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REVIEW ARTICLE

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A systematic review of vestibular stimulation in post-stroke visual neglect

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ABSTRACT

Unilateral visual neglect is a condition that negatively impacts the lives of many stroke survivors. Studies have investigated different forms of vestibular stimulation as a potential therapy, but evidence is yet to be systematically reviewed. We therefore reviewed the effects of vestibular stimulation on outcomes of neglect and activities of daily living (ADL) for people with visual neglect. We searched relevant databases up until September 2022. Eligible articles included any form of vestibular stimulation, study design, or control condition. Included participants were 18 years or older, presenting with neglect following a haemorrhagic or ischaemic stroke. Relevant outcomes were clinically validated measures of neglect and ADL. Cochrane risk of bias tools were used to assess study quality. Meta-analyses and narrative methods were used to synthesize the data. Our search returned 17 relevant studies comprising 180 participants. Meta-analyses showed no difference between galvanic vestibular stimulation and sham conditions on outcomes, whereas caloric vestibular stimulation led to improvement compared to pre-stimulation scores. Narrative syntheses showed mixed results. Clinical and methodological heterogeneity was found both within and between studies. Overall, results were inconsistent regarding the effects of vestibular stimulation as a treatment for neglect. Further trials are warranted but require more careful methodological planning.

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Stroke; Unilateral spatial neglect; Vestibular stimulation; Activities of daily living; Systematic review

Unilateral spatial neglect (also known as neglect) is a primarily an attentional disorder characterized by an inability to report or respond to stimuli in the contralesional side of space (Walker et al., 1991). Unlike other post-stroke visual disorders,

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neglect occurs in the absence of sensory or motor loss (Heilman et al., 1994). Although individuals with neglect are unable to automatically orient their attention towards their contralesional side (Bartolomeo & Chokron, 2002), their conscious adaptation is not impaired (i.e., if their attention is drawn to the neglected side, they can usually report the presence of stimuli; Driver & Mattingley, 1998).

The behavioural effects of neglect are all-encompassing for individuals and their families (Chen et al., 2017). People commonly have difficulties with personal care, as well as daily activities, including reading and writing (Halligan & Robertson, 2014). Understandably, these difficulties can severely limit autonomy (Jehkonen et al., 2000) and quality of life (QoL; Sobrinho et al., 2018). Stroke survivors with neglect also have a poorer long-term prognosis compared to those without (Chen et al., 2015; Katz et al., 1999; Wilkinson et al., 2012).

Neglect most frequently results from right brain damage (Bowen et al., 1999; Esposito et al., 2021). Prevalence estimates for the condition vary widely (e.g., Evald et al., 2021), likely due to the complexity of neglect, which can be motor, representational, or sensory in nature (Williams et al., 2021). Sensory neglect is most widely reported and can be further classified into visual, auditory, tactile, and buccal modalities (André et al., 2000; Bowen et al., 1999). This review will focus on visual neglect (although the different forms of neglect can be difficult to disentangle), given that most standardized outcomes are designed to assess this modality.

Visual neglect can be further divided in terms of its spatial distribution: egocentric, object-centric, or both. The reference frame for egocentric neglect is an individual's body; that is, any stimulus presented to one side of the body midline is ignored. In contrast, allocentric neglect manifests in ignoring one side of an external object (Kerkhoff, 2001). Individuals can have numerous forms of neglect, which interact to form a multitude of unique presentations, making a precise diagnosis difficult (Plummer et al., 2003).

Many neglect assessments have been developed to encapsulate this wide range of deficits (Williams et al., 2021). The most commonly employed is the Behavioral Inattention Test (BIT; Wilson et al., 1987), which aims to measure overall neglect severity. The assessment consists of six subtests, probing individual facets of neglect. These include cancellation tasks, which involve presenting individuals with a stimulus display (aligned to their body midline) and directing them to cross out targets. A failure to cancel stimuli on only one side indicates egocentric neglect. Another common subtest is line bisection, in which participants are instructed to mark the middle of several horizontal lines (which may differ in their relative position to the body midline). Individuals suffering from left-sided neglect (ego- and object-centric) will deviate to the right of the true midline in this task (although there are some exceptions; see Halligan and Marshall 1988). Figure copying of a simple symmetrical object such as a butterfly or a clock is another prevalent subtest, with lateralized omissions indicating object-centric neglect (Friedman, 1991).

Spontaneous recovery from neglect can occur but is mostly confined to the acute and subacute stages (Stone et al., 1992), and is often only partial. Various behavioural, physical, pharmacological, and neuromodulation therapies have been trialled to aid neglect recovery, including prism adaptation, limb activation, visual imagery tasks, eye patching, pharmacotherapy, and transcranial direct current stimulation. While some studies have shown improvements, other evidence from randomized trials has shown that these techniques generate strong placebo effects and that when properly controlled, beneficial results are short-lived or eliminated (Frassinetti et al., 2002; Kerkhoff & Schenk, 2012; Nys et al., 2008; Serino et al., 2009; Turton et al., 2010; Umeonwuka et al., 2020; van der Kemp et al., 2017; Yang et al., 2013).

An alternative emerging therapy is vestibular stimulation. The vestibular system is instantiated across a wide cortical and sub-cortical network (Day & Fitzpatrick, 2005) and contributes to internal, multi-modal representations of space by coding head acceleration, movement and gravitational orientation. Given that these multi-modal spatial representations are disrupted in neglect, it has been proposed that appropriate stimulation of the vestibular nerves may moderate aspects of neglect syndrome (Bense et al., 2001; Miller & Ngo, 2007).

Vestibular stimulation can be delivered via different formats. These include caloric vestibular stimulation (CVS) which is most commonly applied by the introduction of water or air puffs to the external ear canal; and galvanic vestibular stimulation (GVS), where mild electrical currents are applied to the mastoids. Applications of CVS usually irrigate the contralesional ear with cold water on the basis that the contralateral hemisphere is preferentially activated (e.g., Bottini et al., 2001). The effects of GVS are also partially lateralized (right-cathodal, left-anodal GVS [CR-GVS] preferentially activates the right hemisphere; left-cathodal, right-anodal GVS [CL-GVS] activates both hemispheres). Both polarities have been applied in neglect. Motion simulators and vestibular rehabilitation physiotherapy stimulate the vestibular system in a less artificial, lateralized manner. Motion simulators approximate natural movements by rotating or tilting participants to activate the semi-circular canals and otoliths (Palla & Lenggenhager, 2014). Vestibular rehabilitation involves head movement and balance training exercises to encourage habituation and sensory recalibration. It remains unclear how long the post-stimulation effects of vestibular stimulation persist. Some studies have noted a significant sustained effect of GVS on ocular-motor and postural domains after stimulation ceases (Mahmud et al., 2022). However, others show effects are limited to active stimulation (Keywan et al., 2020). Variations in study designs (controls for possible placebo and/or task-dependent learning effects) are thought to underlie these discrepancies. Establishing the longevity of effects is paramount for therapeutic applications.

There is currently no wholly effective treatment for neglect (Longley et al., 2021) so any new, potential form of intervention such as vestibular stimulation

needs to be carefully evaluated. A number of studies have applied vestibular stimulation in neglect, however, there are no existing reviews that systematically assess its efficacy.

Objective

To determine whether people with post-stroke unilateral spatial neglect who receive vestibular stimulation show improvement in neglect symptomology and activities of daily living (ADL) relative to a comparator condition.

Materials and methods

The protocol for this review was registered on the Open Science Framework in May 2020 (https://doi.org/10.17605/OSF.IO/62SM5).

Criteria for considering studies for this review

This systematic review used the Participants, Interventions, Comparisons, Outcomes (PICO) model (Thomas et al., 2019) to design our research question and search strategies. Our PICO components are outlined below.

Population

Study participants had to be adults (≥18 years) who had suffered a stroke according to WHO guidelines (or a clinical definition if not specifically stated i.e., signs and symptoms lasting longer than 24 h), confirmed by neurological examination or brain scan. Participants could be included if they had experienced either a haemorrhagic or ischaemic stroke at any anatomical location. Those in both the acute and chronic phases of the disease were included. Participants with egocentric and/or allocentric neglect were eligible.

Studies involving participants suffering from visual extinction were not included unless they formed part of a mixed population. Individuals suffering from neglect because of a different neurological cause (e.g., tumours or traumatic brain injury) were excluded. If studies included mixed populations, individuals who had suffered a stroke were included if their data had been analysed separately from those with differing aetiology. If stroke survivors had been analysed together with these other individuals, the study was included if they made up more than 50% of this group. The same criterion was applied for studies which pooled groups of stroke survivors both with and without neglect, or with different types of neglect. If individual participants were identified who were suffering from both visual neglect and another form of the disorder (e.g., tactile), or if the type of neglect they were suffering from was not clearly identified, the study was discussed, and a decision made amongst the review team.

Intervention

We included any form of vestibular stimulation delivered in an interventional context (as opposed to diagnostic), including (but not restricted to) GVS, CVS, or vestibular rehabilitation. If vestibular stimulation was used as part of a combined treatment, the study was included if the adjunctive therapy was kept constant across all experimental conditions.

Although prism adaption, neck muscle vibration, and optokinetic stimulation affect the vestibular system as a result of its complex interplay with visual inputs (e.g., Dieterich et al., 1998; Karnath, 1994), the fact that these interventions do not directly stimulate the peripheral vestibular organs or vestibular nerve prompted their exclusion.

Comparator

Studies of any design were included, as it was anticipated that there would be few randomized controlled trials (RCTs) addressing this topic.

Vestibular stimulation could be compared to any control, including alternative interventions, usual care, or no treatment. Controls could also be vestibular stimulation: either a different form, or of the same type but with different parameters e.g., intensity, duration, number of sessions, or frequency (i.e., Hz; including sham stimulation).

Outcomes

Outcomes included any test of visual neglect. After registering the protocol, but before commencing the searches, we decided to also include validated outcomes measuring ADL.

Search methods for identification of studies

CENTRAL, PubMed, WHO ICTRP, PsychINFO, and CINAHL were searched for relevant records. OpenGrey was used to search for grey literature, whilst Latin American and Caribbean Health Science Literature (LILACS) and the African Index Medicus (AIM) were searched for non-English sources. Each database was searched from inception. Search strategies for each of these databases are detailed in Appendix A, and a completed PRISMA checklist in Appendix B.

Data collection and analysis

Records retrieved from the above searches were exported into reference management software (EndNote X9) and duplicates removed. The lead author (CW) screened all the titles and abstracts of the remaining records. The second author (LS), along with three other screeners, split the records between them so that every record was screened by two people. Agreement between screeners was calculated at 90%.

Selection of studies

Full-text articles (if available) of any relevant studies were retrieved and independently screened according to our PICO criteria, recording ineligible studies and the primary reason for their exclusion. Any disagreements were discussed between the first (CW) and second (LS) author. If an agreement could not be reached, another author (DW) was consulted.

Data extraction and management

A Cochrane data extraction form was edited and used to extract data from the included studies.

The following information was extracted:

- Study methods
- Participant information (including method of neglect diagnosis, age, time since stroke, and the presence of visual field defects)
- Description of the intervention (including parameter details such as stimulation frequency, intensity, and duration)
- Outcome measures (including unit of measurement, scales, validation, missing data)
- Results (including means and standard deviations/errors at all available timepoints alongside any other reported results such as mean differences and *p* values).

If these data were not available or unclear from the reports, then we contacted the corresponding authors for further information or clarification. If they had not replied after two contact attempts, the available data were used where possible.

Assessment of risk of bias in included studies

Studies were identified as low, high, or unclear risk of bias within nine different domains. The appropriate Cochrane risk of bias tool for each study type was used. Each study was initially assessed by one author (LS/CW), and another reviewed the form.

Measures of treatment effect

Review Manager 5.4 software (Collaboration, 2014) was used to carry out statistical analyses to determine treatment effects where data could be meaningfully combined. All other data were synthesized narratively.

Comparisons were made at the end of the treatment period. A random-effects model was used for all analyses to adjust for heterogeneity in stimulation

protocols between studies. As all extracted data were continuous and used the same outcome measurement, mean differences (MDs) and 95% confidence intervals (CIs) were calculated. When studies differed in the way that results were reported, values were transformed where possible e.g., if the number of omissions rather than the number of targets cancelled was reported, the number of omissions was subtracted from the highest total score.

Assessment of heterogeneity

For meta-analyses, heterogeneity was visually assessed by looking at the forest plots and considering the extent to which the 95% CIs overlapped. The I^2 statistic was also considered.

Results

Results of the search

The search was first run in May 2020, then re-run in September 2022. These searches returned 7244 and 1215 records respectively, which after deduplication resulted in a combined total of 6190 records to be screened at the title and abstract stage. Due to the broad PICO criteria used, many ineligible records were returned from the original search, which were then excluded at the title and abstract stage of screening. This process left 169 full texts to be assessed, from which 11 records were identified as eligible (see Figure 1). The reference lists of eligible studies and secondary sources were also screened, identifying 6 further records. A total of 17 studies were included in the review (see Figure 1).

Description of included studies

The data from 180 participants from 17 studies were included in this review (Adair et al., 2003; Cappa et al., 1987; Dai et al., 2013; Geminiani & Bottini, 1992; Kang & Oh, 2012; Nakamura et al., 2015; Oppenländer et al., 2015; Rode et al., 2002; Rorsman et al., 1999; Rubens, 1985; Ruet et al., 2014; Storrie-Baker et al., 1997; Sturt & Punt, 2013; Utz, Keller, et al., 2011a; Volkening et al., 2018; Wilkinson et al., 2014; Zubko et al., 2013). This number reflects the small sample sizes in individual studies. Only one study (Wilkinson et al., 2014) conducted a power analysis to determine how many participants would be needed to find an effect.

A summary of study characteristics is shown in Table 1.

Population

All studies included participants with neglect following right hemisphere stroke. Several studies also included control groups without neglect, but data from these groups were not included here. All samples were mixed regarding gender apart

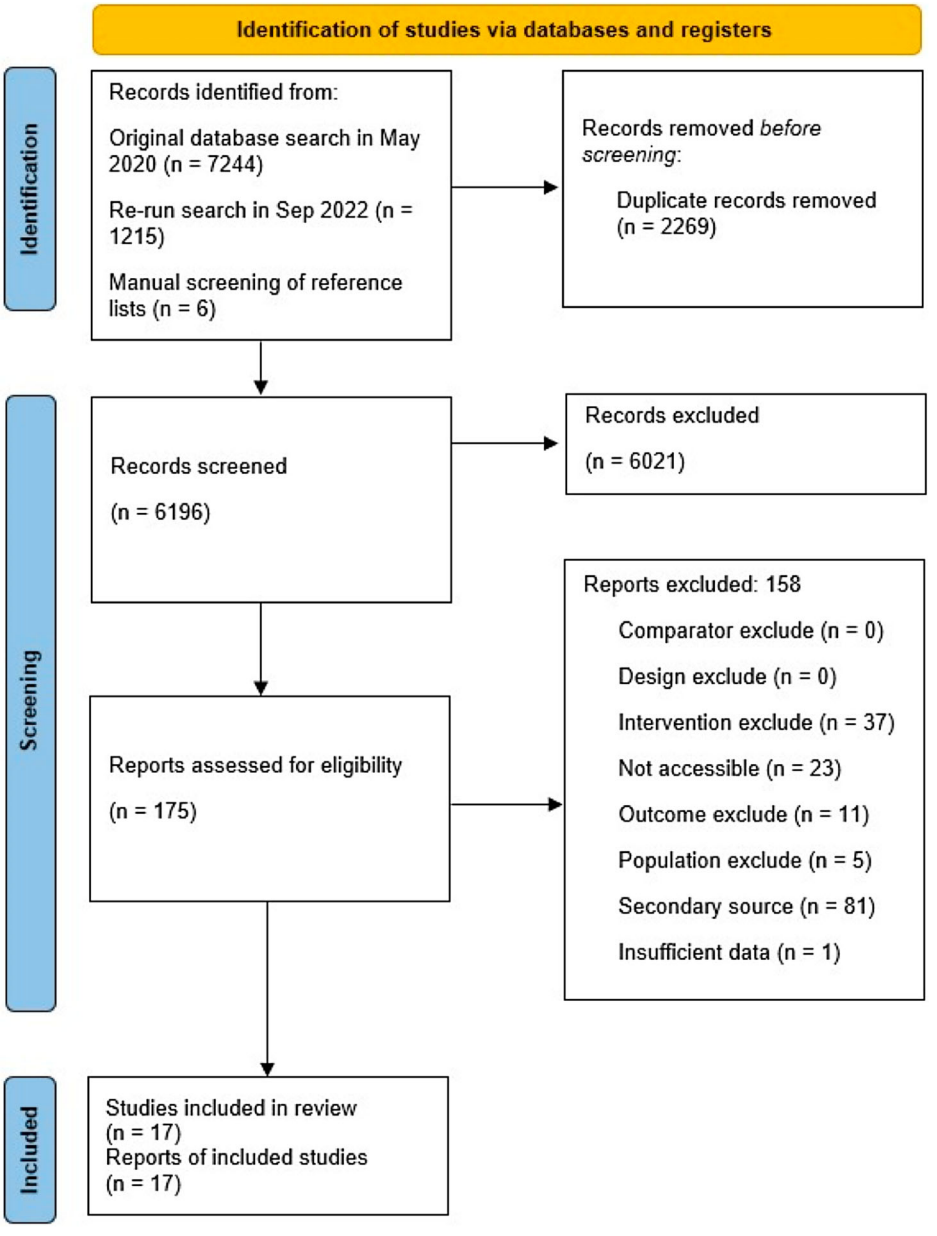

Figure 1. PRISMA flow diagram displaying the results of the search.

from Ruet et al. (2014) (who only recruited males) and those employing a single-case design. Samples were roughly comparable regarding age. Studies were mixed regarding whether participants also had visual field defects, with only two recruiting participants without this impairment (Kang & Oh, 2012; Rode et al., 2002). Length of time since stroke differed widely both within and between studies, the shortest mean being less than two days (Cappa et al., 1987) and the longest more than 38 months (Zubko et al., 2013).

Table 1. Characteristics of included studies.

Study	Design	Intervention parameters	Freq and duration	Method of neglect diagnosis	No. of participants	Mean age (years)	Time since stroke	Presence of visual field defects	Outcome measure(s)
Adair et al., 2003	Pre- and post	CVS (contralesional) – 30ml ice water in the left ear canal	1 session	Any contralateral omissions on the Albert line cancellation test or rightward line bisection beyond the 95% confidence interval for normal subjects	16	64.5	Less than 30 days	Not reported	Line bisection (230mm); mean error in mm. Albert line cancellation task (40 lines); no. of lines cancelled on left and right sides.
Cappa et al., 1987	Case studies	CVS (contralesional) – 20cc of iced water in the left ear for cases 1, 2 and 4; 20 cc of warm water in the right ear for case 1	1 session	Circle cancelling task (3 participants); line crossing test (1 participant). Cut-off values not reported.	4	Case 1: 71 Case 2: 69 Case 3: 57 Case 4: 48	Less than 2 days	All participants had left homonymous hemianopia	Circle cancelling task in 3 participants and line crossing test in 1; percentage of omissions
Dai et al., 2013	RCT (parallel arms, between subjects)	Vestibular rehabilitation (VR) and conventional rehabilitation	10 sessions	BITC (below standard cut-off on at least 2 scales)	[a] VR: 27; Control: 28	[a] VR: 57.21 Control: 64.54	[a] VR: 56.88 Control: 73.88 (mean)	Not reported	Overall BIT-C score (maximum 146); high score is good. Functional Independence Measure (maximum 126); high score is good.
Geminiani & Bottini, 1992	Case studies	CVS (contralesional) – 30cc ice water in the left ear canal	1 session	Modified version of Albert's test. Cut-off values not reported.	5	Not reported	Within one month of stroke	Not reported	Modified version of Albert's test (21 lines); no. of neglect lines on left
Kang & Oh, 2012	Case studies	Whole body tilt and mental practise	19 sessions	> 6.3 mm deviation of the true centre of the line in the line bisection test	3	Case 1: 58 Case 2: 47 Case 3: 58	Case 1 & 2: 7 months Case 3: 23 months	No (hemianopia as exclusion criterio)	Albert test (40 lines); no. of neglected lines
Nakamura et al., 2015	Crossover	Direct current GVS (CL-GVS; CR-GVS, sham). Intensity: 0.4–2.0 mA (threshold found individually).	3×20 min sessions	Score below 131 on Japanese version of the BIT	7	75.4	154.8 days (mean)	Not reported	BIT line cancellation test (36 lines); no. of cancelled lines
Oppenländer et al., 2015	Crossover	Direct current GVS (CL-GVS; CR-GVS, sham). Intensity: 0.7 mA (mean; range: 0.4–1.5 mA; threshold found individually).	3×∼1 h sessions	Number cancellation: centre of cancellation score >0.1. Copy of symmetrical figures: at least 1 omission on the left side. Horizontal line bisection: Mean rightward deviation of	24	63.6 (median)	2 months (median)	7/24 impaired	Cancellation task (200 single-digit numbers); centre of cancellation (scored between −1 and +1, with more extreme scores indicating worse neglect). Figure copying (2 figures);

(*Continued*)

Table 1. Continued.

Study	Design	Intervention parameters	Freq and duration	Method of neglect diagnosis	No. of participants	Mean age (years)	Time since stroke	Presence of visual field defects	Outcome measure(s)
				4.51mm or more. Text copying: at least 1 omission. Cut-off values were determined using healthy controls.					no. of omissions. Line bisection (200mm); mean deviation from true centre in millimetres. Text copying (2 sentences); no. of letters and words omitted.
Rode et al., 2002	Crossover (case study)	CVS (contralesional; ipsilesional; simultaneous). 60cm^3 of 20° water irrigated the external ear canal.	3×30 sec sessions	Drawing tasks (clock and daisy) Line cancellation Line bisection Cut-off values not reported	1	71	Not reported	Unclear	Albert's test (40 lines); no. of cancelled lines. Schenkenberg line bisection; mean percentage horizontal deviation in mm. Copying test (5 items); no. of items drawn symmetrically.
Rorsman et al., 1999	Crossover Exp 1: -no stimulation -stimulation -no stimulation Experiment 2: -no stimulation -no stimulation -stimulation	Direct current CR-GVS. Intensity: individually adjusted to a subsensory threshold (0.7–1.7mA, median 1.15mA)	Line crossing ~60 sec + Star Cancellation ~135 sec×1 session	BIT line crossing and star cancellation. Score below 48% on at least 1 test and no score above 52% on any test.	Experiment 1: 7 Experiment 2: 7	Experiment 1: 73.75 Experiment 2: 73.75	Experiment 1: 5.29 days Experiment 2: 7.86 days (mean)	10 participants had hemianopia. 2 did not and 2 were unclear	BIT line cancellation test (36 lines); no. of cancelled lines. BIT star cancellation (54 stars); no. of cancelled stars.
Rubens, 1985	Crossover	CVS (contralesional; ipsilesional). For contralesional stimulation, 20cc of ice water in left ear followed 30 min later by warm water in right; vice versa for ipsilesional stimulation.	2×30 min sessions	Point to and count people standing around the bed. Read 1-inch-high multisyllabic words. Line crossing. Cut-off score: neglect of one-half or more of visual space on all three tests.	18	62.22	Less than 2 weeks	Left inferior quadrantanopia (n=7); left homonymous hemianopia (n=1); none (n=6). Not tested (n=4)	Word reading (no. of words not reported). Number of words read. Line crossing (25 lines); no. of cancelled lines.
Ruet et al., 2014	Crossover (case studies)	Direct current GVS (CL-GVS; CR-GVS; sham). Intensity: 1.5mA (increased by 0.1mA per second).	3×20 min sessions	Rightwards deviation of more than 6.5mm on a 20cm line bisection test	4	Case 1: 61 Case 2: 38 Case 3: 66 Case 4: 69	Case 1: 3.5 Case 2: 12 Case 3: 3 Case 4: 3	All participants had left homonymous hemianopia	Line bisection (20cm); deviation from centre of line in mm. Star cancellation (56 stars); no of cancelled stars.

Storrie-Baker et al., 1997	Case study	CVS (contralesional) 20 ml of ice water in left ear canal	1×60 sec session	Sunnybrook Neglect Battery. Cut-off value not reported	1	83	12 days	Left homonymous hemianopia	Line bisection (20 cm); percent deviation. Line cancellation (30 lines); no. of cancelled lines.
Sturt & Punt, 2013	Parallel	CVS (Experiment 1: contralesional; Experiment 2: ipsilesional) - 60ml of 20° water in left/ right ear canal	1×60 sec session	Score of 51 or less on the star cancellation test	Experiment 1: [a] RBD+: 6; RBD-: 6; LBD: 6 Experiment 2 (RBD+ only): 6	Experiment 1: [a] RBD+: 75; RBD-: 67.8; LBD: 73 Experiment 2: 74.5	Experiment 1: [a] RBD+: 19.2 days; RBD-: 52.7days; LBD: 47.2 days Experiment 2: 57.5 days (mean)	Not reported	Star cancellation (54 stars); no. of stars cancelled
Utz et al., 2011a	Crossover	Direct current GVS (CL-GVS; CR-GVS; sham). Intensity: 1.5mA (ramped up and down in steps of 0.1mA at the beginning and end of stimulation).	3×20 min sessions	Impairment in at least 3 out of the 6 screening tests (star cancellation, letter cancellation, figure copy, and paragraph reading, number cancellation, and line bisection). Cut-off values for the cancellation and reading tasks were more than 1 omission in the left hemispace. For the figure copying task, any omissions or significant distortions of the left half of copied figures. Cut-off values for line bisection task were derived from healthy controls (−0.34mm deviation to the left and +2.88mm to the right of true centre).	[a] RBD+: 6; RBD-: 11	[a] RBD+: 70.8; RBD-: 70.3	[a] RBD+: 2.6 months; RBD-: 1.9 months (mean)	[a] RBD+: 4 impaired; RBD-: 1 impaired	Adapted Schenkenberg line bisection (17 lines of differing lengths); deviation in mm from centre

(*Continued*)

Table 1. Continued.

Study	Design	Intervention parameters	Freq and duration	Method of neglect diagnosis	No. of participants	Mean age (years)	Time since stroke	Presence of visual field defects	Outcome measure(s)
Volkening et al., 2018	RCT (parallel arms, between participants, randomized)	Direct current GVS (CR-GVS; CL-GVS; sham). Intensity: 1.5mA (ramped up and down in 0.1mA steps).	3×20 min sessions	≤ 135 in the Neglect test (NET), adapted German version of the BIT	[a] CL-GVS: 10 [a] CR-GVS: 11 Sham: 8	[a] CL-GVS: 70.6 [a] CR-GVS: 73 Sham: 70.4	[a] CL-GVS: 1.9 months [a] CR-GVS: 1.3 months Sham: 1.0 months (mean)	[a] CL-GVS: 5/8 impaired [a] CR-GVS: 6/8 impaired Sham: 5/8 impaired	German adaption of the BIT with 17 subtests (maximum 170); higher score is good
Wilkinson et al., 2014	RCT (parallel arms, between participants, randomized)	Noisy current CR-GVS (1-active/9-sham, 5-active/5-sham, and 10-active/0-sham conditions). Intensity: 1 mA mean (0.5– 1.5 mA).	10×25 min sessions	Score ≤129 on the conventional tests of the BIT	[a] [a] 1-active: 15 5-active: 18 10-active: 16	[a] 1-active: 66.9 5-active: 66.0 10-active: 65.7	[a] 1-active: 68 days 5-active: 75 days 10-active: 94 days (median)	People with VFD were included but incidence was not recorded	BITC subtests (maximum 146); higher score is good. Barthel Index (maximum 100); higher score is good.
Zubko et al., 2013	Case studies	Noisy current CR-GVS. Intensity: 90% of cutaneous sensory threshold (1 and 1.5 mA).	5×20 min sessions	Below cut-off on conventional subtests of BIT	2	Case 1: 61 Case 2: 59	Case 1: 8 weeks Case 2: 38 months	Not tested	BIT star and letter cancellation (0–100%); no. of missed targets

Note: Where not all participants were included in our analysis, the included group(s) have been indicated using [a]

Participants in Oppeländer et al.'s study (43) were classified as having neglect (or not) according to which test was used (e.g., a participant who scored below the cut-off on line bisection might not show the same impairment on star cancellation). Therefore, the number of participants differed across outcomes but for simplicity, this information is not reported here.

RBD+ = right brain damage with neglect; RBD- = right brain damage without neglect; LBD = left brain damage; VR = vestibular rehabilitation; BIT= Behavioural Inattention Test.

Studies used a wide range of tests to diagnose neglect. These included different versions of cancellation tasks and line bisection. The cut-off scores and scoring interpretation also varied. For example, some studies (Oppenländer et al., 2015; Utz, Keller, et al., 2011a) used healthy controls to determine cut-offs, whilst others used pre-established scores, or scores determined by the researchers.

Intervention

Of the included studies, eight used GVS as an intervention, seven used CVS, and two used vestibular rehabilitation. Studies varied in terms of the stimulation protocols implemented (e.g., the intensity, duration, and placement of GVS electrodes). For example, whilst some studies tailored the intensity of GVS to each participant's sensory threshold, others used a pre-defined intensity across all participants. All but two of the GVS studies utilized direct-current stimulation (Wilkinson et al., 2014; Zubko et al., 2013; used noisy stimulation). Studies varied in the duration of stimulation per session (∼30 s–60 minutes).

CVS studies all assessed the effects of delivering ice water into the contralesional (left) ear. Three of these studies (Rode et al., 2002; Rubens, 1985; Sturt & Punt, 2013) also investigated the impact of ipsilesional stimulation by delivering ice water into the right ear.

One study compared the effects of vestibular rehabilitation to standard occupational and physical therapy (Dai et al., 2013). Kang and Oh (2012) assessed the effect of a whole-body tilt exercise.

Comparator

Three studies were parallel arm randomized controlled trials (Dai et al., 2013; Volkening et al., 2018; Wilkinson et al., 2014). Four studies used a pseudorandomised crossover design to compare treatment conditions (Nakamura et al., 2015; Oppenländer et al., 2015; Ruet et al., 2014; Utz, Keller, et al., 2011a). All CVS studies (Adair et al., 2003; Cappa et al., 1987; Geminiani & Bottini, 1992; Rode et al., 2002; Rubens, 1985; Storrie-Baker et al., 1997; Sturt & Punt, 2013), apart from one (Rorsman et al., 1999), used non-randomized or case study designs. Other designs included repeated-measures pre and post (Zubko et al., 2013) and multiple baseline case studies (Kang & Oh, 2012).

Outcomes

Many studies used line bisection or cancellation tasks as a primary outcome, but applied different test versions, which differed regarding characteristics such as size, number, and configuration of stimuli on the page. This heterogeneity meant it was not possible to meaningfully combine all outcome measures in meta-analyses, meaning some were instead described narratively.

Dai et al. (2013) assessed ADL using the Functional Independence Measure, whilst Wilkinson et al. (2014) used the Barthel Index.

Assessment of risk of bias in included studies

A summary of risk of bias across studies can be found in Figure 2, the details of which are reported by domain below.

The risk of bias amongst the included studies was low in many domains. However, eight studies were found to have high risk of bias related to certain aspects of their methodology. Risk of bias was most common in the blinding domain, with 13 studies judged as high risk. For studies that used CVS or vestibular rehabilitation, blinding is difficult due to the nature of the intervention. However, issues were also identified within GVS studies. Fifteen studies were judged to be of unclear risk for selective reporting. For this domain, pre-registration details, reporting of all outcomes at all timepoints, and appropriateness of analyses were considered. The carryover effects domain considered the effect of carryover in studies which used a crossover design and therefore did not apply to all studies. All crossover studies (Adair et al., 2003; Cappa et al., 1987; Nakamura et al., 2015; Rorsman et al., 1999) incorporated a washout period of at least 24 h to account for carryover. The period effects domain was judged primarily on the length of time since stroke (alongside the duration of the study) and whether participants were likely past the point of experiencing spontaneous recovery (three months). There were not enough studies included in the review to conduct a sensitivity analysis (including only studies with a low overall risk of bias).

Assessment of treatment effect in included studies

Due to the heterogeneity between studies, it was only possible to pool the data from five studies (Adair et al., 2003; Geminiani & Bottini, 1992; Oppenländer et al., 2015; Sturt & Punt, 2013; Utz, Keller, et al., 2011a), in three random-effects meta-analyses.

Two of these studies (Oppenländer et al., 2015; Utz, Keller, et al., 2011a) used a repeated crossover design in which each participant received CL-GVS, CR-GVS, and sham GVS. As CL- and CR-GVS have been shown to differentially activate the vestibular system, data from each stimulation condition were analysed separately to look at the effects of CL-GVS vs. sham and CR-GVS vs. sham on line bisection. One study was rated as low or moderate risk of bias in all domains (Oppenländer et al., 2015), whilst the other was rated as high risk only for blinding of participants and personnel (Utz, Keller, et al., 2011a). The other meta-analysis considered the effect of contralesional CVS on pre- vs. post-stimulation cancellation scores. Whilst two studies (Geminiani & Bottini, 1992; Sturt & Punt, 2013) were rated as high risk of bias in only one domain (blinding of participants and personnel), one was rated high in five domains (Adair et al., 2003).

Effects of CL-GVS vs. sham and CR-GVS vs. sham on line bisection

The analysis of CL-GVS vs. sham on line bisection, (displayed in Figure 3a), shows a mean difference of −8.96mm (reflecting a reduction in the deviation

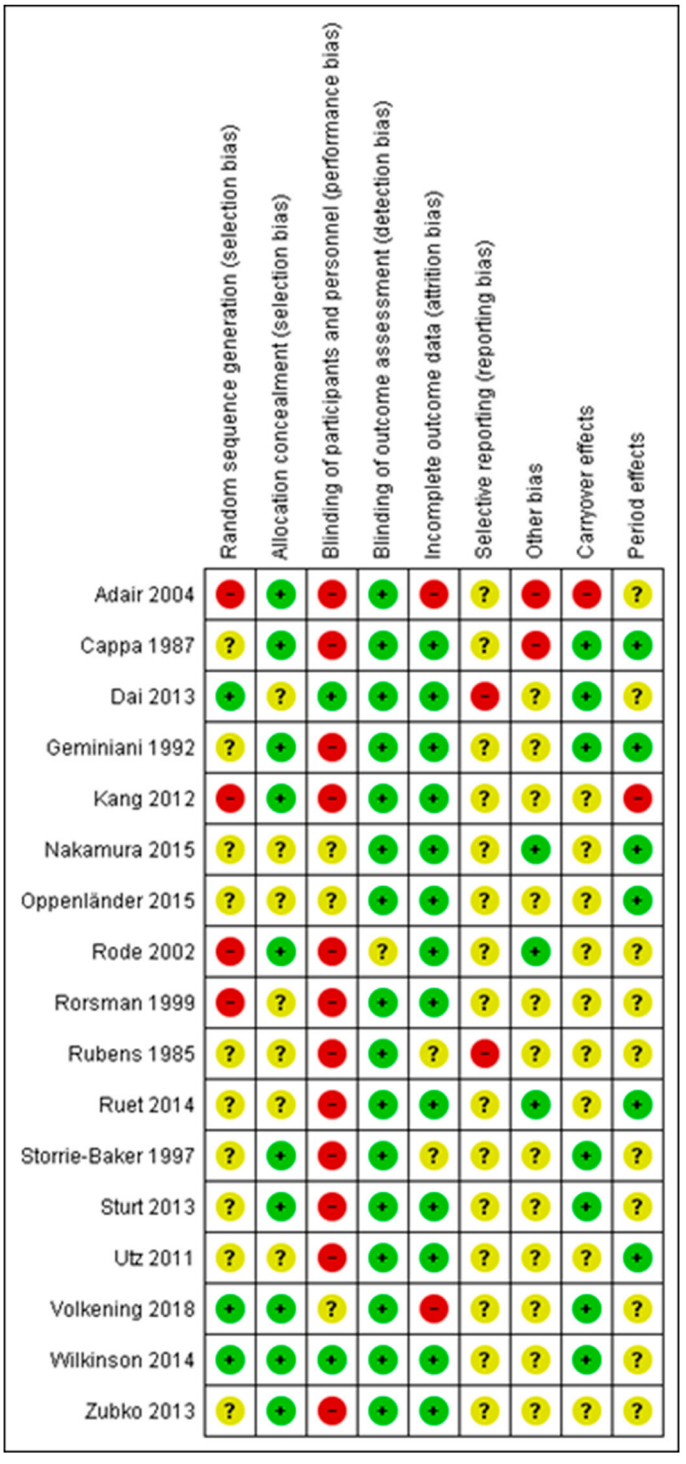

Figure 2. Risk of bias summary for all included studies.

Note: + indicates a study was judged to be at low risk of bias for that domain; ? incidates unclear risk of bias; and - indicates a high risk of bias.

from midline which favours GVS over sham), with 95% CIs spanning from −19.46 to 1.54. However, this result is not statistically significant ($p = .09$), suggesting that there is no reliable difference between the two conditions.

The analysis of CR-GVS vs. sham on line bisection (displayed in Figure 3b), shows a mean difference of −4.44mm and 95% CIs which range from −15.55 to 6.68. Although this estimate favours GVS, the wide range of the CIs means there is uncertainty as to where the true effect may lie, and the non-significant p value (0.43) suggests that there is no reliable difference between the two conditions.

Effect of contralesional CVS on pre- vs. post-stimulation cancellation scores

The analysis, displayed in Figure 4, shows a mean difference of 4.47 and 95% CIs which range from 1.26 to 7.68. This estimate favours post-CVS scores over pre-CVS ones, indicating an improvement in cancellation score after contralesional stimulation. This effect was found to be statistically significant ($p = .006$).

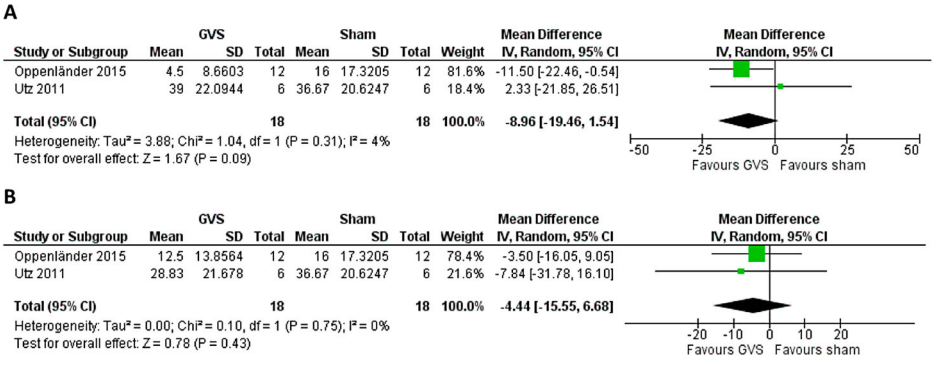

Figure 3. Forest plot displaying the statistical analysis of CL-GVS vs. sham and CR-GVS vs. sham on line bisection.

Note: Boxes and horizontal lines depict the effect estimate and 95% CIs, respectively for each study, whilst the diamond represents the overall effect estimate and 95% CIs. Negative numbers indicate that GVS was more effective than sham and positive values, vice versa (0 = no effect).

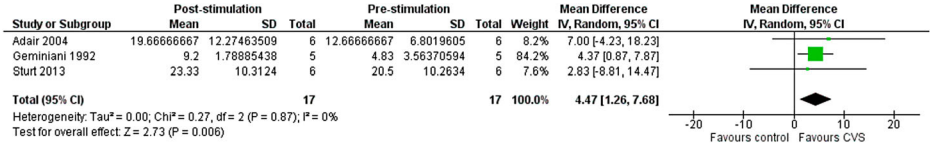

Figure 4. Forest plot displaying the statistical analysis of contralesional CVS pre- vs. post-stimulation cancellation scores.

Note. The boxes and horizontal lines depict the effect estimate and 95% CIs, respectively for each study, whilst the diamond represents the overall effect estimate and 95% CIs. Positive numbers indicate that post-stimulation scores were improved from pre-stimulation scores and negative scores, vice versa (0 = no effect).

Assessment of heterogeneity in included studies

Although the I^2 value for all analyses (which ranges from 0 to 4%) suggests there is very little heterogeneity between studies when taken alone, this is unlikely to reflect the true extent of their statistical differences. The 95% CIs are wide and imprecise, and it is for this reason that they overlap, rather than because the effect estimates for all studies are similar.

Narrative synthesis

Several studies could not be meaningfully combined in a meta-analysis, either because of significant heterogeneity or because they utilized a single-case design.

Narrative results are presented as effect direction plots, whereby an upward pointing arrow (↑) indicates that vestibular stimulation led to a significantly greater improvement than the comparator, a downwards pointing arrow (↓) indicates comparative deterioration, and a sideways arrow (↔) no difference.

Narrative synthesis of studies utilizing GVS

All studies which utilized CL-GVS found that there was no significant difference between this and sham stimulation (or pre vs. post scores for Volkening et al. (2018); see Table 2). Whilst six studies also found no difference between CR-GVS and a comparator, five found that CR-GVS lead to an improvement in neglect test scores compared to sham or pre-test scores.

Narrative synthesis of studies utilizing CVS

All studies but one (Rode et al., which found no difference) found contralesional CVS to improve scores on neglect tests when compared to pre-stimulation performance (see Table 3). Four studies which assessed the effect of ipsilesional CVS found performance was worse post-stimulation, whilst one found no difference between pre- and post-stimulation scores.

Table 2. Effect direction plots for studies utilizing GVS.

Comparison	Study	Direction of effect (CL-GVS)	Direction of effect (CR-GVS)
GVS vs. sham on cancellation score post-intervention	Oppenländer et al., 2015	↔	↑
	Rorsman et al., 1999 exp. 1	n/a	↔
	Rorsman et al., 1999 exp. 2	n/a	↑
	Ruet et al., 2014	↔	↔
	Nakamura et al., 2015	↔	↔
GVS on pre- vs. post-stimulation cancellation score	Zubko et al., 2013	n/a	↑
GVS on pre- vs. post-stimulation BIT/NET score	Volkening et al., 2018	↔	↔
	Wilkinson et al., 2014	n/a	↑
GVS vs. sham on copying score post-intervention	Oppenländer et al., 2015	↔	↑
GVS vs. sham on line bisection post-intervention	Ruet et al., 2014	↔	↔
GVS on pre- vs. post-stimulation Barthel Index score	Wilkinson et al., 2014	n/a	↔

Table 3. Effect direction plots for studies utilizing CVS.

Comparison	Study	Direction of effect (contralesional)	Direction of effect (ipsilesional)
Pre- vs. post-CVS cancellation scores	Cappa et al., 1987	↑ [a]	n/a
	Rode et al., 2002	↑ [a]	↓ [a]
	Rubens, 1985	↑ [a]	↓ [a]
	Storrie-Baker et al., 1997	↑ [a]	n/a
	Sturt and Punt, 2013	n/a (included in meta-analysis)	↔
Pre- vs. post-CVS line bisection scores	Adair et al., 2003	↑	n/a
	Rode et al., 2002	↑	↓
	Storrie-Baker et al., 1997	↑ [a]	n/a
Pre- vs. post-CVS figure copying scores	Rode et al., 2002	↔	↓
Pre- vs. post-stimulation word reading scores	Rubens, 1985	↑ [a]	n/a

Note: Arrows marked with [a] denote a comparison that has not been statistically tested (descriptive analyses only).

Narrative synthesis of studies utilizing motion simulators and vestibular rehabilitation

Vestibular rehabilitation and motion-based stimulation resulted in increased scores post-stimulation in all studies assessed (see Table 4).

Discussion

Summary of main results

This systematic review aimed to evaluate the effects of vestibular stimulation on outcomes of neglect and ADL in people with visual neglect. Seventeen studies were included in the review. Given the heterogeneity of the findings, only three meta-analyses were conducted, with the remaining data summarized narratively. Two meta-analyses indicated no difference between CL-GVS and sham GVS, or CR-GVS and sham GVS in reducing midline deviation during line bisection. Another meta-analysis found that cancellation scores significantly improved after participants received contralesional CVS. Narrative syntheses assessing the effects of GVS, CVS, vestibular rehabilitation, and motion-based stimulation on several neglect and ADL outcomes provided mixed results. Taken together, these comparisons provide tentative evidence for the potential efficacy of vestibular stimulation in neglect.

CVS appeared to show stronger evidence of effect than GVS. There are several potential explanations for this. First, CVS and GVS stimulate the

Table 4. Effect direction plots for studies utilizing vestibular rehabilitation or motion simulators.

Comparison	Study	Direction of effect
Pre- vs. post-stimulation BIT score.	Dai	↑ [a]
Pre- vs. post-stimulation Barthel Index score.	Dai	↑
Pre- vs. post-stimulation cancellation score.	Kang	↑

Note: Arrows marked with an [a] denote a comparison that has not been statistically tested (descriptive analyses only).

vestibular end-organs differently. CVS alters the density of endolymphatic fluid and primarily activates the horizontal canals, whereas GVS alters the firing rate of vestibular afferents stimulating the otoliths and semi-circular canals (Palla & Lenggenhager, 2014). This partly produces differential activation patterns throughout the vestibular cortex. CVS-related clusters involving the postero-medial parietal cortex (associated with spatial and mental imagery), and the caudal part of the anterior cingulate cortex (engaged in directed attention) may underlie this finding (Lopez et al., 2012). Second, CVS and GVS induce divergent behavioural responses; CVS elicits sensations of floating, tilting, or being pulled which can cause temporary vertigo and nausea (Palla & Lenggenhager, 2014) while GVS instead induces rocking and pitching sensations and can cause itching and tingling under the electrodes. These behavioural, attention-grabbing responses are easier to blind with sub-sensory GVS, meaning the accompanying sensations of CVS could have induced a non-specific attentional cue drawing attention to the neglected side. Third, there is no common metric by which "stimulation intensity" can be equated or compared across GVS and CVS which makes it difficult to know if methodological as opposed to genuine physiological differences underlie the variation observed.

Only one study applied vestibular rehabilitation exercises, and another used a motion simulator, which meant that these studies could only be analysed narratively. Neglect symptomology was improved across both studies. Since these techniques provide a better approximation of natural movement and vestibular sensations, they may elicit stronger treatment effects than CVS and GVS (Palla & Lenggenhager, 2014).

These results should be interpreted in the context of methodological limitations and heterogeneity which limited the evidence synthesis. Key issues and recommendations for overcoming these are discussed below.

Sample size and characterization

The studies included for analysis generally drew on small sample sizes; the number of participants included in the two meta-analyses which looked at GVS was only 17 (drawn from the same study samples; Nakamura et al., 2015; Sturt & Punt, 2013) and only 18 participants were included in the meta-analysis investigating CVS (Collaboration, 2014; Dai et al., 2013; Storrie-Baker et al., 1997). This limits the conclusions that can be drawn. Future studies should use *a priori* calculations to ensure sample sizes are adequate; only one study in the review undertook such calculation.

Within these samples, there were significant discrepancies in the reporting of patients' clinical characteristics. An important consideration is when the stroke was acquired due to the likelihood of natural improvement and the potential for neuroplastic change (Adeyemo et al., 2012), especially during earlier stages of recovery. However, only one study considered this variable. In many studies,

the mean time since stroke was less than three months. For those intervention studies which took place over a matter of hours or days this is unlikely to have a significant impact, however, for longer studies (lasting weeks or months) that did not have appropriate control, natural recovery may have confounded the results. Adjusting for time since stroke within statistical analyses or recruiting participants at least three months post-stroke could produce more accurate estimates of treatment effect. Practical considerations, such as participant burden following a recent stroke should also be considered and planned for by involving patients in research design and conduct.

Another confounding clinical characteristic was the presence of visual field defects (VFDs). Few studies reported their incidence, and none cited VFDs as an exclusion criterion. Given that VFDs amplify the effects of neglect (Doricchi & Angelelli, 1999), the impact of vestibular stimulation on neglect can be difficult to disentangle from the influence of VFDs. Future research should adjust for this within statistical analyses or attempt to recruit samples unconfounded by co-occurring VFDs.

Comparability of intervention parameters

Stimulation protocols differed widely, even between studies delivering the same stimulation type. For example, the stimulation intensity, frequency, duration, number of sessions and the interval between them varied significantly across GVS studies. The review data did not allow for subgroup analysis according to such factors, so it is not possible to comment on how these parameters affected results. Unhelpfully, the available evidence is equivocal; Nakamura et al. (2015) reported a significant correlation between total charge applied and neglect improvement, whereas Wilkinson et al. (2014) found that one session of GVS was just as effective as 10 in ameliorating symptoms. Until a clearer consensus is reached on this issue, standardizing a GVS regimen to control for any confounding effects of dose, or conducting systematic dose–response studies which escalate/de-escalate doses according to an adaptive sequence would be a helpful contribution to the literature.

At this stage it is unclear if a higher intensity of stimulation (i.e., higher amplitude/frequency, colder thermal stimulus) will elicit the greatest therapeutic effect. Mild adverse events, such as itching under the electrodes, are more noticeable at higher amplitudes of GVS (Utz, Korluss, et al., 2011b), while in CVS nystagmus and vertigo are initially more common as the temperature declines from 37°C (Lidvall, 1962). Collecting more information on safety and tolerability will be an important step in determining whether vestibular stimulation is likely to be an acceptable and feasible clinical treatment. Although attrition rates were generally low, the use of per protocol analyses made it difficult to determine whether dropout was related to the stimulation protocol. Further research should make this information available and consider intention-to-treat

analyses to establish the viability of the intervention. Checklist tools such as the Template for Intervention Description and Replication (Hoffmann et al., 2014) are available to help researchers provide more complete descriptions of their interventions to facilitate replication and clinical implementation.

Another issue in some studies was the integrity of the blinding procedure. Tailoring GVS intensity to each participant's sensory threshold can help to ensure stimulation is imperceptible. Yet this technique was infrequently utilized, with most studies applying stimulation at a fixed current intensity of 1.5mA. Two reviewed studies cited findings (Gandiga et al., 2006) that 1.5mA is a subsensory level in a stroke population, but this evidence related to a different technique (tDCS) which involves scalp as opposed to mastoidal electrode placement. The average amplitude in studies which individually modified the stimulation threshold was lower than 1.5mA, meaning some participants who received stimulation at 1.5mA are likely to have perceived cutaneous sensation/mild disorientation. Given that thresholding is quick and simple to apply, if studies intend for their stimulation to be subthreshold then tailored thresholding should be implemented to increase concealment.

Justification and reporting of outcomes

Justification for outcome selection was often limited and did not always acknowledge the sensitivity of measures to only a few aspects of neglect. For example, known double dissociations between performance on cancellation tasks and line bisection (Ferber & Karnath, 2001; Halligan & Marshall, 1992; Marshall & Halligan, 1995) indicate that these tests reflect different underlying cognitive processes (ego- and object-centred neglect). This heterogeneity could, to some extent, explain why results varied between studies (see also Williams et al., 2021) and needs to be recognized if any observed treatment effects are to be properly characterized.

Another issue was the standardization and interpretation of the outcomes themselves. Several studies utilized line bisection as an experimental outcome. Although the metric used to score performance was consistent (millimetre deviation from the mean), test versions, and subsequently, line lengths, differed. Line length has been shown to affect performance in bisection, wherein the extent of the rightwards deviation is proportional to the total length of the line (Halligan & Marshall, 1988; Harvey et al., 1995). McIntosh et al. also suggest independently manipulating the locations of the left and right endpoints and recording how the horizontal position of the response varies across trials (as opposed to directional bisection error) to account for line length effects and provide a more sensitive measure of attentional bias (McIntosh et al., 2017).

Similarly, in cancellation tasks the number of distractors (Halligan et al., 1989), targets (Ten Brink et al., 2020), and organization of the stimulus array

(Weintraub & Mesulam, 1988) alter the sensitivity of the measure. If results are to be combined to provide clinically meaningful results, then it is important that such test characteristics are carefully reported and controlled. To this end, open-source platforms provide a means of sharing test stimuli and information on test interpretation.

Outcomes which measure functionality in ADLs were included here to explore whether therapeutic effects (i.e., reduction of neglect symptoms) translate to everyday meaningful activities (e.g., shopping, work, driving). However, of the 17 included studies, only two utilized ADL measures. Future studies should consider including these, particularly if vestibular stimulation techniques are to be adopted clinically. The Catherine Bergego Scale (Azouvi et al., 2003) assesses the impact of neglect on ten everyday situations and has been translated and validated across multiple studies. Other tools (Linacre et al., 1994; Quinn et al., 2011; Schuling et al., 1993) are also commonly used with stroke patients, but there is currently no single, agreed tool to facilitate comparisons between studies.

Limitations

The present systematic review has some limitations. A multitude of terms are used to describe vestibular stimulation within the literature. We therefore found it necessary to adopt broad PICO criteria to encompass these. Consequently, our searches resulted in several different study designs, types of vestibular stimulation, comparators, and outcomes; a heterogeneity that prevented many results from being meaningfully combined in meta-analyses. These discrepancies may have also contributed to the inconsistency of effects detected. Interpretation of the results is also limited by the small number of studies included in the review which were insufficient to conduct a sensitivity analysis (including only studies with a low overall risk or bias), or formally assess for publication bias by means of a funnel plot.

Conclusion

Vestibular stimulation, most notably caloric vestibular stimulation, shows promise as a potential treatment for post-stroke neglect, but conclusions are limited by clinical and methodological heterogeneity. Future research needs to provide more consideration of the homogeneity of samples recruited, adopt *a priori* sample size calculations, select targeted outcome measures, and describe stimulation protocols to address this heterogeneity and assess dose–response.

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Data availability

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Author contributions

Conceptualization: [Charlotte Wheeler, Mohamed Sakel, David Wilkinson], Literature searches: [Charlotte Wheeler, Laura J Smith], Data analysis: [Charlotte Wheeler, Laura J Smith], Writing - original draft preparation: [Charlotte Wheeler, Laura J Smith], Writing – review and editing: [Charlotte Wheeler, Laura J Smith, Mohamed Sakel, David Wilkinson].

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Appendices

Appendix A

Search Strategies

CENTRAL

#1 MeSH descriptor: [Stroke] explode all trees

#2 ((stroke or poststroke or "post-stroke" or cerebrovasc* or brain next vasc* or cerebral next vasc* or cva* or apoplexy* or SAH)):ti,ab,kw

#3 ((brain* or cerebral* or cerebell* or intracran* or intracerebral) near/5 (isch*emi* or infarct* or thrombo* or emboli* or occlus*)):ti,ab,kw

#4 (brain* or cerebral* or cerebell* or intracerebral or intracranial or subarachnoid) near/5 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)

#5 #1 or #2 or #3 or #4

#6 MeSH descriptor: [Visual Perception] explode all trees

#7 MeSH descriptor: [Perceptual Disorders] explode all trees

#8 (hemineglect or hemi-neglect)

#9 ((unilateral or spatial or hemispatial or hemi-spatial or visual) near/5 neglect)

#10 (inattention or hemi-inattention or extinction)

#11 ((perceptual or perception or visual or visuospatial or visuo-spatial or visuoperceptual or visuo-perceptual or attention*) near/5 (disorder* or deficit* or impairment* or abilit* or problem*))

#12 #6 or #7 or #8 or #9 or #10 or #11

#13 #5 and #12

PubMed

("brain injuries/complications"[Mesh] OR stroke[Mesh]) AND (“perceptual disorders”[Mesh] OR “visual perception”[Mesh] OR “vision disorders”[Mesh]) NOT (teen*[TIAB] OR youth*[TIAB] OR adolescen*[TIAB] OR juvenile*[TIAB] OR young adult*[TIAB] OR young person*[TIAB] OR young individual*[TIAB] OR young people*[TIAB] OR young population*[TIAB] OR young man[TIAB] OR young men[TIAB] OR young woman[TIAB] OR young women[TIAB] OR youngster*[TIAB] OR firstgrader*[TIAB] OR second-grader*[TIAB] OR third-grader*[TIAB] OR fourth-grader*[TIAB] OR fifthgrader*[TIAB] OR sixth-grader*[TIAB] OR seventh-grader*[TIAB] OR highschool* OR college* OR secondary school*[TIAB] OR secondary education*[TIAB] OR high school*[TIAB] OR high education[TIAB] OR adolescent[MH] OR young adult[MH])

WHO ICTRP

stroke AND vision OR stroke AND visual perception OR stroke AND neglect OR stroke AND perceptual disorders

PsychINFO

(DE "Cerebrovascular Accidents") AND ((DE "Perceptual Disturbances" OR DE "Agnosia" OR DE "Hallucinations" OR DE "Misophonia" OR DE "Psychedelic Experiences" OR DE "Sensory Neglect") OR (DE "Vision Disorders" OR DE "Balint’s Syndrome" OR DE "Blind" OR DE "Blindsight" OR DE "Eye Disorders" OR DE "Hemianopia" OR DE "Partially Sighted"))

CINAHL
(MH "Stroke+" OR MH "Brain Injuries+/CO") AND (MH "Visual Perception+" OR MH "Perceptual Disorders+" OR MH "Vision Disorders+")

OpenGrey
((stroke OR poststroke OR "post-stroke" OR cerebrovasc* OR brain next vasc* OR cerebral next vasc* OR cva* OR apoplexy*) AND (perceptual OR perception OR visual OR visuospatial OR visuospatial OR visuoperceptual OR visuo-perceptual OR attention*) AND (disorder* OR deficit* OR impairment* OR abilit* OR problem*)) OR "spatial neglect"

LILACS
(stroke OR poststroke OR "cerebrovascular accident" OR CVA) AND (perceptual OR perception OR visual OR visuospatial OR visuo-spatial OR visuoperceptual OR visuo-perceptual OR attention) AND (disorder OR deficit OR problem OR impairment OR neglect) AIM: Title field: stroke poststroke "cerebrovascular accident" CVA

Appendix B

PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarize relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org/

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Appendix B
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	P3-P4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	P4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	P4-P6
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	P5, P7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix A
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	P5-P6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	P6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	P5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	P5-P6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	P6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	P6-P7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	P9
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	P6-7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	P9-P10
	13d		P9-P10

(*Continued*)

Continued.

Section and Topic	Item #	Checklist item	Location where item is reported
		Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	P7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	P7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	P6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A- formal methods not used but certainty of results evaluated within discussion
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	P7-P8; Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	P7; Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	P8-P9; Figure 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figures 3–4, Tables 2–4
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies.	P9-P10
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	P9-P10
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	P9-P10
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A (see item 13f and P7)
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	P8-P9
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A (see item 15)
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	P11-P13
	23b	Discuss any limitations of the evidence included in the review.	P11-P13
	23c	Discuss any limitations of the review processes used.	P13
	23d	Discuss implications of the results for practice, policy, and future research.	P11-P13

(*Continued*)

Continued.

Section and Topic	Item #	Checklist item	Location where item is reported
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	P4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	P4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	P5
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	P14
Competing interests	26	Declare any competing interests of review authors.	P14
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	P24

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.
For more information, visit: http://www.prisma-statement.org/