	Std. Mean Difference (IV, Fixed, 95% CI)	-0.15 [-0.60, 0.30]
1.2.1 CBS	2	36	Std. Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.64, 0.67]
1.2.2 FIM	1	39	Std. Mean Difference (IV, Fixed, 95% CI)	-0.30 [-0.94, 0.33]
1.3 Neglect outcomes: persisting effects	5	98	Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.33, 0.48]
1.3.1 Target cancellation	2	33	Std. Mean Difference (IV, Fixed, 95% CI)	0.41 [-0.30, 1.11]
1.3.2 Line bisection	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.3.3 BIT behavioural subtest	3	65	Std. Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.59, 0.40]
1.4 Neglect outcomes: immediate effects	7	142	Std. Mean Difference (IV, Fixed, 95% CI)	0.08 [-0.26, 0.42]
1.4.1 Target cancellation	3	46	Std. Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.58, 0.60]
1.4.2 Line bisection	1	28	Std. Mean Difference (IV, Fixed, 95% CI)	0.71 [-0.06, 1.48]
1.4.3 BIT behavioural sub- test	3	68	Std. Mean Difference (IV, Fixed, 95% CI)	-0.14 [-0.64, 0.35]



### Analysis 1.1. Comparison 1: Visual interventions versus any control, Outcome 1: Activities of daily living: persisting effects



### Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias

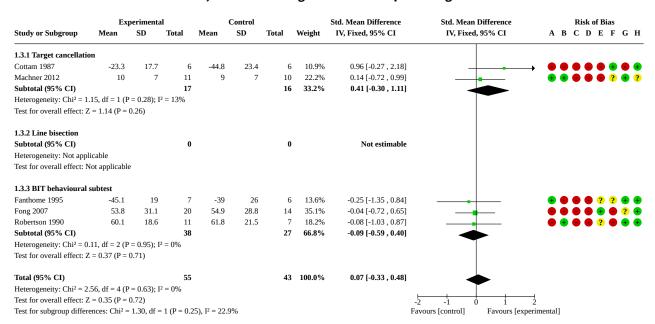
### Analysis 1.2. Comparison 1: Visual interventions versus any control, Outcome 2: Activities of daily living: immediate effects

	-	perimenta			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	ABCDEFGH
1.2.1 CBS										
Machner 2012	-12	9	11	-13	8	10	28.1%	0.11 [-0.74, 0.97]		<b>• • • • • ? • ?</b>
Wu 2013	-10.4	3.2	7	-9.9	4.4	8	20.1%	-0.12 [-1.14, 0.89]		● ● ● ? ● ●
Subtotal (95% CI)			18			18	48.2%	0.02 [-0.64, 0.67]		
Heterogeneity: Chi <sup>2</sup> = 0.	12, df = 1 (P	= 0.73); I	$^{2} = 0\%$						$\top$	
Test for overall effect: Z	= 0.05 (P =	0.96)								
1.2.2 FIM										
Fong 2007	44.3	18.7	20	50.2	19.4	19	51.8%	-0.30 [-0.94, 0.33]		● ● ● ● ● ? ●
Subtotal (95% CI)			20			19	51.8%	-0.30 [-0.94, 0.33]		
Heterogeneity: Not appli	cable									
Test for overall effect: Z	= 0.94 (P =	0.35)								
Total (95% CI)			38			37	100.0%	-0.15 [-0.60 , 0.30]		
Heterogeneity: Chi <sup>2</sup> = 0.5	59, df = 2 (P	= 0.74); I	$^{2} = 0\%$							
Test for overall effect: Z	= 0.65 (P =	0.52)							-2 -1 0 1	
Test for subgroup differe	nces: Chi <sup>2</sup> =	0.47, df =	1 (P = 0.4	9), I <sup>2</sup> = 0%					Favours [control] Favours [exp	erimental]

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- $(F)\ Incomplete\ outcome\ data\ (attrition\ bias)$
- (G) Selective reporting (reporting bias)
- (H) Other bias



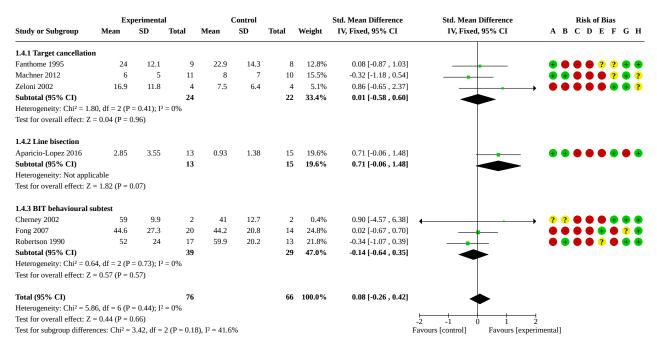
### Analysis 1.3. Comparison 1: Visual interventions versus any control, Outcome 3: Neglect outcomes: persisting effects



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias



### Analysis 1.4. Comparison 1: Visual interventions versus any control, Outcome 4: Neglect outcomes: immediate effects



#### Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias

### Comparison 2. Prism adaptation versus any control

Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
2.1 Activities of daily living: persisting effects	2	39	Std. Mean Difference (IV, Fixed, 95% CI)	-0.29 [-0.93, 0.35]
2.1.1 CBS	2	39	Std. Mean Difference (IV, Fixed, 95% CI)	-0.29 [-0.93, 0.35]
2.1.2 BI	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.1.3 FIM	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.2 Activities of daily living: immediate effects	5	158	Std. Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.12, 0.51]
2.2.1 CBS	5	158	Std. Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.12, 0.51]
2.2.2 BI	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.2.3 FIM	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable



Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
2.3 Neglect outcomes: persisting effects	1	16	Std. Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.96, 1.06]
2.3.1 Target cancellation	1	16	Std. Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.96, 1.06]
2.3.2 Line bisection	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.3.3 BIT behavioural subtest	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.4 Neglect outcomes: immediate effects	5	154	Std. Mean Difference (IV, Fixed, 95% CI)	0.28 [-0.05, 0.60]
2.4.1 Target cancellation	4	120	Std. Mean Difference (IV, Fixed, 95% CI)	0.31 [-0.07, 0.68]
2.4.2 Line bisection	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.4.3 BIT behavioural subtest	1	34	Std. Mean Difference (IV, Fixed, 95% CI)	0.17 [-0.50, 0.85]

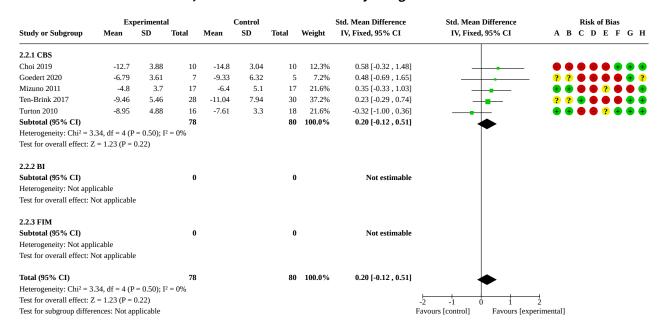
### Analysis 2.1. Comparison 2: Prism adaptation versus any control, Outcome 1: Activities of daily living: persisting effects

	Exp	perimenta	ıl		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	A B C D E F G H
2.1.1 CBS										
Goedert 2020	-7.72	6.36	7	-4.53	4.77	4	26.4%	-0.50 [-1.75, 0.76]		? ? • • • • .
Turton 2010	-5.62	4.28	12	-4.8	3.18	16	73.6%	-0.22 [-0.97, 0.53]	·	● ● ● ? ● ●
Subtotal (95% CI)			19			20	100.0%	-0.29 [-0.93, 0.35]		
Heterogeneity: Chi <sup>2</sup> = 0.14,	, df = 1 (P	= 0.71); I	$^{2} = 0\%$							
Test for overall effect: Z =	0.88 (P = 0	0.38)								
2.1.2 BI										
Subtotal (95% CI)			0			0		Not estimable	·	
Heterogeneity: Not applica	ible									
Test for overall effect: Not	applicable									
2.1.3 FIM										
Subtotal (95% CI)			0			0		Not estimable	·	
Heterogeneity: Not applica	ible									
Test for overall effect: Not	applicable	2								
Total (95% CI)			19			20	100.0%	-0.29 [-0.93 , 0.35]		
Heterogeneity: Chi <sup>2</sup> = 0.14,	, df = 1 (P	= 0.71); I	$^{2} = 0\%$							
Test for overall effect: Z =	0.88 (P = 0	0.38)							-2 -1 0 1	
Test for subgroup difference	es: Not ap	plicable							Favours [control] Favours [6	experimental]
Risk of bias legend										

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- $(G) \ Selective \ reporting \ (reporting \ bias)$
- (H) Other bias



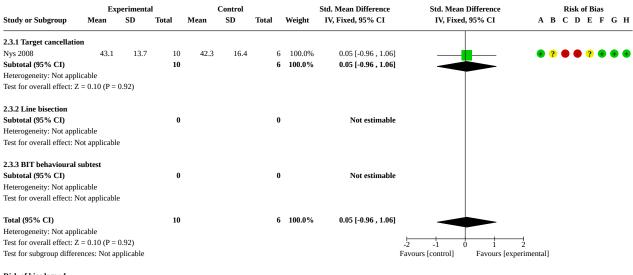
### Analysis 2.2. Comparison 2: Prism adaptation versus any control, Outcome 2: Activities of daily living: immediate effects



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- $(F)\ Incomplete\ outcome\ data\ (attrition\ bias)$
- (G) Selective reporting (reporting bias)
- (H) Other bias



### Analysis 2.3. Comparison 2: Prism adaptation versus any control, Outcome 3: Neglect outcomes: persisting effects



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias

Analysis 2.4. Comparison 2: Prism adaptation versus any control, Outcome 4: Neglect outcomes: immediate effects

	Exp	perimenta	ıl		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	A B C D E F G H
2.4.1 Target cancellation	on									_
Choi 2019	-5	2.21	10	-9.1	1.19	10	7.9%	2.21 [1.05, 3.38]		<b>→ ••••••</b>
Mancuso 2012	16.54	2.25	13	15.89	2.25	9	14.7%	0.28 [-0.58 , 1.13]		? • • • • • • •
Nys 2008	21.5	13.1	10	20.7	19	6	10.5%	0.05 [-0.96 , 1.06]		$\bullet$ ? $\bullet$ $\bullet$ ? $\bullet$ $\bullet$
Ten-Brink 2017	3.03	4.79	29	2.85	5.87	33	43.2%	0.03 [-0.47, 0.53]	<b>———</b>	? ? • • • • • •
Subtotal (95% CI)			62			58	76.3%	0.31 [-0.07, 0.68]		
Heterogeneity: Chi2 = 1	1.72, df = 3 (	P = 0.008	; I <sup>2</sup> = 74%							
Test for overall effect: 2	Z = 1.61 (P =	0.11)								
2.4.2 Line bisection										
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not app										
Test for overall effect: N	Not applicable	2								
2.4.3 BIT behavioural	subtest									
Mizuno 2011	-62.5	15.2	17	-65.7	20.8	17	23.7%	0.17 [-0.50 , 0.85]	<del></del>	
Subtotal (95% CI)			17			17	23.7%	0.17 [-0.50 , 0.85]		
Heterogeneity: Not app										
Test for overall effect: 2	Z = 0.50 (P = 0.50)	0.62)								
Total (95% CI)			79			75	100.0%	0.28 [-0.05 , 0.60]	•	
Heterogeneity: Chi <sup>2</sup> = 1			$I^2 = 66\%$							1
Test for overall effect: 2	,								-2 -1 0 1	2
Test for subgroup differ	ences: Chi <sup>2</sup> =	0.12, df =	1 (P = 0.7	3), I <sup>2</sup> = 0%					Favours [control] Favours [exp	erimental]
Risk of bias legend										
(A) Random sequence g			as)							
(B) Allocation concealn	•	n bias)								
(C) Blinding of particip										
(D) Blinding of personn										
(E) Blinding of outcome		•	bias)							
(F) Incomplete outcome										
(G) Selective reporting	(reporting bia	is)								
(H) Other bias										

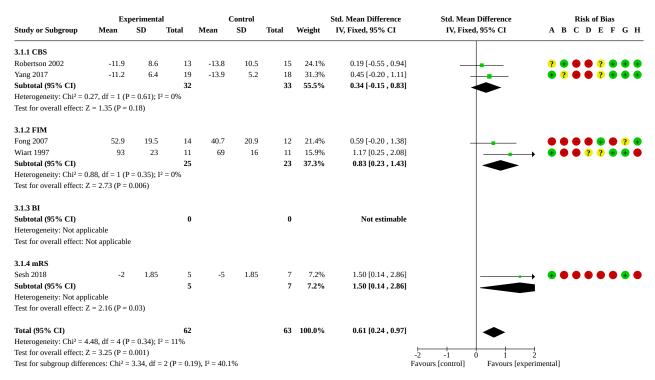


### Comparison 3. Body awareness interventions versus any control

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
3.1 Activities of daily living: persisting effects	5	125	Std. Mean Difference (IV, Fixed, 95% CI)	0.61 [0.24, 0.97]
3.1.1 CBS	2	65	Std. Mean Difference (IV, Fixed, 95% CI)	0.34 [-0.15, 0.83]
3.1.2 FIM	2	48	Std. Mean Difference (IV, Fixed, 95% CI)	0.83 [0.23, 1.43]
3.1.3 BI	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
3.1.4 mRS	1	12	Std. Mean Difference (IV, Fixed, 95% CI)	1.50 [0.14, 2.86]
3.2 Activities of daily liv- ing: immediate effects	7	221	Std. Mean Difference (IV, Fixed, 95% CI)	0.26 [-0.01, 0.53]
3.2.1 CBS	2	76	Std. Mean Difference (IV, Fixed, 95% CI)	0.35 [-0.10, 0.80]
3.2.2 FIM	3	91	Std. Mean Difference (IV, Fixed, 95% CI)	0.39 [-0.04, 0.82]
3.2.3 BI	1	42	Std. Mean Difference (IV, Fixed, 95% CI)	-0.29 [-0.91, 0.32]
3.2.4 mRS	1	12	Std. Mean Difference (IV, Fixed, 95% CI)	0.68 [-0.51, 1.88]
3.3 Neglect outcomes: persisting effects	5	125	Std. Mean Difference (IV, Fixed, 95% CI)	0.36 [0.00, 0.72]
3.3.1 Target cancellation	2	49	Std. Mean Difference (IV, Fixed, 95% CI)	0.50 [-0.08, 1.08]
3.3.2 Line bisection	1	22	Std. Mean Difference (IV, Fixed, 95% CI)	1.09 [0.18, 2.00]
3.3.3 BIT behavioural subtest	2	54	Std. Mean Difference (IV, Fixed, 95% CI)	-0.01 [-0.55, 0.53]
3.4 Neglect outcomes: immediate effects	10	311	Std. Mean Difference (IV, Fixed, 95% CI)	0.16 [-0.07, 0.39]
3.4.1 Target cancellation	7	227	Std. Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.16, 0.37]
3.4.2 Line bisection	1	22	Std. Mean Difference (IV, Fixed, 95% CI)	1.33 [0.39, 2.27]
3.4.3 BIT behavioural subtest	2	62	Std. Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.48, 0.52]
3.5 Discharge destination (home)	1	50	Odds Ratio (M-H, Fixed, 95% CI)	1.40 [0.45, 4.35]
3.6 Adverse events	2	130	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.36 [0.05, 2.61]



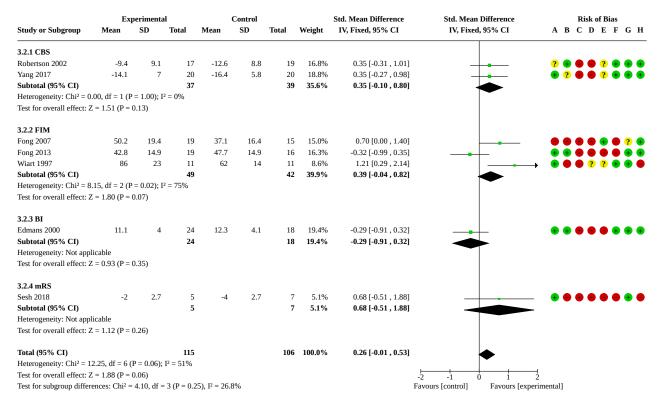
### Analysis 3.1. Comparison 3: Body awareness interventions versus any control, Outcome 1: Activities of daily living: persisting effects



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias



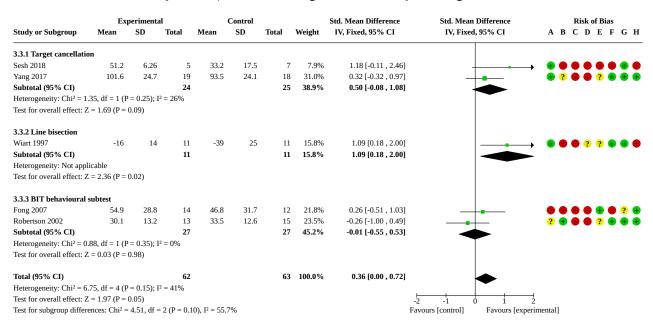
### Analysis 3.2. Comparison 3: Body awareness interventions versus any control, Outcome 2: Activities of daily living: immediate effects



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias



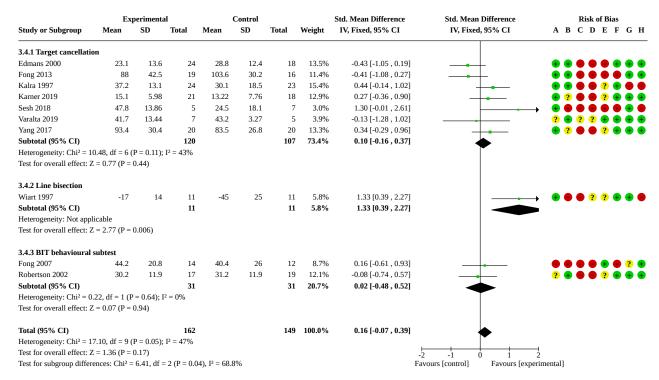
### Analysis 3.3. Comparison 3: Body awareness interventions versus any control, Outcome 3: Neglect outcomes: persisting effects



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias



### Analysis 3.4. Comparison 3: Body awareness interventions versus any control, Outcome 4: Neglect outcomes: immediate effects



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias

Analysis 3.5. Comparison 3: Body awareness interventions versus any control, Outcome 5: Discharge destination (home)

	Experin	nental	Cont	rol		Odds Ratio	Odds Ra	ntio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed,	95% CI
Kalra 1997	16	25	14	25	100.0%	1.40 [0.45 , 4.35]	-	<u> </u>
Total (95% CI)		25		25	100.0%	1.40 [0.45 , 4.35]		
Total events:	16		14					
Heterogeneity: Not app	licable						0.1 0.2 0.5 1	2 5 10
Test for overall effect: 2	Z = 0.58 (P =	0.56)					Favours [control]	Favours [experimental]
Test for subgroup differ	ences: Not a	pplicable						



### Analysis 3.6. Comparison 3: Body awareness interventions versus any control, Outcome 6: Adverse events

	Experin	nental	Cont	rol		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Edmans 2000	0	40	1	40	25.8%	0.14 [0.00 , 6.82]	<b>+</b>
Kalra 1997	1	25	2	25	74.2%	0.50 [0.05, 5.03]	<b>←</b>
Total (95% CI)		65		65	100.0%	0.36 [0.05, 2.61]	
Total events:	1		3				
Heterogeneity: Chi <sup>2</sup> = 0	.32, df = 1 (F	P = 0.57;	$[^2 = 0\%]$				0.1 0.2 0.5 1 2 5 10
Test for overall effect: 2	Z = 1.02 (P =	0.31)					Favours [control] Favours [experimental]
Test for subgroup differ	ences: Not a	pplicable					

### Comparison 4. Mental function interventions versus any control

Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
4.1 Activities of daily living: persisting effects	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
4.1.1 CBS	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
4.1.2 FIM	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
4.1.3 BI	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
4.2 Activities of daily living: immediate effects	1	24	Std. Mean Difference (IV, Fixed, 95% CI)	0.32 [-0.49, 1.12]
4.2.1 CBS	1	24	Std. Mean Difference (IV, Fixed, 95% CI)	0.32 [-0.49, 1.12]
4.2.2 FIM	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
4.2.3 BI	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
4.3 Neglect outcomes: persisting effects	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
4.3.1 Target cancellation	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
4.3.2 Line bisection	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
4.3.3 BIT behavioural subtest	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
4.4 Neglect outcomes: immediate effects	3	84	Std. Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.32, 0.53]
4.4.1 Target cancellation	3	84	Std. Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.32, 0.53]



Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
4.4.2 Line bisection	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
4.4.3 BIT behavioural subtest	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
4.5 Adverse events	1	10	Peto Odds Ratio (Peto, Fixed, 95% CI)	7.39 [0.15, 372.38]

## Analysis 4.1. Comparison 4: Mental function interventions versus any control, Outcome 1: Activities of daily living: persisting effects

	Exp	periment	al		Control			Std. Mean Difference	Std. Mea	n Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rano	lom, 95% CI
4.1.1 CBS										
Subtotal (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applie	able									
Test for overall effect: No	t applicable	e								
4.1.2 FIM										
Subtotal (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applic	able									
Test for overall effect: No	t applicable	е								
4.1.3 BI										
Subtotal (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applic	able									
Test for overall effect: No	t applicable	е								
Total (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applic	able									
Test for overall effect: No	t applicable	e							-100 -50	0 50 100
Test for subgroup differen	nces: Not ap	plicable							Favours [control]	Favours [experimental]



### Analysis 4.2. Comparison 4: Mental function interventions versus any control, Outcome 2: Activities of daily living: immediate effects

	Exp	erimenta	l		Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup M	lean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
4.2.1 CBS									
Kim 2011	-11	5.7	12	-13.2	7.6	12	100.0%	0.32 [-0.49 , 1.12]	<del></del>
Subtotal (95% CI)			12			12	100.0%	0.32 [-0.49 , 1.12]	
Heterogeneity: Not applicabl	e								
Test for overall effect: $Z = 0$ .	77 (P = 0	0.44)							
4.2.2 FIM									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not applicabl	e								
Test for overall effect: Not ap	pplicable								
4.2.3 BI									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not applicabl	e								
Test for overall effect: Not ap	plicable	<u> </u>							
Total (95% CI)			12			12	100.0%	0.32 [-0.49 , 1.12]	
Heterogeneity: Not applicabl	le								
Test for overall effect: $Z = 0$ .	77 (P = 0	0.44)							-2 -1 0 1 2
Test for subgroup differences	s: Not ap	plicable							Favours [control] Favours [experim

Analysis 4.3. Comparison 4: Mental function interventions versus any control, Outcome 3: Neglect outcomes: persisting effects

	Ex	perimen	tal		Control			Std. Mean Difference	Std. Me	an Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Ran	dom, 95% CI
4.3.1 Target cancellati	on									
Subtotal (95% CI)			0			(	)	Not estimable	e	
Heterogeneity: Not app	licable									
Test for overall effect: I	Not applicabl	le								
4.3.2 Line bisection										
Subtotal (95% CI)			0			(	)	Not estimable	e	
Heterogeneity: Not app	licable									
Test for overall effect: I	Not applicabl	le								
4.3.3 BIT behavioural	subtest									
Subtotal (95% CI)			0			(	)	Not estimable	e	
Heterogeneity: Not app	licable									
Test for overall effect: I	Not applicabl	le								
Total (95% CI)			0			(	)	Not estimable	e	
Heterogeneity: Not app	licable									
Test for overall effect: I	Not applicabl	le							-100 -50	0 50 100
Test for subgroup differ	ences: Not a	pplicable							Favours [control]	Favours [experimental]



Analysis 4.4. Comparison 4: Mental function interventions versus any control, Outcome 4: Neglect outcomes: immediate effects

	Exp	erimenta	I		Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup M	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
4.4.1 Target cancellation									
Kim 2011	-8.2	8.3	12	-6.9	7.8	12	28.7%	-0.16 [-0.96, 0.65]	
Park 2015	53.5	2.3	15	53.3	2.8	15	35.9%	0.08 [-0.64, 0.79]	
Welfringer 2011	-6.6	7.3	15	-9.2	7.4	15	35.4%	0.34 [-0.38, 1.07]	
Subtotal (95% CI)			42			42	100.0%	0.10 [-0.32, 0.53]	
Heterogeneity: Chi <sup>2</sup> = 0.83,	df = 2 (P	= 0.66); I	2 = 0%						
Test for overall effect: $Z = 0$	).48 (P = 0	0.63)							
4.4.2 Line bisection									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not applicab	ole								
Test for overall effect: Not a	applicable								
4.4.3 BIT behavioural sub	test								
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not applicab	ole								
Test for overall effect: Not a	applicable								
Total (95% CI)			42			42	100.0%	0.10 [-0.32 , 0.53]	
Heterogeneity: Chi <sup>2</sup> = 0.83,	df = 2 (P	= 0.66); I	2 = 0%						
Test for overall effect: $Z = 0$	).48 (P = 0	0.63)							$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Test for subgroup difference	es: Not ap	plicable							Favours [control] Favours [experimenta

Analysis 4.5. Comparison 4: Mental function interventions versus any control, Outcome 5: Adverse events

	Experii	nental	Cont	rol		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Ferreira 2011	1	5	0	5	100.0%	7.39 [0.15 , 372.38]	
Total (95% CI)		5		5	100.0%	7.39 [0.15 , 372.38]	
Total events:	1		0				
Heterogeneity: Not appl	icable						0.01 0.1 1 10 100
Test for overall effect: Z	L = 1.00 (P =	0.32)					Favours [control] Favours [experimental]
Test for subgroup differen	ences: Not a	pplicable					

### Comparison 5. Movement intervention versus any control

Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
5.1 Activities of daily living: persisting effects	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
5.1.1 CBS	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
5.1.2 FIM	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
5.1.3 BI	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable



Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
5.2 Activities of daily living: immediate effects	3	75	Std. Mean Difference (IV, Fixed, 95% CI)	0.57 [0.09, 1.04]
5.2.1 CBS	3	75	Std. Mean Difference (IV, Fixed, 95% CI)	0.57 [0.09, 1.04]
5.2.2 FIM	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
5.2.3 BI	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
5.3 Neglect outcomes: persisting effects	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
5.3.1 Target cancellation	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
5.3.2 Line bisection	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
5.3.3 BIT behavioural sub- test	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
5.4 Neglect outcomes: im- mediate effects	2	58	Std. Mean Difference (IV, Fixed, 95% CI)	0.57 [0.04, 1.10]
5.4.1 Target cancellation	2	58	Std. Mean Difference (IV, Fixed, 95% CI)	0.57 [0.04, 1.10]
5.4.2 Line bisection	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
5.4.3 BIT behavioural sub- test	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
5.5 Adverse events	1	38	Peto Odds Ratio (Peto, Fixed, 95% CI)	Not estimable



### Analysis 5.1. Comparison 5: Movement intervention versus any control, Outcome 1: Activities of daily living: persisting effects

	Exp	perimen	tal		Control			Std. Mean Difference	Std. Me	ean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Ran	dom, 95% CI
5.1.1 CBS										
Subtotal (95% CI)			0			0	)	Not estimable	!	
Heterogeneity: Not applical	ole									
Test for overall effect: Not a	applicable	2								
5.1.2 FIM										
Subtotal (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applical	ole									
Test for overall effect: Not a	applicable	e								
5.1.3 BI										
Subtotal (95% CI)			0			0	)	Not estimable	1	
Heterogeneity: Not applical	ole									
Test for overall effect: Not a	applicable	2								
Total (95% CI)			0			0	)	Not estimable	<u>!</u>	
Heterogeneity: Not applical	ole									
Test for overall effect: Not a	applicable	e							-100 -50	0 50 100
Test for subgroup difference	es: Not ap	plicable							Favours [control]	

Analysis 5.2. Comparison 5: Movement intervention versus any control, Outcome 2: Activities of daily living: immediate effects

	Exp	perimenta	al		Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
5.2.1 CBS									
Choi 2016	-18.8	4.94	20	-19.61	3.53	18	54.7%	0.18 [-0.46, 0.82]	
Kim 2018	-12.4	3.1	10	-15.2	3.7	10	26.5%	0.79 [-0.13, 1.70]	
Wu 2013	-9.9	4.4	8	-16.3	4.5	9	18.9%	1.36 [0.28, 2.45]	
Subtotal (95% CI)			38			37	100.0%	0.57 [0.09, 1.04]	
Heterogeneity: Chi <sup>2</sup> = 3	3.67, df = 2 (P	= 0.16); I	$^{2} = 46\%$						🕶
Test for overall effect: 2	Z = 2.35 (P =	0.02)							
5.2.2 FIM									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not app	licable								
Test for overall effect: I	Not applicable	2							
5.2.3 BI									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not app	licable								
Test for overall effect: I	Not applicable	e							
Total (95% CI)			38			37	100.0%	0.57 [0.09 , 1.04]	
Heterogeneity: Chi <sup>2</sup> = 3	3.67, df = 2 (P	= 0.16); I	$^{2} = 46\%$						
Test for overall effect: 2	Z = 2.35 (P =	0.02)							$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
Test for subgroup differ	rences: Not ap	plicable							Favours [control] Favours [experimenta
rest for subgroup differ	circes, 140t up	pricable							Tuvous [control] Tuvous [experime



### Analysis 5.3. Comparison 5: Movement intervention versus any control, Outcome 3: Neglect outcomes: persisting effects

	Experi	imental		Control			Std. Mean Difference	Std. Mea	n Difference
Study or Subgroup Mo	ean S	SD Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rand	om, 95% CI
5.3.1 Target cancellation									
Subtotal (95% CI)			0		0	1	Not estimable		
Heterogeneity: Not applicable	2								
Test for overall effect: Not ap	plicable								
5.3.2 Line bisection									
Subtotal (95% CI)			0		0	1	Not estimable		
Heterogeneity: Not applicable	<u>.</u>								
Test for overall effect: Not ap	plicable								
5.3.3 BIT behavioural subte	st								
Subtotal (95% CI)			0		0	1	Not estimable		
Heterogeneity: Not applicable	<u>.</u>								
Test for overall effect: Not ap	plicable								
Total (95% CI)			0		0	1	Not estimable		
Heterogeneity: Not applicable	<u>.</u>								
Test for overall effect: Not ap	plicable							-100 -50	0 50 100
Test for subgroup differences:	Not applie	cable						Favours [control]	Favours [experimental]

## Analysis 5.4. Comparison 5: Movement intervention versus any control, Outcome 4: Neglect outcomes: immediate effects

	Exp	erimenta	l		Control			Std. Mean Difference	Std. Mean	Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed	, 95% CI
5.4.1 Target cancellation	l									
Choi 2016	25.6	11.51	20	19.78	8.93	18	65.8%	0.55 [-0.10 , 1.20]	-	
Kim 2018	18	3.9	10	15.2	4.9	10	34.2%	0.61 [-0.30 , 1.51]	· —	
Subtotal (95% CI)			30			28	100.0%	0.57 [0.04, 1.10]		
Heterogeneity: Chi <sup>2</sup> = 0.01	1, df = 1 (P	= 0.92); I	2 = 0%							•
Test for overall effect: Z =	2.11 (P = 0	0.03)								
5.4.2 Line bisection										
Subtotal (95% CI)			0			0		Not estimable	<b>!</b>	
Heterogeneity: Not application	able									
Test for overall effect: Not	t applicable	:								
5.4.3 BIT behavioural su	ıbtest									
Subtotal (95% CI)			0			0		Not estimable	<u> </u>	
Heterogeneity: Not applica	able									
Test for overall effect: Not	t applicable	!								
Total (95% CI)			30			28	100.0%	0.57 [0.04 , 1.10]	ı	
Heterogeneity: Chi <sup>2</sup> = 0.01	1, df = 1 (P	= 0.92); I	2 = 0%							
Test for overall effect: Z =	= 2.11 (P = 0	0.03)							-2 -1 (	) 1 2
Test for subgroup differen	ices: Not ap	plicable							Favours [control]	Favours [experimenta



Analysis 5.5. Comparison 5: Movement intervention versus any control, Outcome 5: Adverse events

Study or Subgroup	Experir Events	nental Total	Cont Events	trol Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI		Peto Od Peto, Fixe		
	Livents	10(a)	Lvents	10(a)	Weight	1 eto, 1 ixeu, 35 /0 C1		1 610, 1 126	u, 55 /0 C1	
Choi 2016	0	20	0	18	1	Not estimable				
Total (95% CI)		20		18	}	Not estimable				
Total events:	0		0							
Heterogeneity: Not appl	licable						0.01	0.1	10	100
Test for overall effect: N	Not applicabl	le					Favou	rs [control]	Favours [	experimental]
Test for subgroup differen	ences: Not a	pplicable								

### Comparison 6. NIBS versus any control

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
6.1 Activities of daily liv- ing: persisting effects	4	92	Std. Mean Difference (IV, Fixed, 95% CI)	0.35 [-0.08, 0.77]
6.1.1 CBS	3	64	Std. Mean Difference (IV, Fixed, 95% CI)	0.56 [0.04, 1.08]
6.1.2 FIM	1	28	Std. Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.83, 0.65]
6.1.3 BI	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
6.2 Activities of daily liv- ing: immediate effects	8	160	Std. Mean Difference (IV, Fixed, 95% CI)	0.61 [0.27, 0.94]
6.2.1 CBS	6	120	Std. Mean Difference (IV, Fixed, 95% CI)	0.55 [0.17, 0.93]
6.2.2 FIM	1	28	Std. Mean Difference (IV, Fixed, 95% CI)	0.43 [-0.33, 1.18]
6.2.3 BI	1	12	Std. Mean Difference (IV, Fixed, 95% CI)	2.59 [0.90, 4.29]
6.3 Neglect outcomes: persisting effects	5	102	Std. Mean Difference (IV, Fixed, 95% CI)	0.77 [0.29, 1.24]
6.3.1 Target cancellation	4	75	Std. Mean Difference (IV, Fixed, 95% CI)	1.44 [0.83, 2.05]
6.3.2 Line bisection	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
6.3.3 BIT behavioural subtest	1	27	Std. Mean Difference (IV, Fixed, 95% CI)	-0.28 [-1.04, 0.48]
6.4 Neglect outcomes: immediate effects	13	244	Std. Mean Difference (IV, Fixed, 95% CI)	0.75 [0.47, 1.04]
6.4.1 Target cancellation	10	174	Std. Mean Difference (IV, Fixed, 95% CI)	0.72 [0.37, 1.06]
6.4.2 Line bisection	2	42	Std. Mean Difference (IV, Fixed, 95% CI)	2.18 [1.37, 2.98]
6.4.3 BIT behavioural subtest	1	28	Std. Mean Difference (IV, Fixed, 95% CI)	-0.28 [-1.02, 0.47]
6.5 Adverse events	0	0	Peto Odds Ratio (Peto, Fixed, 95% CI)	Not estimable



# Analysis 6.1. Comparison 6: NIBS versus any control, Outcome 1: Activities of daily living: persisting effects

	Exp	erimenta	ıl		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	A B C D E F G H
6.1.1 CBS										
Nyfeller 2019 16c TBS	-5.9	6.28	10	-12.22	7.03		13.9%	0.91 [-0.23, 2.05]		<b>→ • • • ? ? ? • •</b>
Nyfeller 2019 8c TBS	-5.38	4.41	8	-12.22	7.03	4	10.2%	1.18 [-0.15, 2.52]	<u> </u>	<b>→</b>
Yang 2017	-13.9	5.2	18	-15.7	6.6	19	43.0%	0.30 [-0.35, 0.94]		
Subtotal (95% CI)			36			28	67.1%	0.56 [0.04, 1.08]		
Heterogeneity: Chi <sup>2</sup> = 1.85,	df = 2 (P =	0.40); I <sup>2</sup> =	0%							
Test for overall effect: Z = 2	2.11 (P = 0.0	)3)								
6.1.2 FIM										
Iwanski 2020	91.2	24.9	14	93.4	23.1	14	32.9%	-0.09 [-0.83, 0.65]		• ? ? • ? • • •
Subtotal (95% CI)			14			14	32.9%	-0.09 [-0.83, 0.65]		
Heterogeneity: Not applicab	ole									
Test for overall effect: $Z = 0$	0.24 (P = 0.8	31)								
6.1.3 BI										
Subtotal (95% CI)			0			(	)	Not estimable		
Heterogeneity: Not applicab	ole									
Test for overall effect: Not a										
Total (95% CI)			50			42	2 100.0%	0.35 [-0.08, 0.77]		
Heterogeneity: Chi <sup>2</sup> = 3.82, o	df = 3 (P =	0.28); I <sup>2</sup> =	21%							
Test for overall effect: $Z = 1$									-2 -1 0 1	<del></del>
Test for subgroup difference			(P = 0.16)	, I <sup>2</sup> = 49.1%	ó				Favours [control] Favours [ex	perimental]

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias



# Analysis 6.2. Comparison 6: NIBS versus any control, Outcome 2: Activities of daily living: immediate effects

	Exp	perimenta	ıl		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	A B C D E F G H
6.2.1 CBS										
Kim 2018	-12.4	3.1	10	-17.5	4.1	10	11.3%	1.34 [0.35, 2.34]		
Nyfeller 2019 16c TBS	-6.8	7.1	10	-12.5	6.52	5	8.8%	0.77 [-0.35, 1.90]		_ • • • ? ? ? • •
Nyfeller 2019 8c TBS	-7	6.16	10	-12.5	6.52	5	8.7%	0.83 [-0.30, 1.95]		_
Yang 2017	-16.4	5.8	20	-17.9	6.5	20	28.7%	0.24 [-0.38, 0.86]		• ? • • ? • • •
Yi 2016 anodal	-8.4	9	10	-12.3	10.8	5	9.4%	0.38 [-0.70, 1.47]		• ? • • ? • •
Yi 2016 cathodal	-10	6.2	10	-12.3	10.8	5	9.5%	0.27 [-0.81, 1.35]		
Subtotal (95% CI)			70			50	76.4%	0.55 [0.17, 0.93]		
Heterogeneity: Chi <sup>2</sup> = 4.15	5, df = 5 (P =	0.53); I <sup>2</sup> =	0%							
Test for overall effect: Z =	2.84 (P = 0.0	004)								
6.2.2 FIM										
Iwanski 2020	86.2	24.7	14	76.6	18.7	14		0.43 [-0.33 , 1.18]	<del>  • • • • • • • • • • • • • • • • • • •</del>	<b>+</b> ? ? <b>-</b> ? <b>+ + -</b>
Subtotal (95% CI)			14			14	19.7%	0.43 [-0.33 , 1.18]		
Heterogeneity: Not applica										
Test for overall effect: Z =	1.11 (P = 0.2	27)								
6.2.3 BI										
Bang 2015	78.3	3.9	6	69.2	2.4	6	3.8%	2.59 [0.90, 4.29]		228888
Subtotal (95% CI)			6			6	3.8%	2.59 [0.90 , 4.29]		
Heterogeneity: Not applica	able							,		_
Test for overall effect: Z =		003)								
Total (95% CI)			90			70	100.0%	0.61 [0.27, 0.94]	<b>•</b>	
Heterogeneity: Chi <sup>2</sup> = 9.71		,-	28%					_		
Test for overall effect: Z =	,	,						-2	-1 0 1	2
Test for subgroup differen	ces: $Chi^2 = 5$	.56, df = 2	(P = 0.06)	, I <sup>2</sup> = 64.09	6			Fav	vours [control] Favours [exp	erimental]

- (A) Random sequence generation (selection bias)
  (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias



# Analysis 6.3. Comparison 6: NIBS versus any control, Outcome 3: Neglect outcomes: persisting effects

	Exp	perimenta	ıl		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	ABCDEFGI
6.3.1 Target cancellation	on									
Yang 2015 10Hz	-24.44	4.54	10	-45.54	5.74	4	5.0%	4.06 [1.94, 6.18]		· ??? • ? • •
Yang 2015 1Hz	-18.46	4.91	9	-45.54	5.74	3	3.0%	4.91 [2.18, 7.65]		•
Yang 2015 cTBS	-14.79	4.59	9	-45.54	5.74	3	2.3%	5.86 [2.72, 9.01]		•
Yang 2017	93.5	24.1	18	71.9	30.3	19	50.3%	0.77 [0.10, 1.44]		• ? • • ? • •
Subtotal (95% CI)			46			29	60.7%	1.44 [0.83, 2.05]		>
Heterogeneity: Chi <sup>2</sup> = 23	3.51, df = 3 (	P < 0.000	1); I <sup>2</sup> = 87%	ó						
Test for overall effect: Z	= 4.63 (P <	0.00001)								
6.3.2 Line bisection										
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not appl	icable									
Test for overall effect: N	ot applicable	e								
6.3.3 BIT behavioural	subtest									
Iwanski 2020	27	13	13	30.5	11.4	14	39.3%	-0.28 [-1.04, 0.48]		<b>a</b> ? ? <b>a</b> ? <b>a</b> •
Subtotal (95% CI)			13			14	39.3%	-0.28 [-1.04, 0.48]		
Heterogeneity: Not appl	icable									
Test for overall effect: Z	= 0.72 (P =	0.47)								
Total (95% CI)			59			43	100.0%	0.77 [0.29 , 1.24]		
Heterogeneity: Chi <sup>2</sup> = 3!	5.48, df = 4 (	P < 0.0000	)1); I <sup>2</sup> = 89	%						
Test for overall effect: Z	= 3.15 (P =	0.002)							-2 -1 0 1	<b>⊣</b>
Test for subgroup differen	,	,	= 1 (P = 0	0005) 12 =	91.6%			1	Favours [control] Favours [exp	erimental]

- $(A) \ Random \ sequence \ generation \ (selection \ bias)$
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias



# Analysis 6.4. Comparison 6: NIBS versus any control, Outcome 4: Neglect outcomes: immediate effects

	Exp	periment	al		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	A B C D E F G H
6.4.1 Target cancellati	ion									
Kim 2018	18	3.9	10	14.5	3.5	10	9.7%	0.90 [-0.03, 1.84]	-	<b>.</b> • • • • • • •
Koch 2012	42.22	11.5	9	41.5	13.3	9	9.8%	0.06 [-0.87, 0.98]		? ? • • ? • •
Song 2009	-1.51	2.05	7	-5.86	2.89	7	5.2%	1.63 [0.36, 2.89]		· ?? • • ? • • •
Vatanparasti 2019	0.5	1.5	7	2.4	4	7	7.2%	-0.59 [-1.67, 0.49]		? ? • • • ? ? •
Yang 2015 10Hz	-29.01	5.57	10	-49.28	5.41	4	2.3%	3.43 [1.54, 5.33]	_	??? @? # # #
Yang 2015 1Hz	-27.49	5.76	9	-49.28	5.41	3	1.8%	3.53 [1.37, 5.70]		<b>+</b>
Yang 2015 cTBS	-16.54	5.15	9	-49.28	5.41	3	0.9%	5.81 [2.69, 8.93]		<b>.</b>
Yang 2017	83.5	26.8	20	69.1	31.3	20	21.1%	0.48 [-0.15, 1.11]		
Yi 2016 anodal	13.3	8.2	10	8.5	4.9	5	6.9%	0.62 [-0.49, 1.72]		<b>•</b> ? • • ? • •
Yi 2016 cathodal	13.2	8.5	10	8.5	4.9	5	6.9%	0.58 [-0.52 , 1.68]		
Subtotal (95% CI)			101			73	71.9%	0.72 [0.37, 1.06]		
Heterogeneity: Chi <sup>2</sup> = 3	34.95, df = 9 (	P < 0.000	1): I <sup>2</sup> = 749	6						
Test for overall effect:	Z = 4.10 (P <	0.0001)								
6.4.2 Line bisection										
Bang 2015	-5.37	0.4	6	-5.9	0.3	6	4.8%	1.38 [0.07, 2.70]		. ?? • • • • • •
Cha 2016	-19.33	6.87	15	-34.6	4	15	8.2%	2.64 [1.63, 3.66]	_	
Subtotal (95% CI)			21			21	13.0%	2.18 [1.37, 2.98]		1
Heterogeneity: Chi <sup>2</sup> = 2	2.20, df = 1 (P	P = 0.14); 1	[ <sup>2</sup> = 55%							-
Test for overall effect:	Z = 5.31 (P <	0.00001)								
6.4.3 BIT behavioural	l subtest									
Iwanski 2020	18.9	13	14	22.4	11.4	14	15.1%	-0.28 [-1.02, 0.47]		<b>a</b> ? ? <b>a</b> ? <b>a a</b>
Subtotal (95% CI)			14			14		-0.28 [-1.02 , 0.47]		
Heterogeneity: Not app	olicable									
Test for overall effect:		0.46)								
Total (95% CI)			136			108	100.0%	0.75 [0.47 , 1.04]		
Heterogeneity: Chi <sup>2</sup> = 5	56 59 df = 12	(P < 0.00		79%		100	2231070	[3177 ) 210 1]		
Test for overall effect:		,	001),1 /	5,0				Ĕ		٦
	,		- 2 (D < 0	0001) 12 -	80 7%			-2 Em	2 -1 0 1	Z primentall
Test for subgroup diffe	,		= 2 (P < 0	.0001), I <sup>2</sup> =	89.7%			Far	vours [control] Favours [expe	rimental]

#### Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias

Analysis 6.5. Comparison 6: NIBS versus any control, Outcome 5: Adverse events

	Experii	nental	Con	trol		Peto Odds Ratio	Peto Odd	s Ratio
Study or Subgroup	<b>Events</b> Total		Events Total		Weight Peto, Fixed, 95% CI		Peto, Fixed	, 95% CI
Total (95% CI)		(	)		0	Not estimable		
Total events:	0		0					
Heterogeneity: Not app	licable						0.01 0.1 1	10 100
Test for overall effect: I	Not applicab	le					Favours [control]	Favours [experimental]
Test for subgroup differ	rences: Not a	pplicable						

# Comparison 7. Electrical stimulation versus any control

Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
7.1 Activities of daily living: persisting effects	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable



Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
7.1.1 CBS	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
7.1.2 FIM	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
7.1.3 BI	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
7.2 Activities of daily living: immediate effects	1	20	Std. Mean Difference (IV, Random, 95% CI)	-0.54 [-1.44, 0.36]
7.2.1 CBS	1	20	Std. Mean Difference (IV, Random, 95% CI)	-0.54 [-1.44, 0.36]
7.2.2 FIM	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
7.2.3 BI	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
7.3 Neglect outcomes: persisting effects	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
7.3.1 Target cancellation	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
7.3.2 Line bisection	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
7.3.3 BIT behavioural subtest	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
7.4 Neglect outcomes: immediate effects	2	60	Std. Mean Difference (IV, Fixed, 95% CI)	0.99 [0.44, 1.53]
7.4.1 Target cancellation	2	60	Std. Mean Difference (IV, Fixed, 95% CI)	0.99 [0.44, 1.53]
7.4.2 Line bisection	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
7.4.3 BIT behavioural subtest	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable



# Analysis 7.1. Comparison 7: Electrical stimulation versus any control, Outcome 1: Activities of daily living: persisting effects

	Ex	perimen	tal		Control			Std. Mean Difference	Std. Mea	n Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rand	om, 95% CI
7.1.1 CBS										
Subtotal (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applie	cable									
Test for overall effect: No	ot applicabl	e								
7.1.2 FIM										
Subtotal (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applie	cable									
Test for overall effect: No	ot applicabl	e								
7.1.3 BI										
Subtotal (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applie	cable									
Test for overall effect: No	ot applicabl	e								
Total (95% CI)			0			C	)	Not estimable		
Heterogeneity: Not applie	cable									
Test for overall effect: No	ot applicabl	e							-100 -50	0 50 100
Test for subgroup differe	nces: Not a	pplicable							Favours [control]	Favours [experimental]

# Analysis 7.2. Comparison 7: Electrical stimulation versus any control, Outcome 2: Activities of daily living: immediate effects

	erimenta			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
an	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	A B C D E F G H
-12.7	3.88	10	-10.8	2.78	10	100.0%	-0.54 [-1.44, 0.36]	•	$\bullet \bullet \bullet \bullet \bullet \bullet \bullet \bullet$
		10			10	100.0%	-0.54 [-1.44 , 0.36]	<del>T</del>	
3 (P = 0	).24)								
		0			0		Not estimable		
licable									
		0			0		Not estimable		
licable									
		10			10	100.0%	-0.54 [-1.44 , 0.36]		
3(P=0)	).24)							-100 -50 0 50	100
Not app	plicable								experimental]
	12.7 8 (P = 0 licable	12.7 3.88 3 (P = 0.24)	12.7 3.88 10 10 3 (P = 0.24)  0 licable  10 3 (P = 0.24)	0 licable 10 (P = 0.24)	12.7 3.88 10 -10.8 2.78 10 3 (P = 0.24)  0 licable  10 3 (P = 0.24)	12.7 3.88 10 -10.8 2.78 10 10 3 (P = 0.24)  0 0 0 licable  10 10 10	12.7 3.88 10 -10.8 2.78 10 100.0% 10 10 100.0% 3 (P = 0.24)  0 0 licable 10 10 100.0%	12.7 3.88 10 -10.8 2.78 10 100.0% -0.54 [-1.44, 0.36] 10 10 100.0% -0.54 [-1.44, 0.36] 3 (P = 0.24)  0 0 Not estimable licable  10 10 100.0% -0.54 [-1.44, 0.36] 3 (P = 0.24)	12.7 3.88 10 -10.8 2.78 10 100.0% -0.54 [-1.44, 0.36] 10 10 100.0% -0.54 [-1.44, 0.36] 3 (P = 0.24)  0 0 Not estimable licable 10 10 100.0% -0.54 [-1.44, 0.36]

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias



# Analysis 7.3. Comparison 7: Electrical stimulation versus any control, Outcome 3: Neglect outcomes: persisting effects

	Exp	perimen	tal		Control			Std. Mean Difference	Std. Mea	n Difference
Study or Subgroup M	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rand	lom, 95% CI
7.3.1 Target cancellation										
Subtotal (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applicab	ole									
Test for overall effect: Not a	applicable	9								
7.3.2 Line bisection										
Subtotal (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applicab	ole									
Test for overall effect: Not a	applicable	<u> </u>								
7.3.3 BIT behavioural sub	test									
Subtotal (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applicab	ole									
Test for overall effect: Not a	applicable	2								
Total (95% CI)			0			0	)	Not estimable		
Heterogeneity: Not applicab	ole									
Test for overall effect: Not a	applicable	<u>د</u>							-100 -50	0 50 100
Test for subgroup difference	es: Not ap	plicable							Favours [control]	Favours [experimental

# Analysis 7.4. Comparison 7: Electrical stimulation versus any control, Outcome 4: Neglect outcomes: immediate effects

	Exp	perimenta	ıl		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	A B C D E F G H
7.4.1 Target cancellation	ı									
Choi 2019	-5	2.21	10	-8	2.3	10	30.6%	1.27 [0.29, 2.25]		
Polanowska 2009	107.15	20.9	20	83.65	31.6	20	69.4%	0.86 [0.21, 1.51]		<b>+ + + + ? + ? •</b>
Subtotal (95% CI)			30			30	100.0%	0.99 [0.44, 1.53]		
Heterogeneity: Chi <sup>2</sup> = 0.48	8, df = 1 (P	= 0.49); I	$^{2} = 0\%$							
Test for overall effect: Z =	3.56 (P = 0	0.0004)								
7.4.2 Line bisection										
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not applic	able									
Test for overall effect: No	t applicable	9								
7.4.3 BIT behavioural su	ıbtest									
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not applic	able									
Test for overall effect: No	t applicable	2								
Total (95% CI)			30			30	100.0%	0.99 [0.44 , 1.53]		
Heterogeneity: Chi <sup>2</sup> = 0.48	8, df = 1 (P	= 0.49); I	$^{2} = 0\%$							
Test for overall effect: Z =	3.56 (P = 0	0.0004)							-2 -1 0 1	⊣ 2
Test for subgroup differen	ces: Not ap	plicable							Favours [control] Favours [expe	erimental]

- (A) Random sequence generation (selection bias)
- $(B)\,Allocation\,concealment\,(selection\,bias)$
- (C) Blinding of participants
- (D) Blinding of personnel
- $(E) \ Blinding \ of \ outcome \ assessment \ (detection \ bias)$
- (F) Incomplete outcome data (attrition bias)
- $(G) \ Selective \ reporting \ (reporting \ bias)$
- (H) Other bias



# Comparison 8. Acupuncture versus any control

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
8.1 Activities of daily liv- ing: persisting effects	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
8.1.1 CBS	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
8.1.2 FIM	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
8.1.3 BI	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
8.2 Activities of daily living: immediate effects	2	104	Std. Mean Difference (IV, Fixed, 95% CI)	0.65 [0.26, 1.05]
8.2.1 CBS	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
8.2.2 FIM	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
8.2.3 BI	2	104	Std. Mean Difference (IV, Fixed, 95% CI)	0.65 [0.26, 1.05]
8.3 Neglect outcomes: persisting effects	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
8.3.1 Target cancellation	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
8.3.2 Line bisection	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
8.3.3 BIT-behavioural subtest	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable
8.4 Neglect outcomes: immediate effects	2	104	Std. Mean Difference (IV, Fixed, 95% CI)	0.57 [0.18, 0.97]
8.4.1 Target cancellation	1	64	Std. Mean Difference (IV, Fixed, 95% CI)	0.52 [0.03, 1.02]
8.4.2 Line bisection	1	40	Std. Mean Difference (IV, Fixed, 95% CI)	0.65 [0.01, 1.29]
8.4.3 BIT behavioural subtest	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable



# Analysis 8.1. Comparison 8: Acupuncture versus any control, Outcome 1: Activities of daily living: persisting effects

Ехр	erimental			Control			Std. Mean Difference	Std. Mear	n Difference
Study or Subgroup Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixe	d, 95% CI
8.1.1 CBS									
Subtotal (95% CI)		0			0	1	Not estimable		
Heterogeneity: Not applicable									
Test for overall effect: Not applicable	!								
8.1.2 FIM									
Subtotal (95% CI)		0			0	1	Not estimable		
Heterogeneity: Not applicable									
Test for overall effect: Not applicable	!								
8.1.3 BI									
Subtotal (95% CI)		0			0	1	Not estimable		
Heterogeneity: Not applicable									
Test for overall effect: Not applicable	!								
Total (95% CI)		0			0	1	Not estimable		
Heterogeneity: Not applicable									
Test for overall effect: Not applicable	•							-100 -50	0 50 100
Test for subgroup differences: Not ap	plicable							Favours [control]	Favours [experimental]

# Analysis 8.2. Comparison 8: Acupuncture versus any control, Outcome 2: Activities of daily living: immediate effects

	Exp	erimental		(	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD 7	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	A B C D E F G H
8.2.1 CBS										
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not applica	able									
Test for overall effect: Not	t applicable									
8.2.2 FIM										
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not applica	able									
Test for overall effect: Not	t applicable									
8.2.3 BI										
Dolkun 2019	45.59	14.86	32	36.76	13.31	32	62.0%	0.62 [0.12, 1.12]	<del></del>	
Li 2017	53.75	9.16	20	48	6.37	20	38.0%	0.71 [0.07, 1.36]		$\bullet \bullet \bullet \bullet ? \bullet \bullet \bullet$
Subtotal (95% CI)			52			52	100.0%	0.65 [0.26, 1.05]		
Heterogeneity: Chi <sup>2</sup> = 0.05	5, df = 1 (P	= 0.82); I <sup>2</sup> =	0%						•	
Test for overall effect: Z =	3.25 (P = 0	0.001)								
Total (95% CI)			52			52	100.0%	0.65 [0.26 , 1.05]		
Heterogeneity: Chi <sup>2</sup> = 0.05	5, df = 1 (P	= 0.82); I <sup>2</sup> =	0%						•	
Test for overall effect: Z =	3.25 (P = 0	0.001)						-	2 -1 0 1	
Test for subgroup differen	ices: Not ap	plicable						Fa	avours [control] Favours [exp	perimental]

- $(A) \ Random \ sequence \ generation \ (selection \ bias)$
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias



# Analysis 8.3. Comparison 8: Acupuncture versus any control, Outcome 3: Neglect outcomes: persisting effects

Exp	erimental		Control			Std. Mean Difference	Std. Mean	Difference
Study or Subgroup Mean	SD Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed	, 95% CI
8.3.1 Target cancellation								
Subtotal (95% CI)	(	)		0	)	Not estimable	!	
Heterogeneity: Not applicable								
Test for overall effect: Not applicable	!							
8.3.2 Line bisection								
Subtotal (95% CI)		)		0	)	Not estimable	•	
Heterogeneity: Not applicable								
Test for overall effect: Not applicable	!							
8.3.3 BIT-behavioural subtest								
Subtotal (95% CI)		)		0	)	Not estimable	1	
Heterogeneity: Not applicable								
Test for overall effect: Not applicable	!							
Total (95% CI)	(	)		0	)	Not estimable	<u>.</u>	
Heterogeneity: Not applicable								
Test for overall effect: Not applicable	!						-100 -50 (	50 100
Test for subgroup differences: Not app	plicable						Favours [control]	Favours [experimental]

# Analysis 8.4. Comparison 8: Acupuncture versus any control, Outcome 4: Neglect outcomes: immediate effects

	Exper		ıl		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	ABCDEFGH
8.4.1 Target cancellation										
Dolkun 2019	-1.76	0.51	32	-2.07	0.65	32	62.0%	0.52 [0.03, 1.02]		
Subtotal (95% CI)			32			32	62.0%	0.52 [0.03, 1.02]		
Heterogeneity: Not applicab	ole									
Test for overall effect: $Z = 2$	2.06 (P = 0	0.04)								
8.4.2 Line bisection										
Li 2017	-1.2	0.7	20	-1.7	0.8	20	38.0%	0.65 [0.01, 1.29]		$\bullet \bullet \bullet \bullet ? \bullet \bullet$
Subtotal (95% CI)			20			20	38.0%	0.65 [0.01, 1.29]		
Heterogeneity: Not applicab	ole									
Test for overall effect: $Z = 2$	2.00 (P = 0	0.05)								
8.4.3 BIT behavioural sub	test									
Subtotal (95% CI)			0			0		Not estimable		
Heterogeneity: Not applicab	ole									
Test for overall effect: Not a	applicable	ġ.								
Total (95% CI)			52			52	100.0%	0.57 [0.18, 0.97]		
Heterogeneity: Chi <sup>2</sup> = 0.10,	df = 1 (P	= 0.76); I	$^{2} = 0\%$							
Test for overall effect: $Z = 2$	2.86 (P = 0	0.004)							-2 -1 0 1	
Test for subgroup difference	es: Chi² =	0.10, df =	1 (P = 0.7	6), I <sup>2</sup> = 0%					Favours [control] Favours [ex	perimental]

### Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants
- (D) Blinding of personnel
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias

## **ADDITIONAL TABLES**



Study name	Active intervention 1 (subtype)	Active interven- tion 2 (if applica- ble)	Active interven- tion 3 (if applic- able)	Control intervention
Aparicio-Lopez 2016	Visual (eye-patching) + Mental function (cog- nitive rehabilitation)	Mental function (cognitive rehabili- tation)		
Bang 2015	NIBS (tDCS) + Body awareness (mirror therapy)	Body awareness (mirror therapy)		
Cazzoli 2012	NIBS (TBS)			Sham
Cha 2016	NIBS (rTMS)			Sham
Cherney 2003	Visual (scanning)			Attention control
Choi 2016	Movement (upper limb training)			Usual care
Choi 2019	Prism adaptation	Electrical stimula- tion (FES)	Prism adaptation + Electrical stim- ulation (FES)	
Cottam 1987	Visual (scanning)			No treatment
Dolkun 2019	Acupuncture			Usual care
Edmans 2000	Body awareness (perceptual training)			Attention control
Fanthome 1995	Visual (eye movement feedback)			No treatment
Ferreira 2011	Visual (scanning)	Mental function (mental practice)		
Fong 2007	Body awareness (trunk rotation)	Body awareness (trunk rotation) + Visual (eye-patch- ing)		Usual care
Fong 2013	Body awareness (sensory cueing)			Sham
Fu 2017	NIBS (cTBS 80%)	NIBS (cTBS 40%)		
Goedert 2020	Prism adaptation			Usual care
lwanski 2020	NIBS (rTMS) + Visual (scanning)			Sham + Visual (scanning)
Kalra 1997	Body awareness (sensory cueing)			Usual care
Karner 2019	Body awareness (sensory cueing)			Attention control
Katz 2005	Mental function (VR training)	Visual (scanning)		
Kerkhoff 2012	Visual (OKS)	Visual (scanning)		
Kerkhoff 2014	Visual (smooth pursuit training)	Visual (scanning)		



Kim 2011	Mental function (VR training)			Usual care
Kim 2013	NIBS (high-frequency rTMS)	NIBS (low-frequen- cy rTMS)		Sham
Kim 2015	NIBS (1 rTMS) + Visual (scanning)	NIBS (10 rTMS) + Vi- sual (scanning)		
Kim 2018	NIBS (rTMS)	Movement (upper limb training)	NIBS (rTMS) + Movement (up- per limb train- ing)	
Koch 2012	NIBS (cTBS)			Sham
Kutlay 2018	Movement (balance training)			Usual care
Learmonth 2020	NIBS (tDCS)	Movement (visuo- motor feedback)	NIBS (tDCS) + Movement (vi- suomotor feed- back)	Attention control
Li 2017	Acupuncture			Usual care
Luukkainen- Markkula 2009	Body awareness (limb activation)	Visual (scanning)		
Machner 2014	Visual (OKS) + Visual (eye-patching)			Usual care
Mancuso 2012	Prism adaptation			Sham
Mizuno 2011	Prism adaptation			Sham
Nyffeler 2019*	NIBS (8 cTBS) + Visual (smooth pursuit training)	NIBS (16 cTBS) + Visual (smooth pursuit training)		Sham + Visual (smooth pursuit training)
Nys 2008	Prism adaptation			Sham
Pandian 2014	Body awareness (mirror therapy)			Sham
Park 2015	Mental function (mental practice)			Usual care
Park 2015b	Mental function (mental practice)	Electrical stimula- tion		
Polanowska 2009	Electrical stimulation (TENS) + Visual (scanning)			Sham + Visual (scanning)
Raghavan 2017	NIBS (rTMS)			Sham
Robertson 1990	Visual (scanning)			Attention control
Robertson 2002	Body awareness (limb activation) + Visual (scanning)			Sham + Visual (scanning)
Rode 2015	Prism adaptation			Sham



Table 1.	Included studies interventions and	d comparisons (Continued)

Rossit 2019	Movement (visuomotor feedback)			Attention control
Rusconi 2002	Electrical stimulation (TENS) + Mental function (cognitive training)	Mental function (cognitive training)		
Schroder 2008	Electrical stimulation (TENS) + Visual (scanning)	Visual (OKS) + Visu- al (scanning)	Visual (scanning)	
Seniow 2016	Electrical stimulation (TENS) + Visual (scanning)			Sham + Visual (scanning)
Sesh 2018	Body awareness (sensory stimulation)			Usual care
Song 2009	NIBS (rTMS)			Usual care
Ten-Brink 2017	Prism adaptation			Sham
Tsang 2009	Visual (eye-patching)			Usual care
Turton 2010	Prism adaptation			Sham
Van Wyk 2014	Visual (scanning)			Attention control
Varalta 2019	Body awareness (neck taping)			Sham
Vatanparasti 2019	NIBS (cTBS) + Prism adaptation			Sham NIBS + Prism adaptation
Volkening 2016	Electrical stimulation (GVS) + Visual (scanning)			Sham + Visual (scanning)
Welfringer 2011	Mental function (mental practice)			Usual care
Wiart 1997	Body awareness (trunk rotation)			Usual care
Wilkinson 2014	Electrical stimulation (1 GVS)	Electrical stimula- tion (5 GVS)	Electrical stimu- lation (5 GVS)	
Wu 2013	Movement (CIMT)	Movement (CIMT) + Visual (eye-patch- ing)		Usual care
Yang 2015*	NIBS (1 Hz TBS)	NIBS (10 Hz TBS)	NIBS (cTBS)	Sham
Yang 2017	NIBS (rTMS)	NIBS (rTMS) + Body awareness (sensory cueing)		Usual care
Yi 2016*	NIBS (anodal tDCS)	NIBS (cathodal tD- CS)		Sham
Zeloni 2002	Visual (eye-patching)			Usual care

<sup>\*</sup> Denotes studies with multiple entries in Characteristics of included studies table.

CIMT: constraint-induced movement therapy.

cTBS: continuous theta burst stimulation.

GVS: galvanic vestibular stimulation.



OKS: optokinetic stimulation.

rTMS: repetitive transcranial magnetic stimulation.

TBS: theta burst stimulation.

tDCS: transcranial direct current stimulation. TENS: transcutaneous electrical nerve stimulation.

Table 2. Included studies outcome measures used

Study name	Primary outcome	Secondary	outcome measi	are reported	i	Data used in:
	measure reported	Target cancella- tion	Line bisec- tion	ВІТ-В	Other	
Aparicio-Lopez 2016	CBS	х	х			Analysis 1.4
Bang 2015	ВІ		х			Analysis 6.4
Cazzoli 2012	CBS	х	х			No usable data
Cha 2016			х			Analysis 6.4
Cherney 2003				х		Analysis 1.4
Choi 2016	CBS	х	х			Analysis 5.2; Analysis 5.4
Choi 2019	CBS	х				Analysis 2.2; Analysis 2.4; Analysis 7.4
Cottam 1987		х				Analysis 1.3
Dolkun 2019	ВІ	х	х			Analysis 8.2; Analysis 8.4
Edmans 2000	ВІ	х				Analysis 3.2; Analysis 3.4;
Fanthome 1995				х		Analysis 1.3; Analysis 1.4
Ferreira 2011	FIM				х	Table 3; Table 4
Fong 2007	FIM			х		Analysis 1.1; Analysis 1.2; Analysis 1.3; Analysis 1.4; Analysis 3.1; Analysis 3.2; Analysis 3.3; Analysis 3.4
Fong 2013	FIM	х				Analysis 3.2; Analysis 3.4
Fu 2017		х	х			No usable data
Goedert 2020	CBS				х	Analysis 2.1; Analysis 2.2
lwanski 2020	FIM			Х		Analysis 6.1; Analysis 6.2; Analysis 6.3; Analysis 6.4
Kalra 1997	ВІ	х				Analysis 3.4; Analysis 3.6
Karner 2019	SINGER	х	х			Analysis 3.4



Table 2. Included s	ADL test	X				Table 3
	ADL test	x				
Kerkhoff 2012		X	X			Table 3
Kerkhoff 2014	ADL test		х			Table 3
Kim 2011	CBS	х	х			Analysis 4.2; Analysis 4.4
Kim 2013	CBS	х	х			Table 4
Kim 2015		х	х			Table 3
Kim 2018	CBS	Х	х			Analysis 5.2; Analysis 5.4; Analysis 6.2; Analysis 6.4
Koch 2012		х	х	х		Analysis 6.4
Kutlay 2018	FIM	х	х	х		Table 4
Learmonth 2020	SIS	х	х			Table 3; Table 4
Li 2017	BI	х	х			Analysis 8.2; Analysis 8.4
Luukkainen- Markkula 2009	CBS				х	Table 3
Machner 2014	CBS	х	Х			Analysis 1.1; Analysis 1.2; Analysis 1.3; Analysis 1.4
Mancuso 2012		х	х			Analysis 2.4
Mizuno 2011	CBS, FIM			х		Analysis 2.2; Analysis 2.4
Nyffeler 2019	CBS, FIM	х				Analysis 6.1; Analysis 6.2; no usable secondary outcome data
Nys 2008		х	х			Analysis 2.3; Analysis 2.4
Pandian 2014	FIM, mRS	х	х			Table 4
Park 2015		х	х			Analysis 4.4
Park 2015b	CBS	х	х			Table 3
Polanowska 2009		х	х			Analysis 7.4
Raghavan 2017		х	х			No usable data
Robertson 1990	Frenchay Activities Index	х				Analysis 1.3; Analysis 1.4
Robertson 2002	BI	х		Х		Analysis 3.1; Analysis 3.2; Analysis 3.3; Analysis 3.4
Rode 2015	FIM				Х	No usable data



Rossit 2019	SIS			Х	No usable data
Rusconi 2002	BI	х	х		No usable data
Schroder 2008				х	No usable data
Seniow 2016				х	No usable data
Sesh 2018	mRS	х	х		Analysis 3.1; Analysis 3.2; Analysis 3.3; Analysis 3.4
Song 2009		Х	х		Analysis 6.4
Ten-Brink 2017	CBS	х			Analysis 2.2; Analysis 2.4
Tsang 2009	FIM	Х	Х		Table 4
Turton 2010	CBS			Х	Analysis 2.1; Analysis 2.2
Van Wyk 2014	BI	Х			No usable data
Varalta 2019		Х			Analysis 3.4
Vatanparasti 2019	mRS	Х	Х		Analysis 6.4
Volkening 2016				х	No usable data
Welfringer 2011		Х			Analysis 4.4
Wiart 1997	FIM	х	х		Analysis 3.1; Analysis 3.2; Analysis 3.3; Analysis 3.4
Wilkinson 2014	BI			х	Table 3
Wu 2013	CBS				Analysis 1.2;
Yang 2015		х	х		Analysis 6.3; Analysis 6.4
Yang 2017	CBS	х			Analysis 3.1; Analysis 3.2; Analysis 3.3; Analysis 3.4; Analysis 6.1; Analysis 6.2; Analysis 6.3; Analysis 6.4
Yi 2016	CBS	Х	Х	,	Analysis 6.2; Analysis 6.4
Zeloni 2002		Х	X	,	Analysis 1.4

ADL: activities of daily living.

BI: Barthel Index.

CBS: Catherine Bergego Scale.

FIM: Functional Independence Measure.

mRS: modified Rankin Scale.

 ${\bf SINGER: Scores\ of\ Independence\ Index\ for\ Neurological\ and\ Geriatric\ Rehabilitation.}$ 

SIS: Stroke Impact Scale.



Table 3. Results of studies comparing multiple interventions

Study identi- fier	Intervention	Outcome	Mean (SD)	Number of participants	Reported re- sult	
Apari- cio-Lopez 2016	Visual (eye-patching) + Mental function (cognitive rehabilitation)	Immediate ADL (CBS)	10.33 (6.6)	13	"No significant difference"	
2010	Mental function (cognitive rehabilitation)	_	8.83 (6.7)	15	_	
	Visual (eye-patching) + Mental function (cognitive rehabilitation)	Immediate ne- glect (line bi- - section)	2.85 (3.55)	13	"No significan difference"	
	Mental function (cognitive rehabilitation)	- section)	0.93 (1.38)	15	_	
Bang 2015	NIBS (tDCS) + Body awareness (mirror therapy)	Immediate ADL (BI)	78.3 (3.9)	6	Mann-Whitney U, P = 0.004 in – favour of NIBS	
	Body awareness (mirror therapy)	_	69.2 (2.4)	6	+ body aware- ness	
	NIBS (tDCS) + Body awareness (mirror therapy)	Immediate ne- glect (line bi- - section)	5.37 (0.4)	6	Mann-Whitney U, P = 0.031 in	
	Body awareness (mirror therapy)	- section)	5.9 (0.3)	6	<ul><li>favour of NIBS</li><li>+ body aware</li><li>ness</li></ul>	
Choi 2019	Prism adaptation	Immediate ADL	12.7 (3.88)	10	ANOVA, P <  — 0.001 in favour	
	Electrical stimulation (FES)	– (CBS)	14.8 (3.04)	10	of prism adap tation + FES	
	Prism adaptation + Electrical stimulation (FES)	-	10.8 (2.78)	10		
	Prism adaptation	Immediate ne-	8 (2.3)	10	ANOVA, P <  – 0.001 in favour	
	Electrical stimulation (FES)	<ul> <li>glect (target cancellation)</li> </ul>	9.1 (1.19)	10	of prism adap- tation + FES	
	Prism adaptation + Electrical stimulation (FES)	_	5.0 (2.21)	10		
Ferreira 2011	Mental function (mental practice)	Persisting ADL – (FIM)	92.1 (24.4)	5	"No significant – difference"	
	Visual (scanning training)	- (FIIVI)	90.1 (26.5)	5	– difference	
Fong 2007	Body awareness (trunk rotation)	Persisting ADL	52.9 (19.5)	14	"No significant – difference"	
	Body awareness (trunk rotation) + Visual (eye-patching)	– (FIM)	51.5 (21.7)	20	– difference	
	Usual care	_	40.7 (20.9)	12	_	
	Body awareness (trunk rotation)	Immediate ADL	50.2 (19.4)	19	"No significan	
	Body awareness (trunk rotation) + Visual (eye-patching)	– (FIM)	44.3 (18.7)	20	<ul><li>difference"</li></ul>	
		_	37.1 (16.4)	15	_	



	Body awareness (trunk rotation)	Persisting ne- – glect (BIT-B)	54.9 (28.8)	14	"No significant ——— difference"	
	Body awareness (trunk rotation) + Visual (eye-patching)	8.000 (2.1. 2)	53.8 (31.1)	20		
	Usual care	_	46.8 (31.7)	12		
	Body awareness (trunk rotation)	Immediate ne- – glect (BIT-B)	44.2 (20.8)	14	"No significant	
	Body awareness (trunk rotation) + Visual (eye-patching)	= glect (bili-b)	44.6 (27.3)	20	unrerence	
	Usual care	_	4.4 (26)	12		
Fu 2017	NIBS (cTBS 80%)	Immediate ne- – glect (target	No useable da	ta		
	NIBS (cTBS 40%)	cancellation)				
Katz 2005	Mental function (VR training) Immediate ADL		73.7 (14)	11	"No significant	
	Visual (scanning training)	– (FIM)	73.6 (22.8)	8	—— difference	
	Mental function (VR training)	Immediate ne-	14.8 (12.9)	11	No statistical	
	Visual (scanning training)	<ul><li>glect (target cancellation)</li></ul>	14.6 (10.40)	8	comparison reported	
Kerkhoff 2012	Visual (OKS)	Immediate ne- – glect (target	3.3 (4.2)	3	Mann-Whitney U; P < 0.001	
	Visual (scanning training)	cancellation)	9.3 (1.2)	3	In favour of OKS	
Kerkhoff 2014	Visual (smooth pursuit training)	Immediate ADL – (BI)	28 (5)	12	Mann-Whitney U = P > 0.55	
	Visual (scanning training)	– (DI)	26 (8)	12	—— U-F>0.33	
Kim 2013	NIBS (low-frequency rTMS)	Immediate ADL – (CBS)	-5.4 (3.3)	9	"No significant difference"	
(Mean change from baseline	NIBS (high-frequency rTMS)	- (CB3)	-8.6 (3.1)	9	—— difference	
data available only)	Sham	_	-2.6 (1.7)	9		
	NIBS (low-frequency rTMS)	Immediate ne-	16.4 (5.4)	9	"No significant	
	NIBS (high-frequency rTMS) glect (target cancellation)		10.4 (3.6)	9	—— difference	
	Sham	_	3.6 (4.7)	9		
Kim 2015	NIBS (rTMS 1 session)	Immediate ne- – glect (target	16.63 (3.24)	19	ANOVA, P <	
	NIBS (rTMS 10 sessions)	cancellation)	17 (2.85)	15	of 10 sessions	
Kim 2018	NIBS (rTMS)	Immediate ADL – (CBS)	15.2 (3.7)	10	Kruskal-Wallis F	
	Movement (upper limb robot)	<b>–</b> (CD3)	17.5 (4.1)	10	U.15Z	



	NIBS (rTMS)	Immediate ne- glect (target	15.2 (4.9)	10	Kruskal-Wallis F —— = 0.125
	Movement (upper limb robot)	cancellation)	14.5 (3.5)	10	-0.125
Learmonth 2020 (mean change from base-	NIBS (tDCS)	Persisting ne- glect (line bi-	0.20 (49)	5	No statistical comparison re-
	Movement (visuomotor feedback training)	section)	3.39 (4.78)	2	ported
line data only available)	NIBS (tDCS) + Movement (visuomotor feedback training)	_	-0.20 (0.31)	3	
	Attention control	-	0.01 (0.44)	4	
	NIBS (tDCS)	Immediate ne- glect (line bi-	0.68 (2.70)	6	No statistical
	Movement (visuomotor feedback training)	section)	0.64 (1.01)	5	——— comparison re- ported
	NIBS (tDCS) + Movement (visuomotor feedback training)	_	0.12 (0.89)	5	
	Attention control	-	-0.31 (0.56)	5	
Luukkainen- Markkula 2009	Body awareness (arm activation)	Persisting ADL - (CBS)	3.4 (2.4)	6	No statistical comparison re-
	Visual (scanning training)	- (CB3)	6.9 (3.8)	6	ported
	Body awareness (arm activation)	Immediate ADL - (CBS)	5.9 (3.1)	6	No statistical comparison re-
	Visual (scanning training)	- (CD3)	8.9 (5.1)	6	ported
Nyfeller 2019	NIBS (8 cTBS)	Persisting ADL - (CBS)	5.38 (4.41)	8	ANOVA, P = 0.94
	NIBS (16 cTBS)	- (655)	5.9 (6.28)	10	
	Sham		12.2 (7.03)	9	
	NIBS (8 cTBS)	Immediate ADL - (CBS)	7 (6.16)	10	ANOVA, P < 0.02 ——— in favour of 16
	NIBS (16 cTBS)	- (655)	6.8 (7.1)	10	cTBS
	Sham		12.5 (6.52)	10	
Park 2015b	Mental function (mental practice) + electromyogram-	Immediate ADL (CBS)	10.1 (4.6)	16	"No significant difference"
	triggered electrical stimulation	_			
	Mental function (mental practice) + cyclical electrical stimulation		11.2 (4.1)	17	
	Mental function (mental practice) + electromyogram-	Immediate ne- glect (target	13.0 (5.5)	16	"No significant difference"
	triggered electrical stimulation	cancellation)			



	Mental function (mental practice) + cyclical electrical stimulation		11.0 (4.6)	17	
Rusconi 2002	Mental function (cognitive training type 1)	Immediate ADL (BI)	No usable data		
	Mental function (cognitive training type 2)	_			
	Electrical stimulation (TENS) + mental function (cognitive training type 1)	-			
	Electrical stimulation (TENS) + mental function (cognitive training type 2)	_			
	Mental function (cognitive training type 1)	Immediate ne-	No usable data		
	Mental function (cognitive training type 2)	<ul><li>cancellation)</li></ul>			
	Electrical stimulation (TENS) + mental function (cognitive training type 1)	_			
	Electrical stimulation (TENS) + mental function (cognitive training type 2)	_			
Schroder 2008	Electrical stimulation (TENS)	Immediate ne-	No usable data		
	Visual (OKS)	<ul><li>glect (bespoke score)</li></ul>			
Wilkinson	Electrical stimulation (GVS) 1 session	Persisting ADL	64.3 (24.5)	14	"No significant —— difference"
2014	Electrical stimulation (GVS) 5 sessions	_ (BI)	56.9 (25.6)	16	—— difference
	Electrical stimulation (GVS) 10 sessions	-	66.4 (26.5)	14	
	Electrical stimulation (GVS) 1 session	Immediate ADL – (BI)	49.6 (24.1)	13	"No significant —— difference"
	Electrical stimulation (GVS) 5 sessions	– (DI)	60.8 (29.1)	18	—— difference
	Electrical stimulation (GVS) 10 sessions	-	32.6 (31)	15	
Wu 2013	Movement (CIMT) + visual (eye patching)	Immediate ADL	10.4 (3.2)	7	ANOVA, P < 0.01
	Movement (CIMT)	– (CBS)	9.9 (4.4)	8	
	Usual care	_	16.3 (4.5)	9	
Yang 2015	NIBS (1 Hz TBS)	Persisting ne-	18.46 (4.91)	9	ANOVA, P < 0.05
	NIBS (10 Hz TBS)	<ul><li>glect (target cancellation)</li></ul>	24.44 (4.54)	10	_
	NIBS (cTBS)	_	14.79 (4.59)	9	
	Sham	_	15.54 (5.74)	10	



	NIBS (1 Hz TBS)	Immediate ne- glect (target	27.4 (5.76)	9	ANOVA, P < 0.05	
	NIBS (10 Hz TBS) NIBS (cTBS) Sham	cancellation) —— –	29.01 (5.57)	10 9		
			16.54 (5.15)			
			49.28 (5.41)	10		
Yang 2015	NIBS (rTMS)	Persisting ADL —— (CBS)	13.9 (5.2)	18	"No significant	
	NIBS (rTMS) + Body awarenss (sensory cueing)		1.2 (6.4)	19	difference"	
	NIBS (rTMS)	Immediate ADL —— (CBS)	16.4 (5.8)	20	"No significant ——— difference"	
	NIBS (rTMS) + Body awarenss (sensory cueing)	(CB3)	14.1 (7)	20		
	NIBS (rTMS)	Persisting ne-	93.5 (24.1)	18	"No significant ——— difference"	
	NIBS (rTMS) + Body awarenss (sensory cueing)	cancellation)	101.6 (24.7)	19		
	NIBS (rTMS)	Immediate ne-	83.5 (26.8)	20	"No significant difference"	
	NIBS (rTMS) + Body awarenss (sensory cueing)	—— glect (target cancellation)	93.4 (30.4)	20		
Yi 2016	NIBS (anodal tDCS)	Immediate ADL —— (CBS)	8.4 (9)	10	"No significant difference"	
	NIBS (cathodal tDCS)	—— (CB3)	10 (6.2)	10		
	Sham		12.3 (10.8)	10		
	NIBS (anodal tDCS)	Immediate ne-	13.3 (8.2)	10	"No significant	
	NIBS (cathodal tDCS)	cancellation)	13.2 (8.5)	10	—— umerence	
	Sham		8.5 (4.9)	10		

ADL: activities of daily living. CBS: Catherine Bergego Scale.

CIMT: constraint-induced movement therapy. cTBS: continuous theta burst stimulation.

FES: functional electrical stimulation. GVS: galvanic vestibular stimulation.

NIBS: non-invasive brain stimulation. OKS: optokinetic stimulation.

rTMS: repetitive transcranial magnetic stimulation.

TBS: theta burst stimulation.

tDCS: transcranial direct current stimulation.

 $TENS: transcutaneous\ electrical\ nerve\ stimulation.$ 

VR: virtual reality.



Table 4. Results of studies with change from baseline data

Study identi- fier	Intervention	Outcome	Mean change from baseline (SD)	Number of participants	Reported result
Ferreira 2011	Mental practice	Immediate ADL	7.4 (7.3)	5	"No significant dif-
	Scanning training	- (FIM)	10.3 (6.7)	5	- ference"
Kim 2013	Low-frequency rTMS	Immediate ADL - (CBS)	-5.4 (3.3)	9	"No significant dif- ference"
	High-frequency rTMS	(000)	-8.6 (3.1)	9	
	Sham	-	-2.6 (1.7)	9	_
	Low-frequency rTMS	Immediate ne- glect (target can-	16.4 (5.4)	9	"No significant dif- ference"
	High-frequency rTMS	cellation)	10.4 (3.6)	9	
	Sham	-	3.6 (4.7)	9	_
Kutlay 2018	Kinaesthetic ability training	Immediate ADL (FIM)	Median change: 82 (IQR 75.5 to 99)	25	"No significant dif- ference"
	Usual care	-	Median change: 79 (IQR 68.3 to 86.8)	28	_
	Kinaesthetic ability training	Immediate ne- glect (BIT behav-	Median change: 67 (IQR 57.5 to 12)	25	"No significant dif ference"
	Usual care	- ioural)	Median change: 56.5 (IQR 25.75 to 66.5)	28	_
Learmonth	tDCS	Persisting neglect  (line bisection)	0.20 (49)	5	No statistical com
2020	Behavioural training		3.39 (4.78)	2	<ul> <li>parison reported</li> </ul>
	tDCS + Behavioural training	-	-0.20 (0.31)	3	_
	Control behavioural training	-	0.01 (0.44)	4	_
	tDCS	Immediate ne-	0.68 (2.70)	6	No statistical com – parison reported
	Behavioural training	<ul> <li>glect (line bisec- tion)</li> </ul>	0.64 (1.01)	5	
	tDCS + Behavioural training	-	0.12 (0.89)	5	_
	Control behavioural training	-	-0.31 (0.56)	5	-
	tDCS	Persisting depres-	8.25 (9.22)	4	No statistical com
	Behavioural training	- sion (Beck Depres- sion Inventory)	2.00 (1.41)	2	<ul> <li>parison reported</li> </ul>
	tDCS + Behavioural training	-	19.50 (19.09)	2	-



Table 4. Resul	lts of studies with change f	from baseline data (	'Continued)		
	Control behavioural train- ing		17.33 (14.57)	3	
Pandian 2014	Body awareness (mirror therapy)	Persisting neglect (target cancella- — tion)	35 (1.5)	26	ANCOVA, P < 0.0001 in favour of inter- vention
	Sham	— tion)	12 (1.5)	20	Vention
	Body awareness (mirror therapy)	Immediate ne- glect (target can- — cellation)	20 (1)	26	ANCOVA, P < 0.0001 in favour of inter- vention
	Sham	— cellation,	6 (1.25)	20	vention
Tsang 2009	Visual (eye-patching)	Immediate ADL — (FIM)	16 (14.24)	17	"No significant dif- ——— ference"
	Usual care	— (1 IM)	12.41 (14.21)	17	referice
	Visual (eye-patching)	Immediate ne- — glect (target can-	8.65 (13.15)	17	t-test, P = 0.037 in
	Usual care	cellation)	1.88 (5.02)	17	tion

ADL: activities of daily living.
BIT: Behavioural Inattention Test.
FIM: Functional Independence Measure.

CBS: Catherine Bergego Scale.

tDCS: transcranial direct current stimulation.

BIT: Behavioural Inattention Test.

IQR: interquartile range.

rTMS: repetitive transcranial magnetic stimulation.

# APPENDICES

## Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Cerebrovascular Disorders] this term only

#2 MeSH descriptor: [Basal Ganglia Cerebrovascular Disease] explode all trees

#3 MeSH descriptor: [Brain Ischemia] explode all trees

#4 MeSH descriptor: [Carotid Artery Diseases] explode all trees #5 MeSH descriptor: [Cerebrovascular Trauma] explode all trees #6 MeSH descriptor: [Intracranial Arterial Diseases] this term only

#7 MeSH descriptor: [Intracranial Arteriovenous Malformations] explode all trees #8 MeSH descriptor: [Intracranial Embolism and Thrombosis] explode all trees

#9 MeSH descriptor: [Intracranial Hemorrhages] explode all trees

#10 MeSH descriptor: [Intracranial Hemorrhage, Hypertensive] this term only

#11 MeSH descriptor: [Stroke] this term only

#12 MeSH descriptor: [Brain Infarction] explode all trees #13 MeSH descriptor: [Stroke, Lacunar] this term only

#14 MeSH descriptor: [Vasospasm, Intracranial] this term only

#15 MeSH descriptor: [Vertebral Artery Dissection] this term only

#16 MeSH descriptor: [Hypoxia, Brain] explode all trees

#17 (stroke or poststroke or post-stroke or cerebrovasc\* or brain vasc\* or cerebral vasc or cva or apoplex or SAH):ti,ab,kw

#18 ((brain\* or cerebr\* or cerebell\* or intracran\* or intracerebral) near/5 (isch?emi\* or infarct\* or thrombo\* or emboli\* or occlus\*)):ti,ab,kw

#19 ((brain\* or cerebr\* or cerebell\* or intracerebral or intracranial or subarachnoid) near/5 (haemorrhage\* or hemorrhage\* or haematoma\* or hematoma\* or bleed\*)):ti,ab,kw

#20 MeSH descriptor: [Hemiplegia] this term only #21 MeSH descriptor: [Paresis] explode all trees

#22 (hemipleg\* or hemipar\* or paresis or paretic):ti,ab,kw



#23 ((unilateral or visual or hemispatial or attentional or spatial) near/5 neglect):ti,ab,kw

#24 ((cerebral or brain or subarachnoid) near/5 (haemorrhage\* or haemorrhage\* or haematoma\* or hematoma\* or bleed)):ti,ab,kw

#25 ((trauma\* or acquired) near/5 brain injur\*):ti,ab,kw

#26 MeSH descriptor: [Brain Damage, Chronic] explode all trees

#27 MeSH descriptor: [Brain Injuries] this term only #28 MeSH descriptor: [Brain Concussion] explode all trees

#20 MeSi i descriptor. [Drain concussion] explode all trees

#29 MeSH descriptor: [Brain Hemorrhage, Traumatic] explode all trees

#30 MeSH descriptor: [Brain Injury, Chronic] this term only #31 MeSH descriptor: [Diffuse Axonal Injury] this term only #32 MeSH descriptor: [Craniocerebral Trauma] this term only #33 MeSH descriptor: [Head Injuries, Closed] explode all trees

#34 MeSH descriptor: [Intracranial Hemorrhage, Traumatic] explode all trees

#35 MeSH descriptor: [Brain Abscess] explode all trees

#36 MeSH descriptor: [Central Nervous System Infections] explode all trees

#37 MeSH descriptor: [Encephalitis] explode all trees #38 MeSH descriptor: [Meningitis, Viral] explode all trees

#39 (encephalitis or meningitis):ti,ab,kw

#40 MeSH descriptor: [Brain Neoplasms] explode all trees

#41 ((brain or cerebr\*) near/5 (neoplasm\* or lesion\* or tumor\* or tumour\*)):ti,ab,kw

#42 {OR #1-#41}

#43 MeSH descriptor: [Perceptual Disorders] explode all trees

#44 MeSH descriptor: [Perception] explode all trees #45 MeSH descriptor: [Attention] this term only

#46 MeSH descriptor: [Extinction, Psychological] this term only

#47 (hemineglect or hemi-neglect):ti,ab,kw

#48 (unilateral or spatial) near/5 neglect):ti,ab,kw

#49 (perception or inattention or hemi-inattention or attention or extinction):ti,ab,kw

#50 ((perceptual or visuo?spatial or visuo?perceptual or attentional) near/5 (disorder\* or deficit\* or impairment\* or abilit\*)):ti,ab,kw

#51 ((perceptual or visuo?spatial or visuo?perceptual or attention\* or cognit\* or scanning\*) near/5 (training or re-training or rehabilitation or intervention or therapy)):ti,ab,kw

#52 {or #43-#51} #53 #42 AND #52

# Appendix 2. MEDLINE (Ovid) 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 poststroke or post-stroke or apoplex\$ or cerebral vasc\$ or cerebrovasc\$ or cva or SAH).tw.
- 3. ((brain\$ or cerebr\$ or cerebell\$ or intracran\$ or intracerebral) adj5 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$ or occlus\$)).tw.
- 4. ((brain\$ or cerebr\$ or cerebell\$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage\$ or hemorrhage\$ or haematoma\$ or hematoma\$ or bleed\$)).tw.
- 5. exp hemiplegia/ or exp paresis/
- 6. (hemipleg\$ or hemipar\$ or paresis or paretic).tw.
- 7. ((cerebral or brain or subarachnoid) adj5 (haemorrhage or haemorrhage or haematoma or hematoma or bleed)).tw.
- 8. ((trauma\$ or acquired) adj5 brain injur\$).tw.
- 9. exp brain damage, chronic/ or brain injuries/ or exp brain concussion/ or exp brain haemorrhage, traumatic/ or brain injury, chronic/ or diffuse axonal injury/
- 10. craniocerebral trauma/ or exp head injuries, closed/ or exp intracranial haemorrhage, traumatic/
- 11. exp brain abscess/ or exp central nervous system infections/ or exp encephalitis/ or exp meningitis, viral/
- 12. (encephalitis or meningitis).tw.
- 13. exp brain neoplasms/
- 14. ((brain or cerebr\$) adj5 (neoplasm\$ or lesion\$ or tumor\$ or tumour\$)).tw.
- 15. or/1-14
- 16. exp Perceptual Disorders/
- 17. exp perception/
- 18. Attention/
- 19. "Extinction (psychology)"/
- 20. (hemineglect or hemi-neglect).tw.
- 21. ((unilateral or spatial) adj5 neglect).tw.
- 22. (perception or inattention or hemi-inattention or attention or extinction).tw.



- 23. ((perceptual or visuo?spatial or visuo?perceptual or attentional) adj5 (disorder\$ or deficit\$ or impairment\$ or abilit\$)).tw.
- 24. ((perceptual or visuo?spatial or visuo?perceptual or attention\$ or cognit\$ or scanning\$) adj5 (training or re-training or rehabilitation or intervention or therapy)).tw.
- 25. or/16-24
- 26. Randomized Controlled Trials as Topic/
- 27. Random Allocation/
- 28. Controlled Clinical Trials as Topic/
- 29. control groups/
- 30. clinical trials as topic/ or clinical trials, phase i as topic/ or clinical trials, phase ii as topic/ or clinical trials, phase ii as topic/ or clinical trials, phase iv as topic/
- 31. double-blind method/
- 32. single-blind method/
- 33. Placebos/
- 34. placebo effect/
- 35. cross-over studies/
- 36. randomized controlled trial.pt.
- 37. controlled clinical trial.pt.
- 38. (clinical trial or clinical trial phase i or clinical trial phase ii or clinical trial phase iii).pt.
- 39. (random\$ or RCT or RCTs).tw.
- 40. (controlled adj5 (trial\$ or stud\$)).tw.
- 41. (clinical\$ adj5 trial\$).tw.
- 42. ((control or treatment or experiment\$ or intervention) adj5 (group\$ or subject\$ or patient\$)).tw.
- 43. (quasi-random\$ or quasi random\$ or pseudo-random\$ or pseudo random\$).tw.
- 44. ((control or experiment\$ or conservative) adj5 (treatment or therapy or procedure or manage\$)).tw.
- 45. ((singl\$ or doubl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).tw.
- 46. (cross-over or cross over or crossover).tw.
- 47. (placebo\$ or sham).tw.
- 48. trial.ti.
- 49. (assign\$ or allocat\$).tw.
- 50. controls.tw.
- 51. or/26-50
- 52. 15 and 25 and 51

# Appendix 3. Embase (Ovid) search strategy

- 1. cerebrovascular disease/ or brain disease/ or exp basal ganglion hemorrhage/ or exp brain hemangioma/ or exp brain hematoma/ or exp brain hemorrhage/ or exp brain infarction/ or exp brain ischemia/ or exp carotid artery disease/ or exp cerebral artery disease/ or exp cerebrovascular accident/ or exp cerebrovascular malformation/ or exp intracranial aneurysm/ or exp occlusive cerebrovascular disease/ or exp vertebrobasilar insufficiency/
- 2. (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 intracran\$ or intracerebral) adj5 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$ or occlus\$)).tw.
- 4. ((brain\$ or cerebr\$ or cerebell\$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage\$ or hemorrhage\$ or haematoma\$ or hematoma\$ or bleed\$)).tw.
- 5. paralysis/ or exp hemiplegia/ or exp paresis/
- 6. (hempar\$ or hemipleg\$ or paresis or paretic).tw.
- 7. ((trauma\$ or acquired) adj5 brain injur\$).tw.
- 8. exp brain damage, chronic/ or brain Injuries/ or exp brain concussion/ or exp brain hemorrhage, traumatic/ or brain injury, chronic/ or diffuse axonal injury/ or craniocerebral trauma/ or exp head injuries, closed/ or exp intracranial hemorrhage, traumatic/ or exp brain abscess/ or exp central nervous system infections/ or exp encephalitis/ or exp meningitis, viral/
- 9. (encephalitis or meningitis).tw.
- 10. exp brain neoplasms/
- 11. ((brain or cerebr\$) adj5 (neoplasm\$ or lesion\$ or tumor\$ or tumour\$)).tw.
- 12. or/1-11
- 13. exp perception disorder/
- 14. exp perception/
- 15. exp attention/
- 16. visual deprivation/
- 17. (hemineglect or hemi-neglect).tw.
- 18. ((unilateral or spatial or hemi?spatial) adj5 neglect).tw.
- 19. (perception or inattention or hemi-inattention or attention or extinction).tw.
- $20. ((perceptual \, or \, visuo? spatial \, or \, visuo? perceptual \, or \, attentional) \, adj5 \, (disorder\$ \, or \, deficit\$ \, or \, impairment\$ \, or \, abilit\$ \, or \, dysfunction)). tw.$



- 21. ((perceptual or visuo?spatial or visuo?perceptual or attention\$ or cognit\$ or scanning\$) adj5 (training or retraining or rehabilitation or intervention or therapy)).tw.
- 22. or/13-21
- 23. Randomized Controlled Trial/ or "randomized controlled trial (topic)"/
- 24. Randomization/
- 25. Controlled clinical trial/or "controlled clinical trial (topic)"/
- 26. control group/ or controlled study/
- 27. clinical trial/ or "clinical trial (topic)"/ or phase 1 clinical trial/ or phase 2 clinical trial/ or phase 3 clinical trial/ or phase 4 clinical trial/
- 28. Crossover Procedure/
- 29. Double Blind Procedure/
- 30. Single Blind Procedure/ or triple blind procedure/
- 31. placebo/ or placebo effect/
- 32. (random\$ or RCT or RCTs).tw.
- 33. (controlled adj5 (trial\$ or stud\$)).tw.
- 34. (clinical\$ adj5 trial\$).tw.
- 35. ((control or treatment or experiment\$ or intervention) adj5 (group\$ or subject\$ or patient\$)).tw.
- 36. (quasi-random\$ or quasi random\$ or pseudo-random\$ or pseudo random\$).tw.
- 37. ((control or experiment\$ or conservative) adj5 (treatment or therapy or procedure or manage\$)).tw.
- 38. ((singl\$ or doubl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).tw.
- 39. (cross-over or cross over or crossover).tw.
- 40. (placebo\$ or sham).tw.
- 41. trial.ti.
- 42. (assign\$ or allocat\$).tw.
- 43. controls.tw.
- 44. or/23-43
- 45. 12 and 22 and 44

# Appendix 4. CINAHL (Ebsco) search strategy

S1(MH "Cerebrovascular Disorders") OR (MH "Basal Ganglia Cerebrovascular Disease+") OR (MH "Carotid Artery Diseases+") OR (MH "Cerebral Ischemia+") OR (MH "Cerebral Vasospasm") OR (MH "Intracranial Arterial Diseases+") OR (MH "Intracranial Embolism and Thrombosis") OR (MH "Intracranial Hemorrhage+") OR (MH "Stroke") OR (MH "Vertebral Artery Dissections")

S2(MH "Stroke Patients") OR (MH "Stroke Units")

 $S3TI (stroke or poststroke or post-stroke or cerebrovasc^* or brain vasc^* or cerebral vasc or cva or apoplex or SAH) or AB (stroke or post-stroke or post-stroke or cerebrovasc^* or brain vasc^* or cerebral vasc or cva or apoplex or SAH)$ 

S4TI (brain\* or cerebr\* or cerebell\* or intracran\* or intracerebral) or AB (brain\* or cerebr\* or cerebell\* or intracran\* or intracerebral)

S5TI (ischemi\* or ischaemi\* or infarct\* or thrombo\* or emboli\* or occlus\*) or AB (ischemi\* or ischaemi\* or infarct\* or thrombo\* or emboli\* or occlus\*)

S6S4 and S5

S7TI (brain\* or cerebr\* or cerebell\* or intracerebral or intracranial or subarachnoid) or AB (brain\* or cerebr\* or cerebell\* or intracerebral or intracranial or subarachnoid)

S8TI ( haemorrhage\* or hemorrhage\* or haematoma\* or hematoma\* or bleed\* ) or AB ( haemorrhage\* or hemorrhage\* or haematoma\* or hematoma\* or bleed\* )

S9S7 AND S8

S10(MH "Hemiplegia")

S11TI (hemipleg\* or hemipar\* or paresis or paretic) or AB (hemipleg\* or hemipar\* or paresis or paretic)

S12(MH "Brain Injuries") OR (MH "Brain Concussion") OR (MH "Brain Neoplasms+") OR (MH "Brain Damage, Chronic") OR (MH "Head Injuries") OR (MH "Brain Abscess")

S13TI (brain or head or intracran\* or cerebr\* or cerebell\*) N5 (injur\* or contusion\* or hypoxi\* or damage\* or inflamm\* or concussion or trauma\$ or fractur\* or neoplasm\* or lesion\* or tumor\* or tumour\* or cancer\* or infection\*)

S14(MH "Meningitis") OR (MH "Encephalitis")

S15S1 OR S2 OR S3 OR S6 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14

S16(MH "Perceptual Disorders+")

S17(MH "Perception+")

S18(MH "attention")

S19(MH "Unilateral Neglect (Saba CCC)") or (MH "Unilateral Neglect (NANDA)")

S20TI (hemineglect or hemi-neglect) or AB (hemineglect or hemi-neglect)

S21TI (unilateral or spatial) or AB (unilateral or spatial)

S22TI (neglect) or AB (neglect)

S23S21 AND S22

S24TI (perception or inattention or hemi-inattention or attention or extinction) or AB (perception or inattention or hemi-inattention or attention or extinction)



S25TI (perceptual or visuo#spatial or visuo#perceptual or attentional) or AB (perceptual or visuo#spatial or visuo#perceptual or attentional)

S26TI (disorder\* or deficit\* or impairment\* or abilit\*) or AB (disorder\* or deficit\* or impairment\* or abilit\*)

S27S25 and S26

S28TI (perceptual or visuo#spatial or vi

S29TI (training or re-training or rehabilitation or intervention or therapy) or AB (training or re-training or rehabilitation or intervention or therapy)

S30S28 AND S29

S31S16 OR S17 OR S18 OR S19 OR S20 OR S23 OR S24 OR S27 OR S30

S32(MH "Randomized Controlled Trials") or (MH "Random Assignment") or (MH "Random Sample+")

S33(MH "Clinical Trials") or (MH "Intervention Trials") or (MH "Therapeutic Trials")

S34(MH "Double-Blind Studies") or (MH "Single-Blind Studies") or (MH "Triple-Blind Studies")

S35(MH "Control (Research)") or (MH "Control Group") or (MH "Placebos") or (MH "Placebo Effect")

S36(MH "Crossover Design") OR (MH "Quasi-Experimental Studies")

S37PT (clinical trial or randomized controlled trial)

S38TI (random\* or RCT or RCTs) or AB (random\* or RCT or RCTs)

S39TI (controlled N5 (trial\* or stud\*)) or AB (controlled N5 (trial\* or stud\*))

S40TI (clinical\* N5 trial\*) or AB (clinical\* N5 trial\*)

S41TI ((control or treatment or experiment\* or intervention) N5 (group\* or subject\* or patient\*)) or AB ((control or treatment or experiment\* or intervention) N5 (group\* or subject\* or patient\*))

S42((control or experiment\* or conservative) N5 (treatment or therapy or procedure or manage\*)) or AB ((control or experiment\* or conservative) N5 (treatment or therapy or procedure or manage\*))

S43TI ((singl\* or doubl\* or tripl\* or trebl\*) N5 (blind\* or mask\*)) or AB ((singl\* or doubl\* or tripl\* or trebl\*) N5 (blind\* or mask\*))

S44TI (cross-over or cross over or crossover) or AB (cross-over or cross over or crossover)

S45TI (placebo\* or sham) or AB (placebo\* or sham)

S46TI trial

S47TI (assign\* or allocat\*) or AB (assign\* or allocat\*)

S48TI controls or AB controls

S49TI (quasi-random\* or quasi random\* or pseudo-random\* or pseudo random\*) or AB (quasi-random\* or quasi random\* or pseudo-random\*)

S50S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 S51S15 AND S31 AND S50

# Appendix 5. PsycINFO (Ovid) search strategy

- 1. cerebrovascular disorders/ or cerebral hemorrhage/ or exp cerebral ischemia/ or cerebrovascular accidents/ or subarachnoid hemorrhage/
- 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 intracran\$ or intracerebral) adj5 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$ or occlus\$)).tw.
- 4. ((brain\$ or cerebr\$ or cerebell\$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage\$ or hemorrhage\$ or haematoma\$ or hematoma\$ or bleed\$)).tw.
- 5. exp brain damage/ or traumatic brain injury/ or exp brain concussion/ or exp head injuries/
- 6. ((brain or cerebr\$) adj5 (injur\$ or hypoxi\$ or damage\$ or concussion or trauma\$ or neoplasm\$ or lesion\$ or tumor\$ or tumour\$ or cancer \$ or infection\$)).tw.
- 7. exp encephalitis/ or exp meningitis/
- 8. (encephalitis or meningitis).tw.
- 9. exp brain neoplasms/
- 10. ((brain or cerebr\$) adj5 (neoplasm\$ or lesion\$ or tumor\$ or tumour\$)).tw.
- 11. or/1-10
- 12. exp perceptual disturbances/ or exp perceptual distortion/ or exp sensory neglect/
- 13. exp perception/
- 14. exp "Extinction (Learning)"/
- 15. (hemineglect or hemi-neglect).tw.
- 16. ((unilateral or spatial) adj5 neglect).tw.
- 17. (perception or inattention or hemi-inattention or attention or extinction).tw.
- 18. ((perceptual or visuo?spatial or visuo?perceptual or attentional) adj5 (disorder\$ or deficit\$ or impairment\$ or abilit\$)).tw.
- 19. ((perceptual or visuo?spatial ro visuo?perceptual or attention\$ or cognit\$ or scanning\$) adj5 (training or re-training or rehabilitation or intervention or therapy)).tw.
- 20. or/12-19
- 21. clinical trials/ or treatment effectiveness evaluation/ or placebo/
- 22. (random\$ or RCT or RCTs).tw.



- 23. (controlled adj5 (trial\$ or stud\$)).tw.
- 24. (clinical\$ adj5 trial\$).tw.
- 25. ((control or treatment or experiment\$ or intervention) adj5 (group\$ or subject\$ or patient\$)).tw.
- 26. (quasi-random\$ or quasi random\$ or pseudo-random\$ or pseudo random\$).tw.
- 27. ((control or experiment\$ or conservative) adj5 (treatment or therapy or procedure or manage\$)).tw.
- 28. ((singl\$ or doubl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).tw.
- 29. (cross-over or cross over or crossover).tw.
- 30. (placebo\$ or sham).tw.
- 31. trial.ti.
- 32. (assign\$ or allocat\$).tw.
- 33. controls.tw.
- 34. or/21-33
- 35. 11 and 20 and 34

## Appendix 6. US National Institutes of Health Ongoing Trials Register search strategy

( neglect OR hemispatial OR unilateral ) AND AREA[StudyType] EXPAND[Term] COVER[FullMatch] "Interventional" AND AREA[ConditionSearch] (Vertebral Artery OR Brain Infarction OR Intracranial Hemorrhages OR Carotid Artery Diseases OR Brain Ischemia OR Cerebral Hemorrhage OR Cerebrovascular Disorders OR Stroke ) AND AREA[StudyFirstPostDate] EXPAND[Term] RANGE[02/01/2017, 03/25/2020]

#### Basic search:

neglect AND stroke OR hemispatial AND stroke OR neglect AND brain OR hemispatial AND brain OR neglect AND cerebral OR hemispatial AND cerebral

## Appendix 7. World Health Organization International Clinical Trials Registry Platform search strategy

World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch)

#### Basic search

neglect AND stroke OR hemispatial AND stroke OR neglect AND brain OR hemispatial AND brain OR neglect AND cerebral OR hemispatial AND cerebral

# Appendix 8. Previous review search strategy

### **Searching other resources**

For the purpose of this and other reviews (Lincoln 2001; Das Nair 2007), we originally searched simultaneously for trials in four areas of stroke rehabilitation (cognitive rehabilitation, occupational therapy, speech therapy, and treatment for mood disorders) using online computerised bibliographic databases: MEDLINE (1966 to 1998), BIDS Embase (1980 to 1998), CINAHL (1983 to 1998), PsycLIT (1974 to 1998), and CLINPSYCH (1980 to November 1994). We conducted these computerised searches using combinations of the following descriptors/key words: stroke/cerebrovascular accidents/neurological disability and randomised controlled/clinical trials/random allocation/double blind method and rehabilitation/remedial therapy/treatment/intervention and cognitive/unilateral neglect/visuospatial/visuoperceptual/memory/attention span/concentration/hemianopia/attentional deficits/activities of daily living/occupational therapy/leisure/dressing/self-care/domiciliary rehabilitation.

To ensure that studies not listed in the above databases were not overlooked, in 1999 we handsearched all volumes of the journals listed below. The 1999 handsearch included a broad range of journals, as it covered studies in four areas of rehabilitation, only one of which (neglect) was relevant to this specific review. Therefore, for the 2006 update, we checked the Master List of journals that is searched by the Cochrane Collaboration (www.cochrane.us/masterlist.asp). We found that the journals relevant to neglect had been handsearched. The resulting studies would be found from the search of the Cochrane Central Register of Controlled Trials (CENTRAL) carried out quarterly by the Cochrane Stroke Group, and we did not wish to duplicate effort:

- American Journal of Occupational Therapy (1947 to 1998);
- Aphasiology (1987 to 1998);
- Australian Occupational Therapy Journal (1965 to 1998);
- British Journal of Occupational Therapy (1950 to 1998);
- British Journal of Therapy and Rehabilitation (1994 to 1998);
- Canadian Journal of Occupational Therapy (1970 to 1998);
- Clinical Rehabilitation (1987 to 1998);
- Disability Rehabilitation (1992 to 1998), formerly International Disability Studies (1987 to 1991), formerly International Rehabilitation Medicine (1979 to 1986);



- International Journal of Language & Communication Disorders (1998), formerly European Journal of Disorders of Communication (1985 to 1997), formerly British Journal of Disorders of Communication (1977 to 1984);
- Journal of Clinical Psychology in Medical Settings (1994 to 1998), formerly Journal of Clinical Psychology (1944 to 1994);
- Journal of Developmental and Physical Disabilities (1992 to 1998), formerly Journal of the Multihandicapped Person (1989 to 1991);
- Journal of Rehabilitation (1963 to 1998);
- International Journal of Rehabilitation Research (1977 to 1998);
- Journal of Rehabilitation Science (1989 to 1996);
- Neuropsychological Rehabilitation (1987 to 1998);
- Neurorehabilitation (1991 to 1998);
- Occupational Therapy International (1994 to 1998);
- Physiotherapy Theory and Practice (1990 to 1998), formerly Physiotherapy Practice (1985 to 1989);
- Physical Therapy (1988 to 1998);
- Rehabilitation Psychology (1982 to 1998); and
- The Journal of Cognitive Rehabilitation (1988 to 1998), formerly Cognitive Rehabilitation (1983 to 1987).

The pre-1999 searching and selection activities were carried out simultaneously for four reviews.

The National Research Register was searched for the 2012 review; however it has since been archived and not superseded.

We used the three citation index databases Science Citation Index (SCI), Social Sciences Citation Index (SSCI), and Arts and Humanities Citation Index (A&HCI) for citation tracking of relevant included studies.

#### Selection of studies

At least two review authors (NBL, AB for 1999 and 2006 versions; NBL, AB, CH, and AP for 2013 version) independently selected studies to be included in this review using the four inclusion criteria (types of trials, participants, interventions, and outcome measures). We independently assessed the methodological quality of studies, with reference to the *Cochrane Handbook for Systematic Reviews of Interventions* (Cochrane Handbook), and selected, entered, and cross-checked data for analysis. We resolved disagreements by discussion.

## WHAT'S NEW

Date	Event	Description
12 May 2021	New citation required but conclusions have not changed	Despite the inclusion of 65 RCTs, the effectiveness of non-pharmacological interventions for reducing the disabling effects of neglect and increasing independence remains unproven and largely unstudied despite numerous small trials. No rehabilitation intervention for spatial neglect can be supported or refuted based on current evidence
12 May 2021	New search has been performed	We added 44 new trials to 21 of the 23 trials that we included in the previous version. Sixty-five trials (1951 participants) are now included. We excluded 2 previously included studies as either fewer than 50% of participants had neglect, or we were unable to confirm participants had neglect. We have re-written all sections using standard Cochrane sub-headings. We have expanded the inclusion criteria to include any non-pharmacological intervention. Our primary outcome has changed to persisting effects on functional disability to reflect the importance of this outcome for people with stroke. We have changed the comparisons: for this version of the review, we changed the presentation of statistical comparisons using 8 broad treatment types. We have included Patient, Carer, and Public Involvement in Research by consulting with stroke survivors



#### HISTORY

Protocol first published: Issue 2, 2002 Review first published: Issue 2, 2002

Date	Event	Description
17 April 2013	New citation required but conclusions have not changed	Despite the addition of 11 further trials, the key conclusions of this review have not changed greatly since the 2006 version: The effectiveness of cognitive rehabilitation for reducing the disabling effects of neglect and increasing independence remains unproven. No rehabilitation approach can be supported or refuted from current randomised controlled trials
23 September 2012	New search has been performed	We added 11 new trials to the 12 trials that we included in the previous version. Twenty-three trials (628 participants) are now included. We have rewritten the Discussion section using standard Cochrane sub-headings. We have expanded the outcomes: previous versions of the review had functional disability, neglect assessments, and discharge destination as outcomes. For this update, we added a number of secondary outcomes that had been identified as important to stroke survivors. This brings this review in line with other reviews of visual problems after stroke. We have changed the comparisons: for this version of the review, we changed the presentation of statistical comparisons. In particular, we amended the sub-group comparisons of bottom-up and top-down approaches, so that analyses included sub-groups of types of treatment
4 August 2008	Amended	Converted to new review format
26 April 2006	New search has been performed	For this updated review, we excluded several previously included non-randomised trials to reduce bias. We added several new, or newly identified, randomised controlled trials (RCTs), resulting in a review of 306 participants from 12 RCTs

### **CONTRIBUTIONS OF AUTHORS**

The original review, initiated by Nadina Lincoln (published by Lincoln, Bowen, and Dewey in 2002), has been updated several times with input from various review authors. The current (2021) extensive expansion and update was led by Audrey Bowen and was enabled by funding awarded to Verity Longley, Audrey Bowen, Alex Pollock, Christine Hazelton, Claire Mitchell, Calvin Heal, and Andy Vail. Verity Longley conducted most of the updated searches, data collection, analysis, and reporting. Christine Hazelton and Calvin Heal contributed significantly to searches, data collection, and reporting. Gorana Pobric took responsibility for the non-invasive brain stimulation studies. Alex Pollock and Andy Vail led on methodological decision-making and statistical analyses. Claire Mitchell contributed to searches, data collection, and Patient, Carer, and Public Involvement. Kate Woodward-Nutt took responsibility for Patient, Carer, and Public Involvement. All co-authors approved the final report.

## **DECLARATIONS OF INTEREST**

Verity Longley: none known.

Christine Hazelton: payment for a fellowship: my time on this review has been funded in part by a non-clinical lectureship funded by the Stroke Association. Work as a health professional: clinical work as an Optometrist, Glasgow Caledonian University - only a very small amount of this clinical work touches on the topic of interest in this review.

Calvin Heal: none known.

Alex Pollock: none known.

Kate Woodward-Nutt: none known.

Claire Mitchell: none known. Gorana Pobric: none known.



Andy Vail: none known.

Audrey Bowen: grants and contracts: (1) funding for this review update, NIHR NETSCC Incentive Funding; (2) funding for primary research on the topic of this review (e.g. the SPATIAL feasibility study), NIHR RfPB, awarded to SRFT NHS Trust rather than to my University as per NIHR arrangements. Payment for a fellowship: fellowship for Dr Longley under my mentorship, NIHR Development and Skills Enhancement Award, awarded to MMU, where Dr Longley secured an academic post. Published opinions in medical journals, the public press, broadcast and social media relevant to interventions in the work: I have published journal papers and book chapters, and I have edited national guidelines that include the topic of this review (e.g. ICSWP National Clinical Guideline for Stroke 2016, awarded to SRFT NHS Trust rather than to my University as per NIHR arrangements). If you were involved in conducting a study that is eligible for inclusion in this review, what was the funding source for that study? Bowen A (CI), et al. A feasibility study of prisms and therapy in attention loss after stroke (SPATIAL feasibility). NIHR RfPB 249K, 2018-2020.

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

#### SOURCES OF SUPPORT

#### **Internal sources**

· No sources of support provided

## **External sources**

· NIHR DSE award, UK

Funded Verity Longley's time and training

NIHR NETSCC Incentive award, UK

Awarded for the current update

· The Stroke Association, UK

Part-funded Audrey Bowen's post through a readership award

• The RNIB (Royal National Institute for Blind people), UK

Funded Christine Hazelton's time on this update.

• NHS Executive Research and Development Programme Physical and Complex Disabilities, UK

Awarded for the original 2002 review

• The Stroke Association, UK

Part funded Christine Hazelton's time via a non-clinical Lectureship award.

#### DIFFERENCES BETWEEN PROTOCOL AND REVIEW

This review was initiated in 1999 and has undergone many changes. Differences between the previous 2013 version and this update are outlined below.

## **Review title**

Previous versions of this review were titled "Cognitive rehabilitation for spatial neglect following stroke". We decided to broaden the scope of this update beyond cognitive rehabilitation due to the variety of interventions used to rehabilitate this cognitive impairment.

## **Included patients**

Previous versions of this review were confined to trials of participants with stroke. For this updated review, this was expanded to include participants with neglect following any adult-acquired non-progressive brain injury. We expected the majority of such to be stroke patients.

## Types of interventions

Previous versions of this review included only cognitive rehabilitation interventions; however, for this update, we expanded inclusion to any non-pharmacological intervention and thus re-considered any studies previously excluded for this reason. In previous versions of this review, we categorised the type of intervention according to cognitive theory as either a bottom-up or a top-down processing rehabilitation approach. For this update, we categorised interventions into eight broad types based on their approach. Through our knowledge of the field, we were aware of the development since initiation of this review of many non-pharmacological interventions that may not have fallen under the umbrella of cognitive rehabilitation. We therefore expanded our inclusion to be more relevant to clinical practice.



#### Types of outcome measures

For previous versions of this review, we were interested in outcomes at two time points: (1) immediately after completion of an intervention, and (2) persisting beyond completion of an intervention (i.e. follow-up outcome).

For this 2021 update, we designated (1) persisting beyond completion of an intervention (i.e. follow-up outcome) as the primary outcome, and (2) immediately after completion of an intervention as a secondary outcome, to reflect the importance of these outcomes to people with stroke.

In previous versions of the review, we defined the primary outcome as 'ratings on measures of functional disability: activities of daily living (ADL) scales: Barthel Index (BI), Functional Independence Measure (FIM), Frenchay Activities Index (FAI), or neglect-specific ADL measures'. As this was not a comprehensive list of functional disability measures, we extended the scales listed for the 2013 update to be more comprehensive and to avoid having to make decisions after identification of studies. We checked back through the studies included previously and found that this clarification did not lead to any changes to outcomes included from those studies.

# **Analysis**

For this 2021 review update, we analysed outcomes only by subgroup (intervention type), and we omitted analysis of all studies versus any control, as intervention types were not comparable. For all previous versions of this review, we used data recorded at the time of hospital discharge as persisting effects. We re-evaluated this decision for this update and omitted these data from meta-analysis, as they are process dependent.

## INDEX TERMS

## **Medical Subject Headings (MeSH)**

Activities of Daily Living; \*Cognitive Behavioral Therapy; Perceptual Disorders [etiology] [\*rehabilitation]; Randomized Controlled Trials as Topic; Sensation Disorders [etiology] [rehabilitation]; \*Space Perception; Stroke [\*complications]; Stroke Rehabilitation

### MeSH check words

Humans