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HEART & STROKE FOUNDATION
Canadian Partnership for Stroke Recovery

Chapter 13: Neglect and Visuospatial Disorders

Abstract

This review examines the treatment of perceptual disorders following stroke focusing primarily on unilateral spatial neglect. Unilateral spatial neglect is reported in about 25% of stroke patients referred for rehabilitation and is more commonly associated with right parietal lesions. Unilateral spatial neglect has been reported to have a negative impact on functional recovery, length of rehabilitation stay and need for assistance after discharge. In general, rehabilitation interventions to improve neglect may be classified into a) those which attempt to increase the stroke patient's awareness of or attention to the neglected space or b) those which focus on the remediation of deficits of position sense or body orientation. Interventions of the first type included in the present review are: visual scanning retraining, arousal or activation strategies and feedback to increase awareness of neglect behaviours. Identified interventions that attempt to improve neglect by targeting deficits associated with position sense and spatial representation include the use of prisms, eyepatching and hemispatial glasses, caloric stimulation, optokinetic stimulation, TENS and neck vibration. The use of dopaminergic medication therapy and music therapy is also discussed.

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Key Points

The literature is mixed regarding visual scanning training for improving neglect.

Visual scanning training may not be beneficial for improving activities of daily living.

The literature is mixed regarding covert attention training for improving neglect.

Covert attention training may not be beneficial for improving motor rehabilitation or activities of daily living.

The literature is mixed regarding virtual reality-based training for improving neglect and motor rehabilitation.

Virtual reality-based training may not be beneficial for improving learning & memory, or activities of daily living.

Limb activation may not be beneficial for improving neglect, motor rehabilitation, or activities or daily living.

Visuomotor feedback strategies may be beneficial for improving neglect.

Visuomotor feedback strategies may not be beneficial for improving motor rehabilitation or activities of daily living.

The literature is mixed regarding prism adaptation training for improving neglect.

Prism adaptation may not be beneficial for improving motor rehabilitation or activities of daily living.

Trunk rotation therapy may not be beneficial for neglect and activities of daily living

Trunk rotation therapy may be beneficial for motor rehabilitation

General visuospatial/perceptual training may not be beneficial for neglect.

The literature is mixed concerning cueing for improving neglect.

The literature is mixed concerning visual exploration with neck muscle vibration for improving neglect, motor rehabilitation and activities of daily living.

TENS may be beneficial for improving neglect.

The literature is mixed regarding rTMS for improving neglect and motor rehabilitation.

rTMS may not be beneficial for improving activities of daily living

Continuous TBS may be beneficial for improving neglect.

Anodal tDCS may be beneficial for improving neglect.

The literature is mixed regarding dual tDCS for improving neglect.

Galvanic vestibular stimulation (GVS) may not be beneficial for improving neglect

There does not appear to be a difference in efficacy between left, right or sham GVS, and high or low volume GVS

Manual vestibular stimulation may not be beneficial for improving neglect, activities of daily living and motor rehabilitation.

The literature is mixed regarding optokinetic stimulation training for improving neglect.

Functional electric stimulation may be beneficial for improving neglect.

Dopaminergic medications may not be beneficial for improving neglect, learning and memory, and motor rehabilitation.

The literature is mixed concerning rivastigmine therapy for improving neglect.

Nicotine may be beneficial for improving neglect.

The literature is mixed regarding guanfacine for improving neglect.

Citicoline may be beneficial for improving global cognition.

Citicoline may not be beneficial for improving neglect, learning and memory, and motor rehabilitation.

The literature is mixed regarding Selegiline for improving neglect and global cognition.

Selegiline may not be beneficial for improving learning and memory, and activities of daily living.

Piracetam may be beneficial for improving global cognition.

The literature is mixed regarding Piracetam for improving motor rehabilitation.

Piracetam may not be beneficial for improving activities of daily living.

Modified Sackett Scale

Level of evidence	Study design	Description
Level 1a	Randomized controlled trial (RCT)	More than 1 higher quality RCT (PEDro score ≥6).
Level 1b	RCT	1 higher quality RCT (PEDro score ≥6).
Level 2	RCT	Lower quality RCT (PEDro score <6).
	Prospective controlled trial (PCT)	PCT (not randomized).
	Cohort	Prospective longitudinal study using at least 2 similar groups with one exposed to a particular condition.
Level 3	Case Control	A retrospective study comparing conditions, including historical cohorts.
Level 4	Pre-Post	A prospective trial with a baseline measure, intervention, and a post-test using a single group of subjects.
	Post-test	A prospective post-test with two or more groups (intervention followed by post-test and no re-test or baseline measurement) using a single group of subjects
	Case Series	A retrospective study usually collecting variables from a chart review.
Level 5	Observational	Study using cross-sectional analysis to interpret relations. Expert opinion without explicit critical appraisal, or based on physiology, biomechanics or "first principles".
	Case Report	Pre-post or case series involving one subject.

New to the 19th edition of the Evidence-based Review of Stroke Rehabilitation

1) PICO conclusion statements

This edition of Chapter 13: Neglect rehabilitation interventions synthesizes study results from only randomized controlled trials (RCTs), all levels of evidence (LoE) and conclusion statements are now presented in the Population Intervention Comparator Outcome (PICO) format.

For example:

Population: Stroke survivors

Intervention **Comparator**

SPASTICITY			
LoE	Conclusion Statement	RCTs	References
1b	**Bilateral arm training** may not have a difference in efficacy when compared to **TENS** for improving spasticity.	1	Stinear et al. 2014

Outcome

New to these statements is also the use of colours where the levels of evidence are written.

Red statements like above, indicate that the majority of study results when grouped together show no significant differences between intervention and comparator groups.

Green statements indicate that the majority of study results when grouped together show a significant between group difference in favour of the intervention group.

For example:

Population: Stroke survivors

Intervention

MOTOR FUNCTION			
LoE	Conclusion Statement	RCTs	References
1a	**Bilateral arm training** may produce greater improvements in motor function than **conventional therapy**.	4	Meng et al. 2018; Lee et al. 2017; Stinear et al. 2008; Desrosiers et al. 2005

Outcome **Comparator**

Yellow statements indicate that the study results when grouped together are mixed or conflicting, some studies show benefit in favour of the intervention group, while others show no difference between groups.

For example:

Population: Stroke survivors

Outcome **Intervention**

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **CIMT** to improve dexterity when compared to **conventional therapy or motor relearning programmes** during the acute/subacute phase poststroke.	4	Shah et al. 2016; Yoon et al. 2014; Boake et al. 2007; Ro et al. 2006

Comparator

2) Neglect rehabilitation outcome measures

Outcome measures were classified into the following broad categories:

Visuospatial Processing & Neglect: These outcome measures assessed visuospatial processing and orientation to examine neglect severity.

Learning and Memory: These outcomes measures assessed an individual's ability to explicitly and implicitly learn and recall information.

Global Cognition: These outcome measures assessed an individual's overall cognitive processing capability factoring in multiple domains.

Motor Rehabilitation: These outcome measures covered gross motor movements, as well as fine, dexterous movements when using the upper extremities.

Stroke severity: These outcome measures assessed the severity of one's stroke through a global assessment of a multitude of deficits a stroke survivor may experience.

Activities of daily living: These outcome measures assessed performance and level of independence in various everyday tasks.

Outcome measures that fit these categories are described in the next few pages.

Outcome Measure Definitions

Visuospatial Processing & Neglect

Albert's Test: Is a measure used to screen for unilateral spatial neglect in stroke patients. Lines are placed in random orientations on a piece of paper and participants are instructed to cross out the lines. Lines that are left uncrossed on the side corresponding to the participants motor deficit or lesion signify unilateral spatial neglect. It is scored by counting the number of uncrossed lines on each side. Albert's test has shown to have high correlation with Line Bisection Catherine Bergego Scale, Star Cancellation test and Wundt-Jastrow Illusion test as well as good test-retest reliability in detecting unilateral spatial neglect in stroke patients (Argell et al. 1997; Deloche et al. 1996; Fullerton et al. 1986; Massironi et al. 1988).

Auditory Subjective Median Plane (Midline): Is a test of auditory sound localization. Participants are exposed to a binaural white noise stimulus for 3 seconds via headphones. The headphones manipulate different aspects of the auditory stimuli so that they have a different perceived source location. Participants responded in a binary (yes/no) manner as to whether or not they perceived the sound to be originating from their median pane, or if it was to the left or right. Mean deviation from center was used to assess neglect (Kerkhoff et al., 2006).

Baking Tray Task: Is an ecological measure used to detect unilateral spatial neglect. In the test participants are instructed to spread 16 cubes along a 75 x 100cm board as evenly as possible, like "lying out buns on a baking tray". There is no fixed time limit, and it is scored by counting the number of cubes on each half of the tray. Half points are awarded if the cube sits on the midline. This measure has proven to be sensitive in detecting neglect and resistant to practice and set effects. It has been found to have high correlation with the Line Bisection test (Appleros et al. 2004; Bailey et al. 2004; Tham 1996).

Balloons Test: see Bell's Test. Balloons test is a measure of visual inattention. It is a cancellation task similar to Bell's Test. The test has 2 parts: 1) a search of 20 "balloons" (circle with straight line attached) among a much larger number of circles; and 2) a search of 20 circles among a much larger number of "balloons" (Diesfeldt, 2012).

Barrage test: see Albert's test. This test is another name for Albert's test, but will sometimes contain fewer lines than the original when it is described in the literature. (Paolucci et al., 1996).

Behavioural Inattention Test (BIT): Is a battery of tests intended to evaluate the presence and severity of visual neglect. It consists of two subtests, a 'conventional subtest' and a 'behavioural subtest'. The conventional subtest consists of 6 items (eg. Line crossing, letter cancellation, etc…). The behavioural subtest consists of 9- items that are functional activities as opposed to standardized neglect tests (eg. telephone dialing, map navigation etc…). A maximum score for the BIT, the conventional subtest and the behavioural subtest are 227, 146 and 81 respectively, with higher scores indicating more severe impairment. The scale proven to have good test-retest validity and accurately predicts poor functional outcomes in stroke (Jehkonen et al. 2000; Wilson et al. 1987).

Bell's Test: Is a type of cancellation task used to measure visual neglect. Subjects are asked to scan a sheet with 7 columns of drawn stimuli and cross out all target stimuli (i.e. bells). The pattern of scanning can be evaluated as well as the distribution of targets that the subject omits. From this, the pattern and degree of neglect can be determined (Gauthier, Dehaut & Joanette, 1989).

Catherine Bergego Scale: Is a 10-item measure of functioning in everyday tasks used to assess unilateral neglect in stroke patients and anosognosia. A rater will score the patient on a 4-point scale (0 = no neglect, 3 = severe neglect) for each of the items, for example "Forgets to groom or shave left part of his/her face" (Item 1). There is a total score of 30, with higher scores corresponding to greater levels of impairment. The scale has proven to be both reliable and valid in assessing neglect and anosognosia (Azouvi et al. 2003; Azouvi 1996).

Charron Test: Is a measure of visual and attentional processing ability. Subjects are provided with 19 pairs of objects/symbols and 37 pairs of numbers and asked to place a checkmark next to any pairs that are not identical. Their total number of errors are recorded. The test is not standardized and there is a lack of data regarding the test's validity or reliability (Korner Bitensky et al. 1994).

Center of Cancellation: Is a measure allows neglect severity to be evaluated from cancellation tasks, such as the Letter Cancellation test or Bell's test. Using a computer program, participant's responses are recorded and the mean horizontal coordinate for detected items is calculated (Rorden et al. 2010).

Clock Drawing Test: Is a very brief screening tool used to detect cognitive impairment. It can also detect neglect and executive dysfunction. Participants are asked to draw a clock along with numbers and hands denoting a specified time. There are multiple different rating systems, with most classifying the number and type of errors made. The test is valid and reliable as a screening tool, with a high sensitivity and specificity (Duro et al, 2018; Sheehan, 2012).

Coin Sorting: Is a test of neglect, whereby coins of different values are distributed to the left, in front, and to the right of the patient based on a standard arrangement. They are then asked to indicate all of the coins with a particular value. Any omissions are recorded along with the side that the coin was located on (Halligan et al., 1991).

Comb and Razor Test: Is a clinical test for personal neglect (neglect of personal space), in which the participant is given a comb and a razor (or powder compact case for women) and instructed to comb their hair or shave/apply makeup on their face. The number of strokes within 30 seconds are categorized into left, ambiguous or right strokes. The score is most often calculated based on the percent bias of strokes to a particular side. Scores fall anywhere between -1 (total left neglect) and +1 (total right neglect). The test has proven to be highly reliable and be able to distinguish between different known groups of participants (right or left-brain stroke, healthy individuals, extra personal neglect) (Beschin et al. 1997).

Cued Detection Task (Posner Cueing Task): Is a test often used to asses attention. Participants are instructed to look at a fixation point in the middle of the screen and two target areas lie on either side. The participant is instructed to respond once they have detected a stimulus in one of the target areas. During the test, visual cues will precede the stimuli and either cue the participants in the correct direction of stimuli appearance, or the incorrect direction. Individuals with Neglect will be differentially affected by the cueing (Vossel et al., 2010).

Dichotic Listening Task: Is used to assess lateralized auditory perception. Pairs of stimuli are presented to the participant, one in the left ear and one in the right. The participant is instructed to focus on both stimuli, and to repeat them after presentation. Scores are based around the percentage of stimuli identified correctly in both the right ear and left ear separately (Hugdahl et al., 1991).

Extinction Task: Is used to asses visuospatial memory and neglect. Visually presented images are shown in either the right hemifield or the left hemifield, and recall is assessed separately for each hemifield. Any bias in visual memory to one side might indicate a unilateral neglect (Vaes et al., 2016).

Field of View Assessments: Is a measure of functional visual field. It can map an individual's visual field (area that information can be acquired and processed without eye or head movement). The tool consists of a large computer screen and can evaluate visual processing speed, divided attention and selective attention through the completion of 3 computerized tasks. A percentage score is given based on the percentage reduction in useful field of view. The test has been shown to have moderate/high test-retest reliability and good criterion validity in a post-stroke population assessed for driving ability (George & Crotty, 2010; Mazer et al. 2003).

Fluff Test: Is a measure of personal domain in neglect syndrome. The participant is blindfolded and 24 targets are placed on their body. They are kept distracted during the placing of the targets (to prevent counting) and then asked to remove all the pads from their body. Scoring is based on omissions of targets from the left side. This test has demonstrated high test-retest reliability (Cocchini et al. 2001).

Functional Neglect Index: Is a battery devised for a specific study, and consists of a reaching/finding objects task, a picture search task, a stick bisection (line bisection) and a gaze orientation. Each task was rated on a scale from 0-3 and scores were summed, with a higher overall score indicating more severe impairment (Kerkhoff et al., 2014).

Grey Scales: Is a measure used to quantify orienting of visual attention, in which participants are presented with a set of 26 items. Each item is a A4 piece of paper with two rectangles containing semi-continuous shades of grey ranging from black to white at the ends. The two rectangles are identical, but the mirror reverse of one another. The items thus have two grey scales, lying horizontally, one on top of the other. The participant is asked to decide which scale is darker, the top or the bottom (Tant et al. 2002).

Hand Judgement Test: Is a test of the ability of an individual to use mental transformations to identify right and left hands. This test involves line drawings of hands presented to the participant as a palm or the back of a hand in different six planes. The participants are then required to decide if the image is of a right or left hand. Their own hands are not visible during the task (Cooper et al. 1975; Reinhart et al. 2012).

Harrington-Flocks Visual Screener: Is a screening assessment is used to assess any visual field deficits. The test consists of 9 different patterns, each of which is designed to detect a visual field deficit in various locations. The pattern is in fluorescent ink. While the participant stares at a fixation point, a black light is shone on the card for 0.2-0.3 seconds before being turned off. At the point, the participant reports what they have seen. Scores are based on the number of targets missed within the affected field (Harrington & Flocks, 1954).

Joint Position Sense Test (JPST): Is a measure of how well stroke survivors can perceive the position of their joints in motion and standing still. The measure consists of 1 functional task repeated several times. This task involves the patient holding 2 different shaped objects that also weigh different from each other and then told to identify which one weighs more and which one has a stranger shape. The more times the patient (s) identifies which shape is heavier/unique, then the better the outcome. This measure has been shown to have good reliability and validity (Kattenstroth et al. 2013).

Judgement of Drawing of Two Houses: Is a test to investigate blindsight and insight as well as in cases of visual neglect. The participant is presented with two identical drawings of a house differing only by the presence of red flames on the left side of one of the houses. They are then asked to make a same- different judgement (Marshall et al. 1998; Rusconi et al. 2002).

King Devick Test (Subtests 1,2,3): Is a number of tasks that is generally carried out to quickly assess whether or not an individual has had a concussion. The first 3 tasks, however, are related to visual perception and processing. In each of the first three tasks, there are numbers placed on a page, with each task having a different, and progressively more complicated pattern. The participant is asked to read the numbers out loud from left to right as quickly as possible. Time, and errors made are used to assess task performance (Subotic, Ting & Cusimano, 2017).

Landmark Test: Is a test to differentiate between perceptual and motor-based errors made in the line bisection test in spatial neglect patients. In this test participants are presented with lines that are pre-bisected (with the landmark) centrally or asymmetrically to either the left or the right. Each line is presented in three spatial locations relative to the participant's midline (right, middle, left). They were informed that none of the lines were bisected medially and then required to point to the end of line that appeared to be closer to the landmark. Socring is based on the proportion of left and right judgements, particularly on the centrally located landmarks (Harvey et al. 1995).

Lane Tracking Task: Is a driving simulation task, whereby patients are instructed to maintain a position on the road, while 'sidewind' blows them off course. Patients must counteract these perturbations In either direction to maintain the proper position on the road. Mean lateral position and standard deviation are used to reflect their position on track and relative degree of oscillation (van Kessel et al., 2013).

Line Cancellation (Line Bisection) Test: see Bell's Test. AKA Schenkenberg Test. The line cancellation test is another version of a cancellation task used to detect the presence of neglect in stroke. Subjects are asked to cross out lines on a page filled with lines of various orientations. If lines are consistently crossed out closer to one side of each line than another, this can be interpreted as evidence of unilateral visual neglect. Any areas on the page where lines have failed to be crossed can also be used to evaluate neglect (Schenkenberg, Bradford & Ajax, 1980).

Line Crossing Test: See Line Bisection Test. This is a gamified version of the Line Bisection test.

Mobility Assessment Course: Ss an active assessment of neglect. Individuals are instructed to walk or navigate a wheelchair down a corridor without stopping. While navigating the corridor, patients had to point out marked targets that were set long their path. There is no time limit, and scores are computed as the difference between left and right omissions (Ten Brink et al., 2017).

Mone Road Map Test of Direction Sense: Is a measure of right/left orientation with and without mental rotation in space. Subjects must trace a dotted line through a city map and indicate the left/right direction taken at each turn.(Vingerhoets, Lannoo & Bauwens, 1996).

Motor-Free Visual Perception Test (MVPT): Is a measure of visual- perceptual ability independent of motor ability. Spatial relationships, visual discrimination, figure-ground, visual closure and visual memory are assessed. A total raw score is obtained based on the number of correct responses and standard score, percentile rank and age-equivalent score are generated. In the current version (MVPT-4), the test contains 45 items. The MVPT exhibits acceptable construct, content and criterion validity as well as good test-retest reliability and internal consistency (Brown & Peres, 2018).

Munich Reading Texts: Is one standardized version of reading task. There are six 180-word long paragraphs that are designed with simple linguistic structure and relatively short sentences. The task involves reading the text out loud as as quickly and accurately as possible. Any errors or omissions on the left or right side of the paragraph are counted and used to score the test (Kerkhoff et al., 1992).

Neale Analysis of Reading Ability: Is a measure of reading accuracy and comprehension through an orally read text. Participants are required to read a text appropriate to their level and accuracy scores are calculated based on the number of errors made during the reading. Comprehension questions are then asked to evaluate the participants understanding of the text they read (Neale 1997).

Ogden Figure Copying Task: Is a visuomotor figure copying task used to assess neglect. The figure is a small line drawing scene that consists of a (from left to right) a tree, a fence, a house and a different tree. Subjects are asked to copy down the drawing, and any errors or distortions based on the left and right side of the photo are noted and used to assess neglect (Ogden, 1985).

Orientation Lines Test: Is designed to assess visuospatial judgement. A test card is presented with 2 lines placed in various locations, and of different orientations. A reference card is provided, that displays 11 numbered lines all with different orientations. The patient must identify which angle the test card lines are, using the numbered reference line with the same angle. This has been shown as a sensitive measure for those suffering from unilateral brain damage (Benton et al., 1978).

Ota's Task: Is an assessment that is designed to distinguish between object-centered and body-centered forms of neglect. The task consists of 2 tests of similar nature. The first involves a piece of paper with 40 circles distributed randomly on the page. Some of these circles are incomplete, with missing sections either on the right side or the left. The second task involves 40 triangles on a page, also with some of the triangles missing sections on either the right side or the left. Participants are asked to circle the complete shapes and cross out the incomplete ones. Scoring is based on two variables. One is the amount of shapes incorrectly chosen on each side of the paper, and the other is the amount of shapes incorrectly chosen which were incomplete on the left side, versus those incomplete on the right (Ota et al., 2001).

Quadruplet Detection Task: Is a test used to assess visual detection across hemifields, this measure requires participants to detect a coloured shape in one of four quadrants from 3 black shapes. It assesses visual neglect based on response latencies and/or detection rate in regions of the visual field (Lucas et al. 2013; Vuilleamier et al. 2000).

Real Objects Test: Is a measure of visual neglect based off the Line Bisection test but using everyday objects. The test requires participants to reach for an everyday object (rolling pin, towel rail) in the center. Deviations from the center are used to test for the presence of visual neglect (Harvey et al. 2003; Robertson et al. 1997).

Rey-Osterrieth Complex Figure Test: Is a measure of visuo-spatial abilities and visual memory. The test requires the subject to copy a complex geometrical figure and, after an interval, reproduce the figure from memory without forewarning. The most used method of scoring the test is the Osterrieth method, a scoring system that provides a 36-point summary score based to the presence and accuracy of 18 units of the figure. The test has been shown to have excellent interrater reliability and good discriminant validity (Salvadori et al. 2018).

Rivermead Perceptual Assessment Battery: Is a test that consists of 16 different subtests, which can be divided into 8 different categories (form constancy, body image, cube copying, sequencing, object copying, figure ground, inattention and spatial awareness). It has been shown to have good inter-rater reliability, and correlates well with other psychological and behavioural assessment of visual perception (Lincoln & Edmans, 1989).

Semi-structured Scale for the Functional Evaluation of Hemi-attention: Used to functionally evaluate hemineglect, this scale includes two subscales corresponding to extra-personal space and personal space. Extra-personal space tasks include serving tea, dealing cards to four people sitting round a square table, describing three complex pictures, and describing a room. Personal space tasks include use of everyday objects: razor or make-up, comb, glasses. Items are scored from 0 (normal) -3 (severe). Inter- rater reliability has been reported as good (Azouvi, 1996; Zoccolotti et al. 1991).

Sentence Reading Test: A measure of visual spatial neglect, in which participants are required to read 6 sentences aloud. Scores are based on number of sentences read without omissions (Paolucci et al. 1996).

Single and Double-digit Cancellation: See Letter Cancellation Test. A target number (between 1 and 9) is randomly intermixed, with an even number of digits on the left and right side, with distractor numbers between 1 and 9. The participant is required to cross out all the occurrences of the target number. Scores are calculated based on the number of targets omitted in the right and left hemifields. The same procedure is followed for double- digit cancellation, however, the participant is given two numbers as targets (i.e. 3 and 6) (Kerkhoff et al. 2013).

Star Cancellation Test: Is part of a collection of cancellation tests which require the patient to mark/cancel target items printed on a paper placed directly in front. The target items for cancellation may be single target items (without distractors) e.g. Line Cancellation Test; target items (with distractors) e.g. Bells Test, Star Cancellation Test and Mesulam shape cancellation test (Parton et al., 2004). This test consists of a random array of verbal and non-verbal stimuli. The stimuli are 52 large stars (14mm), 13 randomly positioned letters and 19 short (3-4 letters) words are interspersed with 56 smaller stars (8mm) which comprise the target stimuli. The patient is instructed to cancel all the small stars. Two examples of small stars are pointed out and cancellation of two central stars is demonstrated. As with the letter cancellation task, the test sheet can be subdivided into columns to calculate the number and location of errors.

Subjective Neglect Questionnaire: Is a questionnaire for detecting everyday problems typical of individuals with unilateral spatial neglect. Participants are asked to rate the frequency of 19-neglect related issues, such as bumping into furniture, telling time or navigating wheelchair, occurring within the past month. The questionnaire has been found to correlate with the star cancellation test significantly, however neglect participants have often been found to rate their experiences differently from their relatives (Towle et al. 1991).

Tangent Screen Exam: Is a comprehensive assay of an individual's visual field. It requires the participant to focus on the center of a screen, while targets are presented in their periphery. Participants will inform the assessor when they are able to see the target. Using this information, a detailed map of the visual field can be produced, and any deficits identified (West, 1988).

Target Cancellation: See Bell's Test. This is a measure of spatial neglect, in which the participant is required to circle targets that have been mixed in with distractors in 7 columns on sheet of paper. The angular gyrus is critical for task performance. This measure has been found to correlate highly with the Line Bisection test but is more sensitive (Gauthier et al. 1989; Molenberghs et al. 2011).

Testing Battery for Attentional Performance: Is a series of tests developed to assess all facets of attentional processing. The computerized testing consists of 13 sub-tests (eg. Alertness, Eye Movements, Working Memory etc…) that assess various components of cognition and behaviour related to attention (Zimmermann & Fimm, 1993).

Toulouse Pieron Cancellation Test: Is a form of cancellation tests which require the patient to mark/cancel target items printed on a paper placed directly in front. The Toulouse-Piéron Cancelation Test (TP) is a classic psychometric tool for the assessment of selective/sustained attention, processing speed and visuo-perceptual abilities. The TP can be administered individually or in group and the completion time is 10 minutes. The test consists of a blank sheet of paper with twenty-five lines and forty small squares per line. The squares are distinguished from each other through the orientation of the rows on the outer surface: in each square the stroke is oriented in eight possible directions. The subject is required to cross out three targets presented in the header. For each line the evaluator must register the total number of hits (H), i.e., the number of targets correctly crossed out by the subject, errors (E), i.e., when irrelevant targets are crossed out in violation of the instructions (false-positives), and omissions (O), i.e., when the targets are not crossed out (false-negatives) (Lima et al. 2021).

Unawareness and Behavioural Neglect Index: See Catherine Bergego Scale. This measure is based off the Catherine Bergego Scale, but also contains six measures intended to evaluate level of awareness in daily life. It is a 10- item scale with the remaining four measures of behavioural neglect in activities of daily living. The index is measured on a four- point scale (0 behavior never occurs – 3 behaviour occurs daily) (Kerkhoff et al. 2014).

Verbal Cancellation Test (Letter Cancelation): Is another form of cancellation test (see Ballon's and Bell's Tests). This one howevever uses letters and other 'verbal' stimuli as opposed to non-verbal symbols (Brucki & Nitrini, 2008).

Vienna Test System – Peripheral Perception: Is an assessment of peripheral perception, included in the neuropsychological test and training program "Vienna Test System Neuro". The test is a modified tangent screen test, where an individual is asked to track a target on a computer screen while lights are flashed in different peripheral locations. The participant then identifies when they have seen a peripheral stimulus (Cazzoli et al., 2012).

Visual Scanning Tasks: can take on many forms but comprise of the same basic principles. Often a photo or a group of symbols is used. In this task, the individual is asked to identify certain target stimuli or objects within an image, and the number of stimuli omitted on either side of the photo are used to assess neglect (Cazzoli et al., 2012)

Visual Subjective Straight Ahead: Is a task used to assess neglect. It involves a luminous rod that p[patients are instructed to translate and rotate so as to align it with the longitudinal midline axis of the head and body (Saj et al., 2006).

Wundt- Jastrow Illusion Test: Is used for detection of unilateral neglect, this test has 40 differing stimuli consisting of two fans identical in shape and surface. Each of the pairs of fans has one of two orientations (right or left direction and upward or downward convexity). The participant is the required to indicate which of the two fans is larger, the top or the bottom (Massironi et al., 1988).

Learning & Memory

Corsi Vertical Span Test: Is a measure designed to assess memory independently from unilateral neglect. It is a measure of short-term visuospatial and working memory. The examiner taps a series of blocks in succession, one at a time, then the participant is asked to tap the blocks either in the same sequence (forward test) or in reverse (backward test). Backwards tests are thought to involve executive function to a greater degree. The test can also be computerized. The 'vertical' aspect simply means the blocks are aligned vertically on the participants midline, so as to prevent any unilateral neglect from affecting the results. This test can also be computerized. Span tests have shown to be valid assessments of working memory and are specific, however their sensitivity and symptom validity are variable (Wentink et al. 2016; Berch, Krikorian & Huha, 1998).

Global Cognition

Mini Mental Status Examination (MMSE): Is a brief screening tool and quantitative assessment of cognitive impairment. It is one of the most commonly used instruments for this purpose. The exam consists of 11 questions/tasks in 7 cognitive domains: 1) orientation to time; 2) orientation to place; 3) registration of 3 words; 4) attention and calculation; 5) recall of 3 words; 6) language; and 7) visual construction. The test is scored out of 30 possible points, with a score of 18-24 denoting mild impairment and a score of 0-17 denoting severe impairment. The test has been found to be valid as a screening tool, and is sensitive for detecting moderate/severe impairment, but not mild impairment. It has good interrater reliability. The MMSE is appropriate for screening for post-stroke cognitive impairment (Bour et al. 2010; Tombaugh & McIntyre, 1992; Dick et al. 1984).

Ravens Coloured Progressive Matrices: Is a measure of intelligence that consists of a series of multiple-choice items of abstract reasoning. Each item depicts an abstract pattern in a two by two or three by three matrix; all cells contain a figure except for one cell in the corner. Participants are asked to identify the missing segment that would best complete the pattern. The test is shown to be a reliable measure of visuoperceptual, and memory cognitive functioning in persons with motor impairment and speech deficits (Brouwers et al. 2009; Pueyo et al. 2008).

Reaction Time Assessments: Reaction time assessments measure both the processing speed and motor output of responding to a given stimulus (Woods et al. 2015). There is a wide array of reaction time assessments that are designed to mimic the underlying topic being studied. In post-stroke rehabilitation, reaction time is essential to determining driving ability (breaking reaction) among other activities of daily living.

Trail-making Test A: Is a neuropsychological instrument often used in patients with suspected cognitive impairment to measure the cognitive domains of processing speed, sequencing, mental flexibility, and visual-motor skills. The most widely used version comprises of 2 parts: A and B. In part A, the patient uses a pencil to connect a series of 25 encircled numbers in numerical order. In part B, the patient connects 25 encircled numbers and letters in numerical and alphabetical order, alternating between the numbers and letters. The primary variable of interest is the total time to completion for parts A and B, which is used to obtain a ratio of total time to complete part B/A for all trials. A lower value (closer to 1.0) is indicative of better performance. Part A of the measure is thought to be a test of visual search and motor speed skills, whereas part B is considered also to be a test of higher-level cognitive skills such as mental flexibility. The measure has excellent construct validity and interrater reliability, however may be susceptible to practice effects at shorter intervals (Bowie & Harvey 2006; Piper et al. 2015).

Trail-making Test B: Is a neuropsychological instrument often used in patients with suspected cognitive impairment to measure the cognitive domains of processing speed, sequencing, mental flexibility, and visual-motor skills. The most widely used version comprises of 2 parts: A and B. In part B, the patient connects 25 encircled numbers and letters in numerical and alphabetical order, alternating between the numbers and letters. The primary variable of interest is the total time to completion for parts A and B, which is used to obtain a ratio of total time to complete part B/A for all trials. A lower value (closer to 1.0) is indicative of better performance. Part A of the measure is thought to be a test of visual search and motor speed skills, whereas part B is considered also to be a test of higher-level cognitive skills such as mental flexibility. The measure has excellent construct validity and interrater reliability, however may be susceptible to practice effects at shorter intervals (Bowie & Harvey 2006; Piper et al. 2015).

Test of Everyday Attention (TEA): Is a measure of attention. The test attempts to assess attention in an ecologically valid manner. It consists of 8 subtests including tests of: sustained attention (elevator counting and lottery), selective attention (map search and telephone search) switching attention (visual elevator), working memory (elevator counting with distraction and auditory elevator with reversal), and divided attention (telephone search while counting). The test has been shown to have good/excellent test-retest reliability in a chronic stroke population (Chen et al. 2013; Robertson et al. 1994).

Wechsler Adult Intelligence Scale (WAIS): Is a widely used IQ test designed to measure a person's intelligence and cognitive ability. The original WAIS was created in 1955, and there have been many revisions since, including the WAIS-R, WAIS-III, and WAIS-IV. WAIS-R is a revised form of the WAIS and consists of six verbal (information, comprehension, arithmetic, digit span, similarities, vocabulary) and five performance (picture arrangement, picture completion, block design, object assembly, digit symbol) subtests. The current edition, WAIS-IV, includes four core indices measuring verbal comprehension, perceptual reasoning, working memory, and processing speed. The WAIS scales have long been considered the gold standard measure of intellectual functioning and have demonstrated excellent validity and reliability (Denhart 2018).

Motor Rehabilitation

Action Research Arm Test (ARAT): Is a commonly used observational measure to quantify upper extremity motor rehabilitation after stroke. It consists of 4 subtests: grasp, grip, pinch and gross motor. It is scored on a scale from 0 (no movement) to 3 (normal movement). ARAT has been shown to have good predictive validity in mild to moderate stroke without severe cognitive impairment as well as excellent test-retest and interrater reliability (Chen et al. 2012; Platz et al. 2005).

Box and Block Test (BBT): Is a measure of gross unilateral manual dexterity in stroke survivors. This measure consists of 1 functional task. This task involves a patient moving as many wooden blocks as possible from one end of a partitioned box to the other, in a span of 60 seconds. Patients are scored based on the number of blocks they transfer (the higher the blocks transferred, the better the outcome). The measure has been shown to have good reliability and validity. (Higgins et al. 2005; Platz et al. 2005).

Fugl-Meyer Assessment: Is one of the most commonly used measures of motor impairment post-stroke (Gladstone et al. 2002). The five domains of the assessment include motor rehabilitation, sensory function (maximum score of 24), balance (maximum score of 14), joint range of motion (maximum score of 44), and joint pain (maximum score of 44).The domain of motor rehabilitation can be divided into upper extremity (maximum score of 66) and lower extremity (maximum score of 34) subscales. Each of the subscales or domains can be administered individually to stand on their own. This assessment has demonstrated excellent Inter/intra-rater reliability, internal consistency, and criterion validity (Duncan et al. 1983; Lin et al. 2004; Malouin et al. 1994).

Functional Test for the Hemiparetic Upper Extremity (FTHUE): Is a measure used to quantify functional movement ability of the hemiparetic arm in stroke patients. The test consists of a series 17 timed activities of daily living that focus on completion of everyday tasks involving the impaired limb (e.g., zipping a jacket, placing a pillow in a pillowcase). The tasks are arranged in seven levels by degree of difficulty ranging from simple single joint movements at the shoulder to complex multi-joint movements involving the hand and arm. The test has been shown to have high inter- and intra-rater reliability (Wilson et al. 1984).

Motricity Index: Is a measure of motor rehabilitation involving strength testing of six muscle actions. The muscle actions are graded and assigned weighted scores based on movement present and resistance taken. Weighted scores for each action are then added to obtain scores for each of the three subscales of the measure (arm, leg, and trunk). Each section is scored from 0 to 100, where 0 indicates complete motor rehabilitation loss. The measure is found to be reliable and valid for use with stroke patients (Safaz et al. 2009; Cameron & Bohannon 2000).

Nine Hole Peg Test (9HPT): Is a measure of overall manual dexterity in stroke survivors. The measure consists of 1 functional task. Patients are asked to take 9 pegs out of a container and insert them into the pegboard. Once all 9 pegs are inserted, they are then taken out of the pegs as quickly as possible and placed back in the container. Patients are scored on how quickly they can insert and take out the pins, so the faster the time, the better the outcome. This measure has been shown to have good reliability and concurrent validity (da Silva et al. 2017).

Rivermead Mobility Index (RMI): Is a self-reported measure of the ability of a stroke patient to complete functional tasks. This measure consists of 15 functional tasks (e.g. turning over in bed, stairs, walking outside) which are then rated on 2-point scale completed by the patient in the form of a questionnaire (0=cannot complete task, 1=can complete task). This measure is has been shown to have good reliability and validity (Lennon et al. 2000; Colleen et al. 1991).

Trunk Control Test: Is a measure that assesses the level of motor impairment a stroke patient has in the trunk/abdominal region. This measure consists of 4 functionals tasks (e.g. roll to weak side, roll to strong side, balance on a sitting position at the edge of a bed, and sit up from lying down). For each task the patient receives points (0=cannot complete task, 12=completes task with some assistance, 25=completes task independently) for a maximum of 100 points. This measure has been shown to have good reliability and validity (Duarte et al. 2002; Franchignoni et al. 1997).

Wolf Motor Function Test: Is a measure that quantifies upper extremity motor ability in stroke survivors. The measure consists of 17 tasks (e.g. lifting arm up using only shoulder abduction, picking up a pencil, picking up a paperclip). These tasks are then subdivided into 3 areas: functional tasks, measures of strength, and quality of movement. Patients are scored on a 6-point scale (1=cannot complete task, 6=completes task as well as the unaffected side. This measure has been shown to have good reliability and validity (Wolf et al. 2005; Wolf et al. 2001).

Stroke Severity

Canadian Neurological Scale (CNS): Is a measure used to assess neurological status of acute phase stroke patients. Ten clinical domains including motor rehabilitations, both weakness and response of arm, face and legs are measured along with mentation (speech, orientation and level of consciousness). The scale has demonstrated reliability and concurrent validity (Cote et al. 1989; Cote et al. 1986).

National Institutes of Health Stroke Scale (NIHSS): Is a measure of somatosensory function in stroke patients during the acute phase of stroke. This measure contains 11 items and 2 of the 11 items are passive range of motion (PROM) assessments delivered by a clinician to the upper and lower extremity of the patient. The other 9 items are visual exams conducted by the clinician (e.g. gaze, facial palsy dysarthria, level of consciousness). Each item is then scored on a 3-point scale (0=normal, 2=minimal function/awareness). This measure has been shown to have good reliability and validity (Heldner et al. 2013; Weimar et al. 2004).

Modified Rankin Scale (MRS): Is a measure of functional independence for stroke survivors. The measure contains 1 item. This item is an interview that lasts approximately 30-45 minutes and is done by a trained clinician. The clinician asks the patient questions about their overall health, their ease in carrying out ADLs (cooking, eating, dressing) and other factors about their life. At the end of the interview the patient is assessed on a 6-point scale (0=bedridden, needs assistance with basic ADLs, 5=functioning at the same level as prior to stroke). This measure has been shown to have good reliability and validity (Quinn et al. 2009; Wilson et al. 2002).

Activities of Daily Living

Activities of Daily Living Questionnaire: consists of 30 items which can be grouped into 6 subscales based on the type of problem (personal care, reaching, grasping, spatial orientation, time orientation, awareness of the deficit). Answers were recorded by a family member or hospital staff, and each item was rated on a scale from 0-3, where higher scores indicated greater levels of impairment. This Questionnaire was a modified and extended version Towle and Lincoln's questionnaire (see Subjective Neglect Questionnaire) (Schindler et al., 2002).

Barthel Index (BI): Is a measure of one's ability to perform activities of daily living. The scale consists of 10 items: personal hygiene, bathing, feeding, toilet use, stair climbing, dressing, bowel control, bladder control, ambulation or wheelchair mobility and chair/bed transfers. Each item has a five-stage scoring system and a maximum score of 100 points, where higher scores indicate better performance. The scale is suitable for monitoring on the phone and is shown to have a high inter-rater reliability (Park 2018).

Functional Independence Measure (FIM): Is an 18-item outcome measure composed of both cognitive (5-items) and motor (13-items) subscales. Each item assesses the level of assistance required to complete an activity of daily living on a 7-point scale. The summation of all the item scores ranges from 18 to 126, with higher scores being indicative of greater functional independence. This measure has been shown to have excellent reliability and concurrent validity in its full form (Granger et al. 1998, Linacre et al. 1994; Granger et al. 1993).

Help Index (Help Scale): A measure of stroke patients' functionality in activities of daily living. Participants perform 10 activities of daily living and are rated by a nurse on a scale from one (no help needed) to five (fully reliant on nurse for completion of task). Items are as follows: 1. Correct arm placing, 2. Correct leg placing. 3. Dressing. 4. Shaving/combing. 5. Orienting in the rehabilitation ward. 6. Orienting in the patient's room. 7. Eating. 8. Putting on glasses. 9. Finding persons or objects in the room. 10. Transfers from bed to chair and back (Kerkhoff et al. 2014).

Veteran Low Vision Visual Functional Questionnaire: The Veterans Affairs Low-Vision Visual Functioning Questionnaire-48 (VA-LV-VFQ48) is a 48-item questionnaire produced by Stelmack et al. 2005 to determine the patient centered outcome of low-vision patients undergoing low vision rehabilitation (LVR) (di Maggio et al. 2020). The 48-item content reflects the activities that are targeted by, which depend heavily on vision, and are important to most patients. The self-reported answers are similar to ADLs and IADLs such as getting dressed and reading signs. There is strong test–retest concordance with an ICC of 0.98 (95% confidence interval [CI]: 0.96 – 0.99) (Stekmack et al. 2004).

Introduction: Rehabilitation of Neglect Following a Stroke

Defining Neglect

Unilateral spatial neglect is one of the disabling features of a stroke, and is defined as a failure to report, respond, or orient to sensory stimuli presented to the side contralateral to the stroke lesion site (Heilman & Watson, 1985). Many terms are used interchangeably in the literature to describe unilateral spatial neglect, including unilateral neglect, hemi-inattention, visual neglect and hemi spatial neglect. Clinically, the presence of severe unilateral spatial neglect is apparent when a patient often collides into his/her surroundings, ignores food on one side of the plate, and attends to only one side of his/her body (Wyness, 1985). However, symptoms of unilateral spatial neglect have to be quite severe for this impairment to be observed easily during the performance of functional activities (Cherney et al., 2001; Mesulam, 2000) and are more obvious when present during the early stages post stroke. More subtle forms of unilateral spatial neglect may go undetected in a hospital setting but are a major concern for client function and safety upon discharge. Mild symptoms of unilateral spatial neglect become apparent during high-level activities such as driving, working or while interacting with others.

Neglect is a complex combination of clinical presentation that differs from patient to patient. Unilateral spatial neglect can be classified into egocentric and allocentric.

- Egocentric neglect: Neglect of the own body or personal space, tendency to neglect the opposite side of the lesion, in reference to the midline the body.
- Allocentric neglect: Can present in 2 ways, either peripersonal neglect or extrapersonal neglect.
    - Peripersonal neglect refers to neglect towards the contralesional side of object/environment within the patient's normal reach (within reaching space).
    - Extrapersonal neglect refers to neglect towards the contralesional side of each object/environment beyond the patient's normal reach (beyond reaching space).

Incidence of Neglect

Reported incidence of unilateral spatial neglect ranges from 8% to 95%, however, sample selection, definitions of unilateral spatial neglect and methods used to assess unilateral spatial neglect are not consistent in all studies that report its incidence (Bowen et al., 1999). Pedersen et al. suggested that the 23% rate of occurrence found in the Copenhagen stroke study is a more reasonable estimate (Pedersen et al., 1997). More recently, Appelros et al. (2002) reported 23% of patients included in a stroke incidence study to have visual-spatial neglect while 8% were reported to have personal neglect. The presence of neglect has been associated with both severity of stroke and age of the individual (Appelros et al., 2002; Pedersen et al., 1997; Ringman et al., 2004), but not with gender, prior stroke, comorbidities or handedness (Pedersen et al., 1997; Ringman et al., 2004). Linden et al. (2005) reported that elderly stroke patients with persistent neglect 20 months following the stroke event demonstrated more visual field impairments, cognitive impairments and dementia than stroke patients with no neglect. The frequency of these impairments was associated with the severity of neglect. The most common cognitive impairment among stroke patients with neglect was reported to be apraxia, either constructional or ideational-instrumental (Linden et al., 2005).

Anatomical Substrates of Neglect

Unilateral spatial neglect is more common in patients with right-sided lesions than left. In the Copenhagen Stroke Study (Pedersen et al., 1997), 42% of individuals with a right-sided lesion were reported to have unilateral spatial neglect compared to only 8% of patients with a left hemisphere lesion. A study of 1,282 acute stroke patients (Ringman et al., 2004) revealed that 43% of patients with right-sided lesions experienced neglect compared to 20% of patients with left-sided lesions ($p<0.001$). At 3 months following stroke onset, 17% of patients with right-sided lesions continued to suffer from neglect compared to only 5% of patients with left-sided lesions.

There is evidence from positron emission tomographic (PET) scan analyses (Corbetta et al., 1993) and a systematic review of 17 studies (Bowen et al., 1999) that the right hemisphere regulates attention. Neuroanatomical findings have identified that the left hemisphere is responsible for modulating arousal and attention for the right visual field, whereas the right hemisphere controls these processes in both right and left visual fields (Feinberg et al., 1990). This may explain why unilateral spatial neglect is not typical for those with left hemisphere damage (LHD) post-stroke because the intact right hemisphere is capable of compensating for perceptual deficits that result from LHD (Feinberg et al., 1990) (See Figure 1. for an illustration of visual neglect and the compensatory action of the right hemisphere).

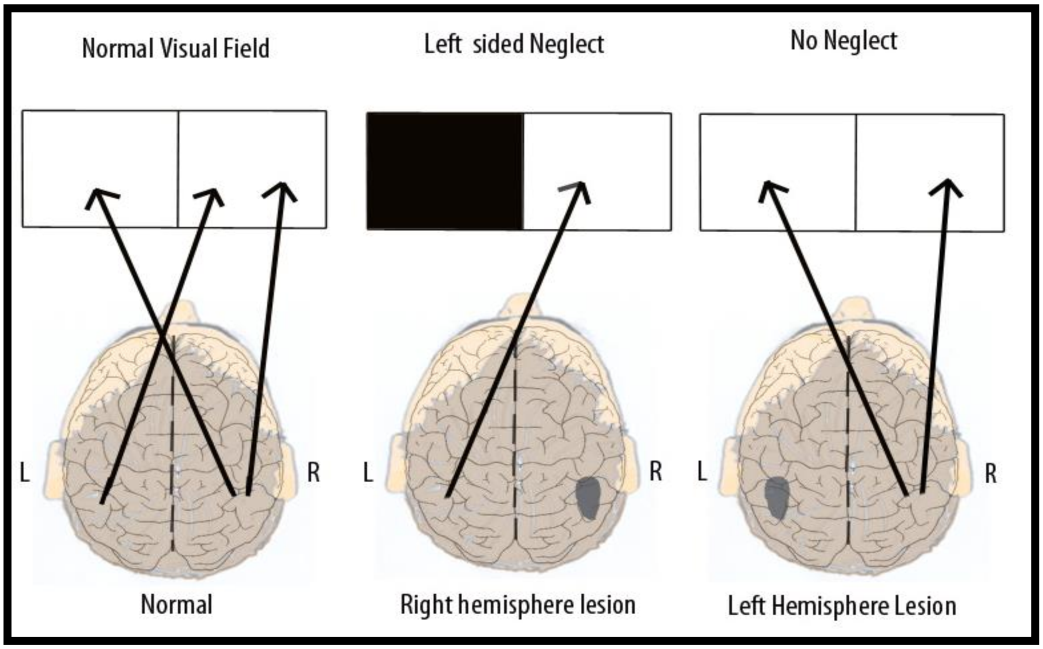


Figure 1. Lesion location and resulting neglect

In a review of the literature, Ferro et al. (1999) reported that more severe and more stable neglect has been associated with parietal and frontoparietal lesions. Paolucci et al. (2001) reported unilateral spatial neglect in right brain damaged individuals post stroke to be more frequently associated with MCA territory infarcts with large, cortical frontal temporoparietal lesions ($p<0.001$) and with cortical parietotemporal lesions ($p<0.05$). A study of 1,282 patients with acute stroke reported that unilateral neglect was most frequently associated with cortical lesions and in the temporal, parietal, and frontal lobes (Ringman et al., 2004).

Spontaneous Recovery and Neglect

It has been reported that incidence of unilateral spatial neglect declines one month or more following the stroke event (Katz et al., 1999; Paolucci et al., 2001). In their 1999 review, Ferro and colleagues reported that, in many cases, the most conspicuous manifestations of hemi-spatial neglect resolved spontaneously within the first 4 weeks following a stroke event (Ferro et al., 1999). While further recovery may continue over the period of one year, it is not as significant as the recovery seen in the acute phase post stroke.

The degree of recovery may vary according to type of neglect. Appelros and colleagues demonstrated that patients experiencing neglect of peripersonal space experienced complete recovery less often than those patients experiencing either neglect of far space or of personal space (Appelros et al., 2004). In the latter cases, complete recovery was seen by 6 months post stroke in 52% and 46% of cases, respectively compared with 13% of patients experiencing neglect of peripersonal space. For all three types of neglect, there were no further significant improvements seen from 6 months to one-year post stroke (Appelros et al., 2004).

The Impact of Neglect Post-Stroke

Unilateral spatial neglect has been reported to have a negative impact on functional recovery, length of rehabilitation stay, and need for assistance after discharge. While the majority of patients diagnosed with visuospatial inattention post-stroke recover by three months, those with severe visuospatial inattention on initial presentation have the worst prognosis (Diamond, 2001). Paolucci et al. (2001) reported unilateral spatial neglect to be a clearly negative prognostic factor. The presence of unilateral spatial neglect was associated with poorer functional outcome, poorer mobility, longer length of stay in rehabilitation and a greater chance of institutionalization upon discharge from rehabilitation. A 2005 study reported the presence of unilateral spatial neglect to be a significant predictor of length of stay (Gillen et al., 2005). In that study, patients with right-sided stroke and unilateral spatial neglect were matched for severity of functional deficits (FIM scores) at admission to rehabilitation with patients with right-sided stroke and no unilateral spatial neglect. It was determined that among patients with similar functional deficits, the presence of unilateral spatial neglect was associated with longer lengths of stay and slower rates of improvement (Gillen et al., 2005).

Patients with unilateral spatial neglect may be more impaired at the beginning of rehabilitation than patients without unilateral spatial neglect (Katz et al., 1999), particularly if they are experiencing both spatial and personal neglect (Wee & Hopman, 2008). While significant gains may be made throughout the course of rehabilitation, patients with unilateral neglect, whether left or right, spatial or personal, tend to be more functionally disabled at discharge (Wee & Hopman, 2008). Wee and Hopman (2008) reported that the presence of both unilateral spatial neglect and unilateral personal neglect was associated with increased safety risk (e.g. collisions with objects or people, risk to unattended side of the body, lack of insight regarding cause of injury), decreased likelihood of discharge home, longer lengths of stay in rehabilitation, increased incidence of shoulder or hand complications and lower FIM scores at admission and discharge from stroke rehabilitation (Wee & Hopman, 2008). Similar results were also observed in a more recent study conducted by Timbeck et al. (2013). The authors found that visuospatial neglect was significantly associated with worse admission and discharge FIM scores and found that all six individuals with neglect were discharged to a supportive living environment.

The presence of unilateral spatial neglect has been identified as a significant predictor of functional dependence in ADLs (Appelros et al., 2002; Katz et al., 1999) and poorer performance in IADLs at six months (Katz et al., 1999) and one year post discharge from rehabilitation (Jehkonen et al., 2000). The presence of unilateral spatial neglect explained 73% of the total variance in IADL at a three-month follow up, 64% at six months and 61% at one-year in 57 subjects post stroke (Jehkonen et al., 2000). Appelros et al. (2003) reported unilateral spatial neglect to be a significant predictor of both mortality (OR=2.7) and dependency (OR=4.0) one year after the stroke event. In addition, substantial proportions of individuals (79 – 82%) with neglect require home assistance following discharge (Appelros et al., 2003; Katz et al., 1999) or may be discharged to nursing home care (Appelros et al., 2003; Paolucci et al., 2001).

It should be noted that not all authors report strong associations between neglect and functional outcome. Pedersen et al. (1997) found hemi-neglect to have no influence on functional prognosis, length of rehabilitation or mortality. A review of studies evaluating the impact of neglect on functional outcomes following stroke found that, in 25 of 26 studies from 1996 – 2005, neglect was reported to be a significant predictor of poorer functional outcome either alone or in combination with one or more variables such as age, hemiparesis, severity of stroke, anosognosia or other cognitive impairments (Jehkonen et al., 2006). The authors note that the reported relationship between neglect and functional outcome is dependent upon both how and when variables are assessed, which potential predictors are included in the analysis and how patients are selected for study inclusion. Definitions of neglect were inconsistent and few studies provided detailed operational definitions of the construct (Jehkonen et al., 2006).

Language impairments reported in those with LHD post-stroke can influence the validity of assessments requiring receptive and expressive speech, such that this population is frequently excluded in studies evaluating unilateral spatial neglect. For example, when assessed with the Rivermead Perceptual Assessment Battery (Whiting et al., 1985), 47% of non-dysphasic subjects with LHD post stroke were identified as having unilateral spatial neglect (Barer et al., 1990). When individuals with language deficits were included in the sample, almost every dysphasic subject (97%) with LHD screened positive for unilateral spatial neglect within 48 hours post-stroke (Barer et al., 1990), suggesting that the lack of assessment of patients with aphasia may account, in part, for the low incidence of unilateral spatial neglect reported in those with LHD. While unilateral spatial neglect is commonly associated with a right-sided stroke, evidence from the literature suggests that all patients with stroke might benefit from unilateral spatial neglect screening.

Screening and Assessments for Neglect

Clinicians are responsible to systematically screen all stroke patients for unilateral spatial neglect as a routine part of clinical examination. The Canadian Best Practice Recommendations for Stroke Care 2013 emphasize the all patients with stroke should be screened for perceptual deficits as part of the broader rehabilitation assessment process. Clinical Guidelines for Stroke have recommended that it is “best practice” for acute care clinicians to screen for cognitive deficits, which include visual perception and unilateral spatial neglect, during routine neurological examination within 48 hours of the client regaining consciousness post-stroke (Royal College of Physicians, 2012). Clinicians have the responsibility to systematically screen all clients for cognitive impairments and disabilities post stroke, including unilateral spatial neglect, with the use of standardized assessment tools and stroke scales (Agency for Health care Policy and Research (AHCPR), 1994; Kelly-Hayes et al., 1998; Royal College of Physicians, 2012; VA DoD Clinical Practice Guideline, 2010).

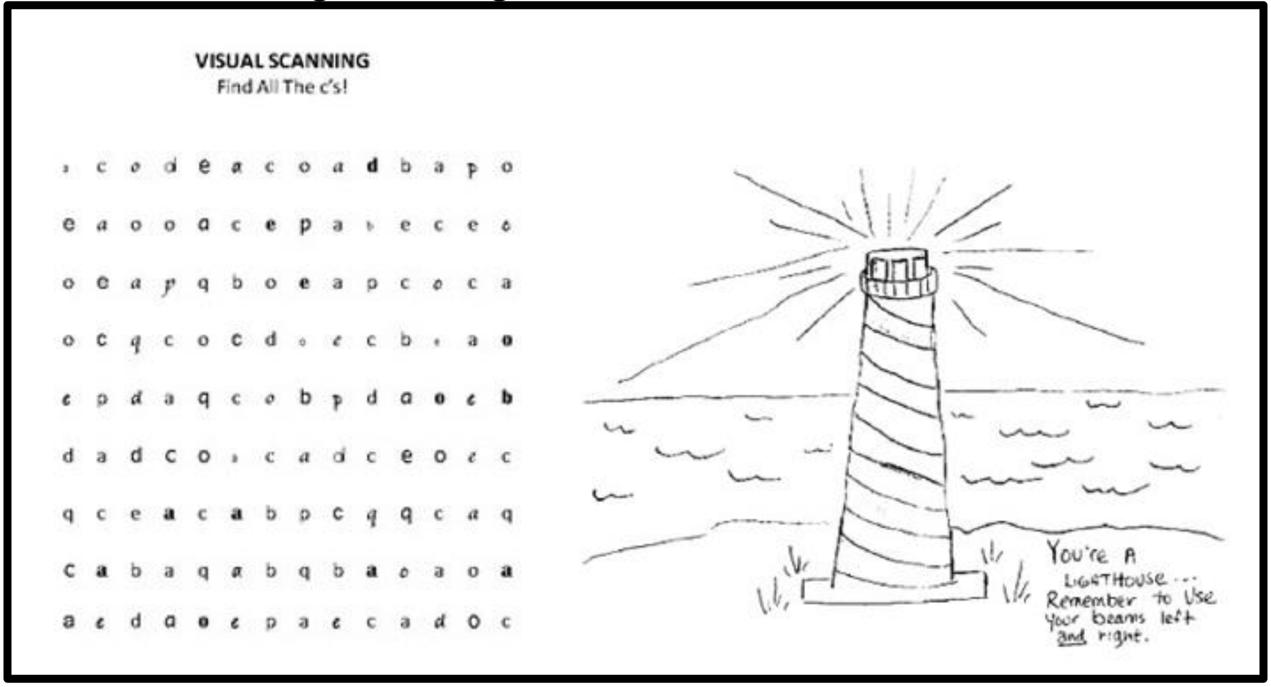
Screening and assessment can be performed via pen & paper test, observation of behaviour/activity or a combination of both. As unilateral spatial neglect is a complex disorder with both an egocentric and allocentric component, it is important to note that a single test may detect a specific type of neglect, thus a battery of tests are often more sensitive that single test (Parton et al., 2004).

A literature review reported that there are currently 61 standardized and non-standardized assessment tools available to assess unilateral spatial neglect in each of the hemispaces at both impairment and disability levels (Menon & Korner-Bitensky, 2004). Common pen and paper tests for screening are the Line Bisection Test and Cancellation Tests. There are various versions of cancellation tests which require the patient to mark/cancel target items printed on a paper placed directly in front. The target items for cancellation may be single target items (without distractors) e.g. Line Cancellation Test; target items (with distractors) e.g. Bells Test, Star Cancellation Test and Mesulam shape cancellation test (Parton et al., 2004).

Behavioural/activity observations are also used to assess client's personal space by assessing their performance in functional activities, such as using a comb or applying makeup as in Comb and Razor Test and Catherine-Bergego Scale which is comprised of 10 different daily activities including grooming and eating (Azouvi et al., 2003). A combination of pen and paper tests and observation of behavioural/ activity e.g. Behavioural Inattention Test is used to assess unilateral spatial neglect in more detail, though it is more time consuming.

Behavioural therapy-based Intervention

Visual Scanning Training



Adopted from: https://www.teacherspayteachers.com/Product/Visual-Scanning-A-to-Z-3765433 and https://www.sciencedirect.com/topics/psychology/cancellation-test

Individuals with neglect are unable to visually scan their whole environment (Weinberg et al., 1977), particularly experiencing deficits on the side affected by their stroke (Ladavas et al., 1994). The literature concerning remediation of visuospatial deficits encompasses two basic approaches: (1) abilities and behaviours (visual scanning or visual perception), and (2) functional or constructional activities requiring spatial ability (Cicerone et al., 2000; Pierce & Buxbaum, 2002). The goal of these interventions is to improve visual functioning, allowing individuals to re-learn to scan and explore the affected hemifield.

14 RCTs evaluated visual scanning interventions for the rehabilitation of neglect. Six RCTs compared visual scanning to conventional rehabilitation in (Chan & Man, 2013; Modden et al., 2012; Ferreira et al., 2011; Niemeier et al., 2001; Paolucci et al., 1996; Antonucci et al., 1995). Visual scanning was also investigated in combination with saccade training and task-specific training to task specific training alone in one RCT (van Wyk et al., 2014). Dual task visual scanning was compared to single task visual scanning in one RCT (van Kessel et al., 2013). Visual scanning was also compared to limb activation and prism adaptation in one RCT (Prifitis et al., 2013). Computerized visual scanning was compared to standard computer use in one RCT (Robertson et al., 2020). DYNAVISION was compared to a waitlist control in one RCT (Crotty et al., 2009). Neuro Vision Tech was compared to individualized therapy in one RCT (Crotty et al., 2018). While Usual Field of View (UFOV) was compared to a computer-based visuoperception intervention in one RCT (Mazer et al., 2005).

The methodological details and results of all 14 studies are presented in Table 1.

Table 1. RCTs evaluating visual scanning interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Visual Scanning Training vs. Conventional Rehabilitation		
Chan & Man (2013) RCT (6) N_{Start}=40 N_{End}=40 TPS=Acute	E: Visual Scanning Training + Conventional Rehabilitation C: Conventional Rehabilitation Only Duration: 45min/d, 3d/wk for 4wk	• Catherine Bergego Scale (+exp) • Mini Mental State Examination (-) • Modified Barthel Index (-) • Behavioural Inattention Test - Conventional Subtest (-)
Modden et, al. (2012) RCT (7) N_{start}=45 N_{end}=42 TPS=Subacute	E1: Computerized Compensatory Therapy E2: Restorative Computerized Training C: Standard Occupational Therapy Duration: 30min/d, 5d/wk for 3wk	E1/E2 vs C Testing Battery for Attentional Performance: • Visual Field (-) • Phasic Alertness (-) • Visual Scanning (-) • Behavioural Inattention Test: Cancellation Tasks (-) Reading Performance: • Errors (-) • Speed (-) • Barthel Index (-) E1 vs E2 Testing Battery for Attentional Performance: • Visual Field (-) • Phasic Alertness (-) • Visual Scanning (-) • Behavioural Inattention Test: Cancellation Tasks (-) Reading Performance: • Errors (-) • Speed (-) • Barthel Index (-)
Ferreira et al. (2011) RCT (5) N_{start}=10 N_{end}=10 TPS=Chronic	E1: Visual Scanning Training + Physical Therapy (PT) E2: Mental Practice Training + PT C: PT only Duration: 1hr/d, 2d/wk for 5wk	E1 vs C • Behaviour Inattention Test (+exp$_1$) • Functional Independence Measure • Total Score (-) • Self-Care: (+exp$_1$) E2 vs E1/C • Behaviour Inattention Test (-) • Functional Independence Measure • Total Score (-) • Self-Care: (-)
Niemeier et al. (2001) RCT (5) N_{start}=19 N_{end}=19 TPS=Acute	E: Lighthouse Strategy Training + Usual Rehabilitation (3x 30min sessions) C: Waiting list with No Treatment Duration: Until Discharge (avg 3wks)	• Route-Finding Task (+exp) • Rancho Los Amigos Cognitive and Behavioural Scale (-) • Mesulam Verbal Cancellation Test (-) Functional Independence Measure: • Walking/Wheelchair (+exp) • Problem Solving (+exp) • Attention (-) • Safety Judgement (-) • Grooming (-) • Feeding (-) • Bathing (-) • Dressing (-) • Toileting (-) • Reading (-) • Writing (-) • Community Re-entry (-)
Paolucci et al. (1996)	E: Neglect Specific Training	• Rivermead Mobility Index (+exp)

Cross-over RCT (6) N_{start}=59 N_{end}=51 TPS=Subacute	C: General Cognitive Treatment Duration: 1hr/d, 5d/wk for 8wk	• Barthel Index (+exp) • Canadian Neurological Scale (-) • Letter Cancellation Test (+exp) • Albert's Barrage Test (-) • Wundt-Jastrow Area Illusion Test (+exp) • Sentence Reading Test (+exp)
Antonucci et al. (1995) RCT (4) N_{start}=20 N_{end}=20 TPS=Subacute	E: Immediate Visual Scanning Treatment + Conventional Rehabilitation C: General Cognitive Intervention Duration: 45min/d, 5d/wk for 8wk	• Letter Cancellation Test (+exp) • Albert's Barrage Test (-) • Sentence Reading Test (+exp) • Wundt-Jastrow Area Illusion Test (+exp) • Semi-structured Scale for the Functional Evaluation of Hemi-Inattention - Extrapersonal Space (-)
Saccade Training + Visual Scanning + Task Specific Activities vs Task Specific Activities Alone		
van Wyk et al. (2014) RCT (8) N_{Start}=24 N_{End}=24 TPS=Acute	E: Saccadic Eye Movement Training + Visual Scanning Exercises + Task-specific Activities C: Only Task-specific Activities Duration: 1hr/d, 5d/wk for 4wk Statistical Analysis: ANOVA	• King-Devick Test Subtest 1 (-) • King-Devick Test Subtest 2 (-) • King-Devick Test Subtest 3 (+exp) • Barthel Index (+exp) • Star Cancellation Test (+exp)
Dual Task Visual Scanning vs. Single Task Visual Scanning		
van Kessel et al. (2013) RCT (6) N_{Start}=29 N_{End}=29 TPS=Subacute	E: Dual Task Visual Scanning Training C: Single Task Visual Scanning Training Duration: 1hr/d, 5d/wk for 6wk	• Behavioural Inattention Test - Conventional Subtest (-) • Bell's Cancellation Test (-) • Grey Scales Index (-) • Word Reading Task (-) • Semi-structured Scale for the Functional Evaluation of Hemi-attention (-) • Subjective Neglect Questionnaire (-) • Single and Dual Lane Tracking (-)
Visual Scanning vs Limb Activation vs Prism Adaptation		
Priftis et al. (2013) RCT (5) N_{Start}=33 N_{End}=31 TPS=Subacute	E1: Visual Scanning Training E2: Limb activation Treatment E3: Prism Adaptation Duration: 20min, 2x/d 5d/wk for 2wk	E1 vs E2 • Fluff Test (-) • Comb and Razor Test (-) • Semi-structured Scale for the Functional Evaluation of Hemi-Inattention (-) • Room Description (-) • Picture Scanning (-) • Menu Reading (-) • Coin Sorting (-) • Catherine Bergego Scale (-) E1 vs E3 • Fluff Test (-) • Comb and Razor Test (-) • Semi-structured Scale for the Functional Evaluation of Hemi-Inattention (-) • Room Description (-) • Picture Scanning (-) • Menu Reading (-) • Coin Sorting (-) • Catherine Bergego Scale (-)
Computer-Based Visual Scanning vs Standard Computer Use		
Robertson et al. (1990) RCT (6) N_{start}=36 N_{end}=32 TPS=Chronic	E: Computer Scanning + Attentional Training C: Recreational Computing Duration: 45min/d, 3d/wk for 4wk Statistical Analysis: Mann-Whitney U Test	• Behavioural Inattention Test (-) • Wechsler Adult Intelligence Scale (-) • Neale Reading Test (-) • Letter Cancellation Test (-) • Rey-Osterreith Test (-)

Visual Scanning vs Covert Attention		
Modden et al. (2012) RCT (7) N_{start}=45 N_{end}=42 TPS=Subacute	E1: Computerized Compensatory Therapy E2: Restorative Computerized Training C: Standard Occupational Therapy Duration: 30min/d, 5d/wk for 3wk	E1/E2 vs C Testing Battery for Attentional Performance: • Visual Field (-) • Phasic Alertness (-) • Visual Scanning (-) • Behavioural Inattention Test: Cancellation Tasks (-) Reading Performance: • Errors (-) • Speed (-) • Barthel Index (-) E1 vs E2 Testing Battery for Attentional Performance: • Visual Field (-) • Phasic Alertness (-) • Visual Scanning (-) • Behavioural Inattention Test: Cancellation Tasks (-) Reading Performance: • Errors (-) • Speed (-) • Barthel Index (-)
DYNAVISION vs Waitlist Control		
Crotty et al. (2009) RCT (7) N_{Start}=26 N_{End}=23 RPS=Subacute	E: Visual Scanning Training using the DYNAVISION Device C: Waitlist Control Duration: E=40min/session, 3 sessions/wk, 6wks C=6wks	• Standardized On-Road Driving Assessment (-) • Abilities in Response Time Measures (-) • Visual Scanning Analyzer (-) • Adelaide Driving Self-Efficacy (-)
Neuro Vision Tech vs Individualized Therapy		

Crotty et al. (2018)
RCT (6)
N_{Start}=24
N_{End}=24
TPS=Subacute
	E: Visual Scanning Training using the Neuro Vision Tech Program
	C: Individualized Therapy recommended by Clinicians
	Duration: 3 sessions/wk, 7wks
		• Mobility Assessment Course
		  • Both Sides (-)
		  • Affected Side (-)
		• Visual Scanning Assessment (-)
		  • Reading Speed (-)
		• National Eye Institute Visual Functioning Questionnaire (-)
		  • General Health (-)
		  • General Vision (-)
		  • Near Activities (-)
		  • Distance Activities (-)
		  • Social Functioning (-)
		  • Mental Health (-)
		  • Role Difficulties (-)
		  • Dependency (-)
		• Veteran Low Vision Visual Functional Questionnaire
		  • Visual Ability (-)
		  • Reading (-)
		  • Mobility (-)
		  • Visual Information (-)
		  • Visual Motor (-)
		• Mayo Portland Adaptability Inventory (-)
		• Behavioural Inattention Test (-)
		  • Conventional (-)
		  • Behavioural (-)

Computer-Based Useful Field of View vs Computer-Based Visuoperception		
Mazer et al. (2003) RCT (5) N_{Start}=97	E: Computer-Based Visual Scanning C: Computer-Based Traditional Visuoperception Treatment Program	• Useful Field of View (+exp) • Complex Reaction Timer (-) • Motor-Free Visual Perception Test (-)

N_{End}=84 TPS=Subacute	Duration: 30-60min/session, 2-4 sessions/wk, 20 sessions total	• Single Letter Cancellation Task (-) • Double Letter Cancellation Task (-) • Money Road Map Test of Direction Sense (-) • Trail Making Test A (-) • Trail Making Test B (-) • Bells Test (-) • Charron Test (-) • Test of Everyday Attention (-) • On-Road Driving Evaluation (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Visual Scanning Training

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the use of **visual scanning** for improving neglect when compared to **conventional rehabilitation**.	6	Chan & Man, 2013; Modden et al., 2012; Ferreira et al., 2011; Niemeier et al., 2001; Paolucci et al., 1996; Antonucci et al., 1995
1b	There is conflicting evidence about the use of **saccade training + visual scanning + task specific activities** for improving neglect when compared to **task specific activities alone**.	1	van Wyk et al., 2014
1b	**Dual-task visual scanning** may not have a difference in efficacy compared to **Single-task visual scanning** for improving neglect.	1	van Kessel et al., 2013
2	**Visual scanning** may not have a difference in efficacy compared to **limb activation** or **prism adaptation** for improving neglect.	1	Prifitis et al., 2013
2	**Visual scanning** may not have a difference in efficacy compared to **mental practice** for improving neglect.	1	Ferreira et al., 2011
1b	**Visual scanning** may not have a difference in efficacy compared to **covert attention** for improving neglect.	1	Modden et al., 2012
1b	**DYNAVISION** may not have a difference in efficacy compared to **waitlist control** for improving neglect.	1	Crotty et al., 2009
1b	**Neuro vision tech** may not have a difference in efficacy compared to **individualized therapy** for improving neglect.	1	Crotty et al., 2018
2	**Computer-based useful field of view** may not have a difference in efficacy compared to **computer-based visuoperception** for improving neglect.	1	Mazer et al., 2003

GLOBAL COGNITION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Visual scanning** may not have a difference in efficacy compared to **conventional rehabilitation** for improving global cognition.	2	Chan & Man, 2013; Niemeier et al., 2001

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Visual scanning** may produce greater improvements in motor rehabilitation than **conventional rehabilitation**.	1	Paolucci et al., 1996
2	**Computer-based useful field of view** may not have a difference in efficacy compared to **computer-based visuoperception** for improving motor rehabilitation.	1	Mazer et al., 2003

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Visual scanning** may not have a difference in efficacy compared to **conventional rehabilitation** for improving stroke severity.	1	Paolucci et al., 1996

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Visual scanning** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	5	Chan & Man, 2013; Modden et al., 2012; Ferreira et al., 2011; Niemeier et al., 2001; Paolucci et al., 1996
1b	**Saccade training + visual scanning + task specific activities** may produce greater improvements in activities of daily living than **task specific activities alone**.	1	Van Wyk et al., 2014
2	**Visual scanning** may not have a difference in efficacy compared to **mental practice** for improving activities of daily living.	1	Ferreira et al., 2011
1b	**Visual scanning** may not have a difference in efficacy compared to **covert attention** for improving activities of daily living.	1	Modden et al., 2012
1b	**Neuro vision tech** may not have a difference in efficacy compared to **individualized therapy** for improving activities of daily living.	1	Crotty et al., 2018

Key Points

The literature is mixed regarding visual scanning training for improving neglect.

Visual scanning training may not be beneficial for improving activities of daily living.

Covert Attention Training

Adopted from : https://www.seevividly.com/info/Lazy_Eye_Treatments/Eye_Exercises/Brock_String

Lesions caused by cerebrovascular events can cause impairment of the ability to covertly attend to visual stimuli (Morrow & Ratcliff, 1988). Covert attention is a process where an individual attends to stimuli without moving their eyes (Findlay, 2003). Interventions aiming to improve covert attention in patients with hemispatial neglect have implemented visual fixation training. By fixating focus on a target and covertly attending to stimuli in the fringe or periphery, these interventions look to reteach covert attention to patients with post-stroke neglect.

Five RCTs were found evaluating covert attention interventions for neglect rehabilitation. Two of these studies compared covert attention to standard care (Rowe et al., 2017; Modden et al., 2012). One study compared covert attention and visual stimulation (Keller et al., 2010). One study compared covert attention to optokinetic stimulation (Elshout et al., 2016).

The methodological details and results of all five RCTs are presented in Table 2.

Table 2. RCTs evaluating covert attention training for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Covert Attention vs Standard Care		
Rowe et al. (2017) RCT (5) N_{Start}=87 N_{End}=71 TPS=Subacute	E1: Fresnel Prism Glasses E2: Visual Fixation Training C: Standard Care Duration: min 2hr/d, 5d/wk, 6wks for E1; min 30min/d, 5d/wk, 6wks for E2	<u>E1 vs C</u> • Visual Field Assessment (-) • Reading Ability (-) • Visual Function Questionnaire (-) • Rivermead Mobility Index (-) • Nottingham Extended Activities of Daily Living Assessment (-) <u>E2 vs C</u> • Visual Field Assessment (-) • Reading Ability (-) • Visual Function Questionnaire (+exp2) • Rivermead Mobility Index (-) • Nottingham Extended Activities of Daily Living Assessment (-) <u>E1 vs E2</u> • Visual Field Assessment (-) • Reading Ability (-) • Visual Function Questionnaire (+exp2) • Rivermead Mobility Index (-) • Nottingham Extended Activities of Daily Living Assessment (-)
Modden et, al. (2012) RCT (7) N_{start}=45 N_{end}=42 TPS=Subacute	E1: Computerized Compensatory Therapy E2: Restorative Computerized Training C: Standard Occupational Therapy Duration: 30min/d, 5d/wk for 3wk	<u>E1/E2 vs C</u> Testing Battery for Attentional Performance: • Visual Field (-) • Phasic Alertness (-) • Visual Scanning (-) • Behavioural Inattention Test: Cancellation Tasks (-) Reading Performance: • Errors (-) • Speed (-) • Barthel Index (-) <u>E1 vs E2</u> Testing Battery for Attentional Performance: • Visual Field (-) • Phasic Alertness (-) • Visual Scanning (-) • Behavioural Inattention Test: Cancellation Tasks (-) Reading Performance: • Errors (-) • Speed (-) • Barthel Index (-)
Covert Attention vs Visual Stimulation		
Keller et al. (2010) RCT (7) N_{Start}=20 N_{End}=20 TPS=Subacute	E: Multimodal Audiovisual Fixation Stimulation Training C: Visual Stimulation Training Duration: 30 min/session, 20 sessions over 3wks	• Visual Exploration (+exp) • Reading Time (+exp) • Search Time/Object (+exp) • Activities of Daily Living (+exp) • Number of Saccades (+exp) • Amplitude of Saccades (+exp)
Covert Attention vs Optokinetic Stimulation		
Elshout et al. (2016) RCT (4) N_{Start}=30	E: Covert Attention Training C: Computer-based Optic Flow Training Duration: 1hr/d, 5d/wk, 8wks	• Goldmann Perimetry (+con) • Humphrey Perimetry (-) • Reading (-)

N_{End}=27 TPS=Chronic		
Covert Attention vs Fresnel Prism Glasses		
Rowe et al. (2017) RCT (5) N_{Start}=87 N_{End}=71 TPS=Subacute	E1: Fresnel Prism Glasses E2: Visual Fixation Training C: Standard Care Duration: min 2hr/d, 5d/wk, 6wks for E1; min 30min/d, 5d/wk, 6wks for E2	E1 vs E2 • Visual Field Assessment (-) • Reading Ability (-) • Visual Function Questionnaire (+exp2) • Rivermead Mobility Index (-) • Nottingham Extended Activities of Daily Living Assessment (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Covert Attention Training

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Covert attention** may not have a difference in efficacy compared to **standard care** for improving neglect.	2	Rowe et al., 2017; Modden et al., 2012
1b	**Covert attention** may produce greater improvements in neglect than **visual stimulation.**	1	Keller et al., 2010
2	There is conflicting evidence about the use of **covert attention** for improving neglect when compared to **optokinetic stimulation.**	1	Elshout et al., 2016
2	**Covert attention** may not have a difference in efficacy compared to **Fresnel prism glasses** for improving neglect.	1	Rowe et al., 2017

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Covert attention** may not have a difference in efficacy compared to **standard care** for improving motor rehabilitation.	1	Rowe et al., 2017
2	**Covert attention** may not have a difference in efficacy compared to **Fresnel prism glasses** for improving motor rehabilitation.	1	Rowe et al., 2017

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Covert attention** may not have a difference in efficacy compared to **standard care** for improving activities of daily living.	2	Rowe et al., 2017; Modden et al., 2012
1b	**Covert attention** may produce greater improvements in activities of daily living than **visual stimulation.**	1	Keller et al., 2010
2	**Covert attention** may not have a difference in efficacy compared to **Fresnel prism glasses** for improving activities of daily living.	1	Rowe et al., 2017

Key Points

The literature is mixed regarding covert attention training for improving neglect.

Covert attention training may not be beneficial for improving motor rehabilitation or activities of daily living.

Virtual Reality-Based Rehabilitation

Adopted from: https://gettecla.com/blogs/news/virtual-reality-is-transforming-the-healthcare-and-rehab-industry

Traditionally, post-stroke neglect rehabilitation has been constrained to real-world therapies. More recently, virtual reality-based approaches are becoming more viable as technology becomes more realistic, user-friendly and affordable. A 2015 systematic review from Pedroli and colleagues outlined three ‘critical challenges’ that need to be addressed when designing virtual-reality interventions. They are: (1) using an ergonomic design that enables those in wheelchairs or with hemiparesis; (2) software that is user friendly for clinical staff and patients; and (3) costs that are affordable for all patients (Pedroli et al., 2015).

Six RCTs were found evaluating computer-based interventions for neglect rehabilitation. Three of these RCTs compared virtual reality training to conventional training (Choi et al., 2021; Jo et al., 2012; Kim et al., 2011). One RCT compared immersive virtual reality to desktop screen virtual reality (Gamito et al., 2014). One RCT compared virtual reality attention training to computer-based visual scanning (Katz et al., 2005). One RCT compared simulator-based driving training to cognitive training (Akinwuntan et al., 2010).

The methodological details and results of all six RCTs are presented in Table 3.

Table 3. RCTs evaluating virtual reality-based rehabilitation interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample $Size_{start}$ Sample $Size_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Virtual Reality Training vs. Conventional Rehabilitation		

Choi et al. (2021)
RCT (8)
N_{Start}=24
N_{End}=24
TPS=Subacute
	E: Virtual Reality-Based Digital Practice
	C: Conventional Rehabilitation
	Duration: Digital Practice 30min, 3d/wk, 4wks
	Conventional Training 1-hr therapy session, 5 d/wk, 4wks
		• Line Bisection Test (+exp)
		• Modified Barthel Index (-)
		• Catherine Bergego Scale (-)
		• Motor-Free Visual Perception Test (+exp)
		  • Response Behavior Left (+exp)
		  • Response Behaviour Right (-)
		  • Performance Behavior Left (+exp)
		  • Performance Behavior Right (+exp)
		  • Processing Time (+exp)
		• Rotation Angle (+exp)
		  • Mean Change Head Rotation Velocity (+exp)

Maier et al. (2020) RCT (4) N_{Start}=38 N_{End}=32 TPS=Chronic	E: Computer-based Virtual Reality Cognitive Training C: Cognitive Tasks to be Completed at Home Duration: 30 min/day, 5 days/wk, 6wks	• Attention (-) • Memory (-) • Executive Function (-) • Spatial Awareness (-) • Generalized Cognitive Functioning (-)

Jo et. al. (2012)
RCT (6)
N_{start}=29
N_{end}=27
TPS=Chronic
	E: Virtual Reality Training
	C: Conventional Rehabilitation
	Duration: 60min/d, 5d/wk for 4wk
		Motor-Free Visual Perception Test:
		  • Total Score (+exp)
		  • Response Time (+exp)
		  • Visual Discrimination (+exp)
		  • Figure Constancy (+exp)
		  • Visual Closure (-)
		  • Visual Memory (-)
		  • Spatial Relation (-)
		  • Wolf Motor Function Test (-)

Kim et al. (2011) RCT (4) N_{start}=24 N_{end}=21 TPS=Acute	E: Virtual Reality Training C: Conventional Rehabilitation (visual tracking, reading, etc.) Duration: 30min/d, 5d/wk for 3wks	• Star Cancellation Test (+exp) • Line Bisection Test (-) • Catherine Bergego Scale (+exp) • Korean-Modified Barthel Index (-)
Immersive Virtual Reality vs Desktop Screen Virtual Reality		
Gamito et al. (2014) RCT (4) N_{Start}=17 N_{End}=17 TPS=Subacute	E1: Immersive Virtual Reality Cognitive Training E2: Desktop Screen Based Virtual Reality Duration: 1 session/wk, 12wks	• Wechsler Memory Scale (-) • Rey-Osterrieth Complex Figure (-) • Toulouse Pieron Cancellation Test (-)
Virtual Reality Attention Training vs Computer-Based Visual Scanning		
Katz et al. (2005) RCT (6) N_{Start}=19 N_{End}=19 TPS=Subacute	E: Virtual Reality Street Crossing Attention Training C: Computer-Based Visual Scanning Duration: 45 min/session, 3sessions/wk, 4wks	• Functional Independence Measure (-) • Mesulam Scores (+exp) • Activities of Daily Living (+exp) • Virtual Reality Street Crossing Accidents (+exp) • Real Street Crossing Results • Mean Number of Times Participants Looked to the Left Before Crossing (-)

		• Decision Time to Cross the Street per Vehicle (-)
Simulator-Based Driving Training vs Cognitive Training		
Akinwuntan et al. (2010) RCT (5) N_{Start}=81 N_{End}=67 TPS=Subacute	E: Simulator-Based Driving Training C: Traditional Cognitive Training Duration: 1 hr/session, 3 sessions/wk, 5wks	• Useful Field of View (-) • Divided Attention Test Subtest (-) • Selective Attention Subtest (-) • Speed of Processing Subtest (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Virtual Reality-based Rehabilitation

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the use of **virtual reality-based training** for improving neglect when compared to **conventional rehabilitation.**	4	Choi et al., 2021; Maier et al., 2020; Jo et al., 2012; Kim et al., 2011
2	**Immersive virtual reality** may not have a difference in efficacy compared to **desktop virtual reality** for improving neglect.	1	Gamito et al., 2014
1b	**Virtual reality attention training** may produce greater improvements in neglect than **computer-based visual scanning.**	1	Katz et al., 2005
2	**Simulator-based driving training** may not have a difference in efficacy compared to **cognitive training** for improving neglect.	1	Akinwuntan et al., 2010

GLOBAL COGNITION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Virtual reality-based training** may not have a difference in efficacy compared to **conventional rehabilitation** for improving global cognition.	1	Maier et al., 2020

LEARNING & MEMORY			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Immersive virtual reality** may not have a difference in efficacy compared to **desktop virtual reality** for improving learning & memory.	1	Gamito et al., 2014

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the use of **virtual reality-based training** for improving motor rehabilitation when compared to **conventional rehabilitation.**	2	Choi et al., 2021; Jo et al., 2012

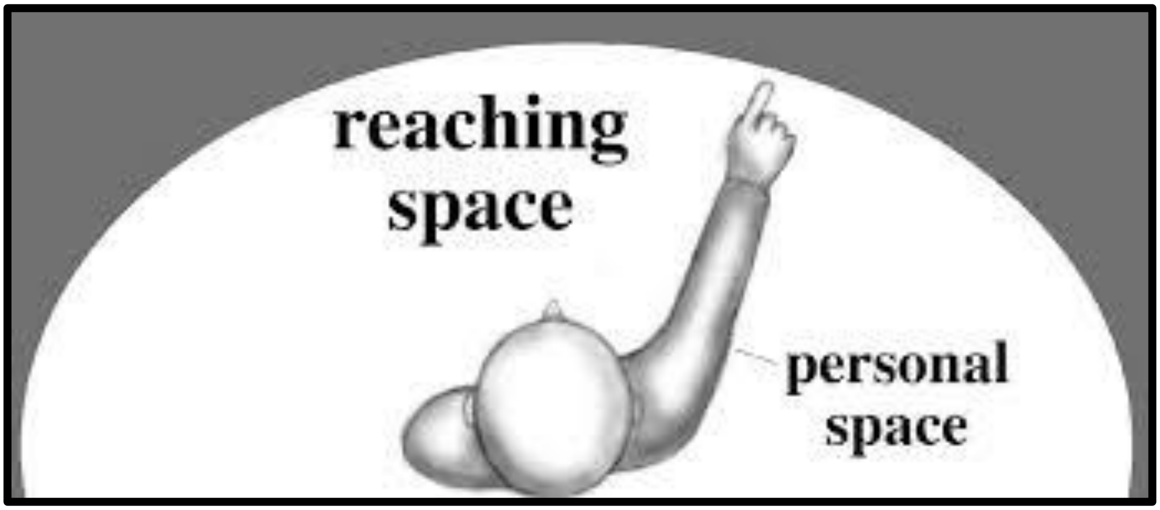
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Virtual reality-based training** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	2	Choi et al., 2021; Kim et al., 2011
1b	There is conflicting evidence about the use of **virtual reality attention training** for improving activities of daily living when compared to **computer-based visual scanning.**	1	Katz et al., 2005

Key Points

The literature is mixed regarding virtual reality-based training for improving neglect and motor rehabilitation.

Virtual reality-based training may not be beneficial for improving learning & memory, or activities of daily living.

Limb Activation



Adopted from: https://www.tandfonline.com/doi/abs/10.1080/09602010244000228?journalCode=pnrh20

Limb activation therapy for neglect is based on activating spatial and motor representations of specific areas which are not being attended to. By increasing this activation, an individual can increase the representation of that spatial sector. In one of the first studies examining this intervention for neglect treatment, Robertson and North (1992) showed that only when the contralateral limb was activated in the contralesional space, patients saw an improvement in neglect. In addition, they also showed that this improvement was independent of the visual cue provided by seeing the limb and could be elicited from movement alone. Additionally, there is mixed results concerning whether passive movement can ameliorate neglect as well (Frassinetti et al., 2001; Ladavas et al., 1997; Robertson & North, 1993) Considering the high prevalence of motor impairment post-stroke, passive movement could prove an effective and accessible treatment for many. The literature on limb activation has shown mixed results both for and against its effectiveness, and more work will need to be done to replicate positive results to concretely establish its effectiveness.

Nine RCTs were found evaluating limb activation interventions for neglect rehabilitation. Three RCTs compared limb activation to conventional rehabilitation (Fong et al., 2013; Wu et al., 2013; Karla et al., 1997). Two RCTs compared limb activation to attentional training programs (Reinhart et al., 2012; Robertson et al., 2002). One RCT compared limb activation to visual scanning training, and prism adaptation (Prifitis et al., 2013). One RCT compared hand intrinsic muscle movement to common upper extremity tasks (Ma et al., 2019). Two RCTs examined robot-assisted therapy compared to conventional rehabilitation; one evaluated the use of robot-assisted arm therapy (Chen et al., 2021); one evaluated the use of robot-assisted left-hand training (Park et al., 2021).

The methodological details and results of all nine RCTs are presented in Table 4.

Table 4. RCTs evaluating limb activation interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Limb Activation vs Conventional Rehabilitation		
Fong et al. (2013) RCT (9) N_{Start}=40 N_{End}=35 TPS=Subacute	E: Conventional Rehabilitation + Cued Arm Movements C: Conventional Rehabilitation + Instructions to Move as Much As Possible Duration: 3hr/d, 5d/wk for 3wk Statistical Analysis: ANOVA	• Functional Independence Measure- Motor Subscale (-) • Functional Test for Hemiplegic Upper Extremity (-) Behavioural Inattention Test Conventional Subtest: • Cancellation Tasks (-) • Drawing Tasks (+exp) Fugl-Meyer Assessment - Upper Extremity • Motor Subscore (-) • Hand Subscore (-)
Wu et al. (2013) RCT (7) N_{Start}=27 N_{End}=24 TPS=Chronic	E1: Constraint Induced Therapy + Eye Patching (6hr/d) E2: Constraint Induced Therapy C: Conventional Rehabilitation (2hr/d) Duration: 5/wk for 3wk Statistical Analysis: Independent T-Test	E1 vs E2 • Catherine Bergego Scale (-) Eye Movement Variables: • Number of Left Fixation Points (+exp$_2$) • Fixation Amplitude (-) • Left Fixation Time (-) Arm-trunk Movement Variables: • Reaction Time (-) • Time of Peak Velocity (+exp$_1$) • Movement Time (-) • Total Distance (-) • Trunk Lateral Shift: (+exp$_1$) E1/E2 vs C • Catherine Bergego Scale (+exp$_1$,+exp$_2$) Eye Movement Variables: • Number of Left Fixation Points (+exp$_2$) • Fixation Amplitude (-) • Left Fixation Time (-) Arm-trunk Movement Variables: • Reaction Time (+exp$_2$) • Time of Peak Velocity (+exp$_1$) • Movement Time (-) • Total Distance (-) • Trunk Lateral Shift (-)
Kalra et al. (1997) RCT (7) N_{start}=50 N_{end}=46 TPS=Acute	E: Spatiomotor Cueing of Affected Limb in Deficit Hemispace C: Conventional Therapy Duration: 45min/d, 1d/wk for 12wk Statistical Analysis: Mann-Whitney U Test	Rivermead Perceptual Assessment Battery: • Cancellation (+exp) • Body Image (+exp) • Picture Matching (-) • Object Matching (-) • Size Recognition (-) • Series (-) • Missing Article (-) • Sequencing-pictures (-) • Right/Left Copying (-) • Word Colour Matching (-) • 3-dimensional Copying (-) • Figure Ground Discrimination (-) • Animal Halves (-)
Limb Activation vs Attentional Training		
Reinhart et al. (2012) RCT Cross-over (6) N_{start}=8 N_{end}=8 TPS=Subacute	E1: Passive Left Limb Activation E2: Alertness Cueing Duration: 2 sessions of 1hr Statistical Analysis: ANOVA	• Hand Judgement Task (+exp)

Robertson et al. (2002) RCT (6) N_{start}=40 N_{end}=36 TPS=Subacute	E: Limb Activation Treatment + Perceptual Training C: Perceptual Training Duration: 45min/d, 3d/wk for 4wk Statistical Analysis: ANOVA	• Motricity Index (+exp) • Barthel Index (-) • Catherine Bergego Scale (-)
Limb Activation vs Visual Scanning vs Prism Adaptation		
Priftis et al. (2013) RCT (5) N_{Start}=33 N_{End}=31 TPS=Subacute	E1: Visual Scanning Training E2: Limb Activation Treatment E3: Prism Adaptation Duration: 20min, 2x/d 5d/wk for 2wk Statistical Analysis: Mann-Whitney U Test	E2 vs E1 • Fluff Test (-) • Comb and Razor Test (-) • Semi-structured Scale for the Functional Evaluation of Hemi-Inattention (-) • Room Description (-) • Picture Scanning (-) • Menu Reading (-) • Coin Sorting (-) • Catherine Bergego Scale (-) E2 vs E3 • Fluff Test (-) • Comb and Razor Test (-) • Semi-structured Scale for the Functional Evaluation of Hemi-Inattention (-) • Room Description (-) • Picture Scanning (-) • Menu Reading (-) • Coin Sorting (-) • Catherine Bergego Scale (-)
Hand Intrinsic Muscle Movement vs Common Upper Extremity Task		
Ma et al. (2019) RCT (6) N_{Start}=20 N_{End}=20 TPS=Chronic	E: Task Application After Hand Intrinsic Muscle Treatment C: Common Upper Extremity Task Duration: 30min/d, 5d/wk, 2wks	• Albert's Test (+exp) • Line Bisection Test (+exp)
Robot-Assisted Therapy vs Conventional Rehabilitation		
Chen et al. (2021) RCT (8) N_{Start}=20 N_{End}=20 TPS=Subacute	E: Robot-Assisted Arm Therapy C: Conventional Therapy Duration: 45min/d, 5d/wk, 4wks	• Behavioral Inattention Test (+exp) • Catherine Bergego Scale (-) • Fugl-Meyer Assessment for Upper Extremity (+exp) • Modified Barthel Index (-) • World Health Organization Disability Assessment Schedule Version 2.0 - Social Participation (+exp)
Park et al. (2021) RCT (8) N_{Start}=24 N_{End}=24 TPS=Chronic	E: Robot-Assisted Left-Hand Training C: Conventional Treatments for Neglect Symptoms Duration: 30 min/session, 5 sessions/wk, 4wks	• Line Bisection Test (+exp) • Albert's Test (+exp) • Catherine Bergego Scale (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
$+exp_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Limb Activation

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Limb activation** may not have a difference in efficacy compared to **conventional rehabilitation** for improving neglect.	3	Fong et al., 2013; Wu et al., 2013; Karla et al., 1997
1a	There is conflicting evidence about the use of **limb activation** for improving neglect when compared to **visual training**.	2	Reinhart et al., 2012; Robertson et al., 2002
1b	**Constraint induced therapy with eye patching** may not have a difference in efficacy compared to **constraint induced therapy alone** for improving neglect.	1	Wu et al., 2013
2	**Limb activation** may not have a difference in efficacy compared to **visual scanning** or **prism adaptation** for improving neglect.	1	Prifitis et al., 2013
1b	**Hand intrinsic muscle movement** may produce greater improvements in neglect than **common upper extremity tasks.**	1	Ma et al., 2019
1b	There is conflicting evidence about the use of **robot-assisted arm therapy** for improving neglect when compared to **conventional rehabilitation**.	1	Chen et al., 2021
1b	**Robot-assisted left-hand training** may produce greater improvements in neglect than **conventional rehabilitation.**	1	Park et al., 2021

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Limb activation** may produce greater improvements in motor rehabilitation than **visual training**.	1	Robertson et al., 2002
1b	**Limb activation** may not have a difference in efficacy compared to **conventional rehabilitation** for improving motor rehabilitation.	1	Fong et al., 2013
1b	**Constraint induced therapy** may not have a difference in efficacy compared to **conventional rehabilitation or constraint induced therapy alone** for improving motor rehabilitation.	1	Wu et al., 2013
1b	**Robot-assisted arm therapy** may produce greater improvements in motor rehabilitation than **conventional rehabilitation**.	1	Chen et al., 2021

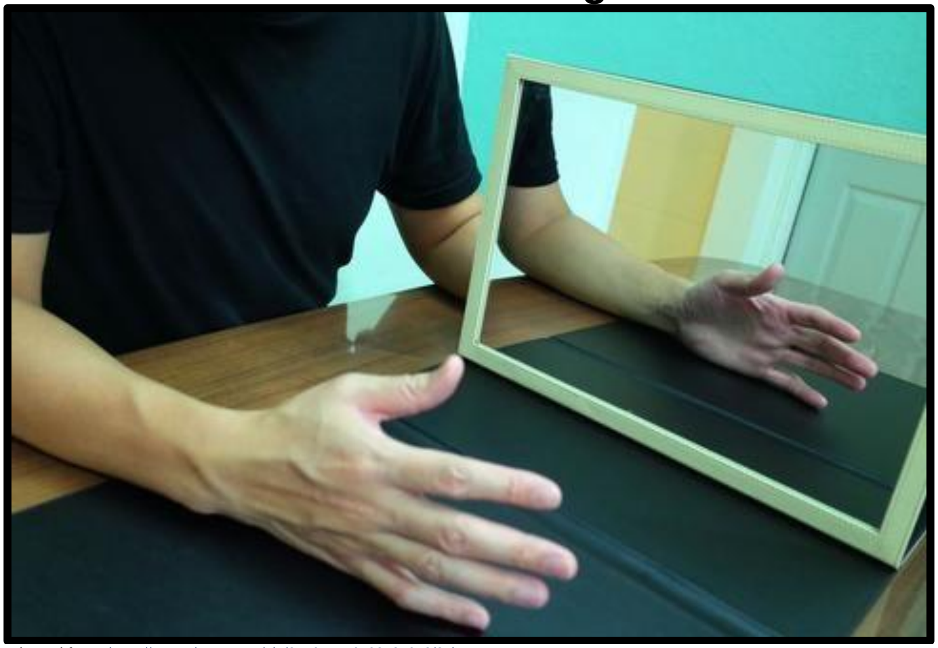
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Limb activation** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	1	Fong et al., 2013

1b	**Limb activation** may not have a difference in efficacy compared to **visual training** for improving activities of daily living.	1	Robertson et al., 2002
1b	**Robot-assisted arm therapy** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	1	Chen et al., 2021

Key Points

Limb activation may not be beneficial for improving neglect, motor rehabilitation, or activities or daily living.

Visuomotor Feedback Strategies



Adapted from: https://www.pinterest.ca/pin/371054456792134018/?nic=1a

A common feature of neglect is that those who suffer from it are usually unaware of the deficit, having no conscious recognition of any problems as they occur (Bisiach et al., 1986). Although popular, some interventions like visual scanning receive criticism because they rely on the self-awareness and intention of the participant. Therefore, therapies that provide direct feedback (externally or internally) can aid in the acknowledgement of when a perceptual error is occurring and allow the individual to properly correct it. These types of strategies allow for 'trial-and-error' learning, whereas before the error itself could not be apparent. By establishing this feedback loop the necessary conditions for operant conditioning can be maintained and training can have the potential to be more effective.

Nine RCTs were found that evaluated feedback strategy interventions for neglect rehabilitation. One RCT compared visuomotor feedback training to an attentional control (Rossit et al., 2019). One RCT evaluated a balance feedback training system compared to conventional rehabilitation (Kutlay et al.,2018). Three RCTs examined mirror therapy: one compared mirror training and sham training (Pandian et al., 2014); one compared mirror therapy to a no-mirror control group (Dhole et al., 2009); and one examined three groups which were an individual mirror therapy group, a group mirror therapy group and a control with restricted view on the affected arm (Thieme et al., 2013). One RCT compared rod balancing at center procedure to a rod balancing on the right-side procedure (Harvey et al., 2003). One RCT compared eye-tracking feedback glasses to conventional rehabilitation (Fanthome et al., 1995). One RCT examined visuomotor imagery therapy compared to standard care (Welfringer et al., 2011). One RCT compared a visual perception motion tracking programme to a cognitive rehabilitation control program (Kang et al., 2009).

The methodological details and results of all nine RCTs are presented in Table 5.

Table 5. RCTs evaluating visuomotor feedback interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Visuomotor Feedback Training vs Attentional Control		
Rossit et al. (2019) RCT (7) N_{Start}=20 N_{End}=19 TPS=Subacute	E: Visuomotor Feedback Training C: Attentional Control Duration: 2 experimenter-led sessions, 30min ea. 30 min/session, 5 sessions/wk, 2wks	• Line Bisection (+exp) • Behavioural Inattention Test (-) • Stroke Impact Scale-ADL/IADL (+exp) • Stroke Impact Scale - Hand Function (-) • Stroke Impact Scale - Stroke Recovery (-) • Balloons Test (-) • Landmark Task (-) • Subjective Straight-Ahead Description Task (-) • Room Description Task (-)
Balance Feedback Training vs Standard Rehabilitation		
Kutlay et al. 2018 RCT (7) N_{start}=64 N_{end}=53 TPS=Subacute	E: Kinesthetic Ability Training (KAT) + Standard Rehabilitation + visual scanning) C: Standard Rehabilitation + visual scanning) Duration: 30min/d, 5d/wk for 4wk Statistical Analysis: Mann-Whitney U Test	• Behavioural Inattention Test (-) • Functional Independence Measure (-)
Mirror Training vs Control		
Pandian et al. (2014) RCT (8) N_{Start}=48 N_{End}=46 TPS=Acute	E: Mirror Training C: Sham Mirror Training Duration: 1.5hr/d, 5d/wk for 4wk Statistical Analysis: ANOVA	• Star Cancellation Test (+exp) • Line Bisection Test (+exp) • Picture Identification Task (+exp)

Dhole et al. (2009)
RCT (6)
N_{Start}=48
N_{End}=36
TPS=Subacute
	E: Mirror Therapy
	C: Control Therapy (No Mirror)
	Duration: 30 min/d, 5 d/wk, 6wks
		• Motor Function (-)
		• Finger Motor Score (+exp)
		  • Range of Motion (-)
		  • Surface Sensitivity-Light Touch (+exp)
		  • Proprioception (-)
		• Improvement in Signs of Hemineglect in Right-Handed Patients (+exp)
		• Activities of Daily Living Capacity (-)

Individual Mirror Therapy vs Group Mirror Therapy vs Restricted View on Affected Arm		

Thieme et al. (2013)
RCT (8)
N_{Start}=60
N_{End}=49
TPS=Subacute
	E1: Individual Mirror Therapy
	E2: Group Mirror Therapy
	C: Restricted View on the Affected Arm
	Duration: 30 min/session, 4 sessions/wk, 5wks
		E1 vs C
		• Action Research Arm Test (-)
		• Fugl-Meyer (FM) - Motor (-)
		• Barthel Index (-)
		• Stroke Impact Scale (-)
		• FM - Sensory (-)
		• FM - Range of Motion (-)
		• FM - Pain (-)
		• Modified Ashworth Scale (MAS)
		  • Finger (-)
		  • Wrist (-)
		• Star Cancellation Test (+exp1)
		E2 vs C
		• Action Research Arm Test (-)
		• Fugl-Meyer (FM) - Motor (-)
		• Barthel Index (-)
		• Stroke Impact Scale (-)
		• FM - Sensory (-)
		• FM - Range of Motion (-)
		• FM - Pain (-)
		• Modified Ashworth Scale (MAS)
		  • Finger (-)

		• Wrist (-) • Star Cancellation Test (-) E1 vs E2 • Action Research Arm Test (-) • Fugl-Meyer (FM) - Motor (-) • Barthel Index (-) • Stroke Impact Scale (-) • FM - Sensory (-) • FM - Range of Motion (-) • FM - Pain (-) • Modified Ashworth Scale (MAS) • Finger (+exp1) • MAS - Wrist (-) • Star Cancellation Test (-)
Rod Lifting Balance Training at Center vs Rod Lifting Balance Training at Right Side		
Harvey et al. (2003) RCT (4) N_{start}=14 N_{end}=14 TPS=Chronic	E: Rod Lifting and Balancing at Central Point C: Rod Lifting and Balancing at Right Side Duration: 45min/d, 2d/wk for 6wk Statistical Analysis: ANOVA	• Landmark Test (+exp) • Line Bisection Test (-) • Real Objects Test (-)
Eye Tracking Feedback vs No Treatment		
Fanthome et al. (1995) RCT (5) N_{start}=18 N_{end}=18 TPS=Subacute	E: Eye-tracking Feedback Training Glasses C: No Neglect Treatment Duration 40min/d, 4d over 4wk Statistical Analysis: ANOVA	Behaviour Inattention Test: • Conventional Subtest (-) • Behavioural Subtest (-) • Eye Movement (-)
Visuomotor Imagery Therapy vs Standard Care		
Welfringer et al. (2011) RCT (7) N_{Start}=30 N_{End}=30 TPS=Subacute	E: Visuomotor Imagery Therapy C: Standard Care with No Supplementary Therapy Duration: 30 min/session, 2 sessions/d, 3wks	• Bells Cancellation (-) • Reading (-) • Flower Copying (-) • Clock Drawing (-) • Body Touching (-) • Visual Arm Imagery (-) • Kinaesthetic Arm Imagery (-) • Sensation (-) • Action Research Arm Test (-)
Visual Perception Motion Tracking Programme vs Cognitive Rehabilitation Program		
Kang et al. (2009) RCT (7) N_{Start}=16 N_{End}=16 TPS=Subacute	E: Interactive Computerized Visual Perception Rehabilitation Programme using CAMSHIFT Motion Tracking Technology C: PSS CogRehab Program Duration: 30 min/session, 3 sessions/wk, 4wks	• Mini-Mental Status Examination (-) • Motor-Free Visual Perception Test (-) • Korean Version - Modified Barthel Index (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Visuomotor Feedback Strategies

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Visuomotor feedback training** may not have a difference in efficacy compared to **an attentional control** for improving neglect.	1	Rossit et al., 2019
1b	**Kinesthetic ability training** may not have a difference in efficacy compared to **conventional rehabilitation** for improving neglect.	1	Kutlay et al., 2018
1a	**Mirror training** may produce greater improvements in neglect than **conventional rehabilitation.**	3	Pandian et al., 2014; Thieme et al., 2013; Dhole et al., 2009
1b	**Individual mirror therapy** may not have a difference in efficacy compared to **group mirror therapy** for improving neglect.	1	Thieme et al., 2013
2	**Rod lifting and balancing at center** may not have a difference in efficacy compared to **rod lifting and balancing on the right side** for improving neglect.	1	Harvey et al., 2003
2	**Eye tracking feedback glasses** may not have a difference in efficacy compared to **conventional rehabilitation** for improving neglect.	1	Fanthome et al., 1995
1b	**Visuomotor imagery therapy** may not have a difference in efficacy compared to **standard care** for improving neglect.	1	Welfringer et al., 2011
1b	**Visual perception motion tracking programs** may not have a difference in efficacy compared to **cognitive rehabilitation** for improving neglect.	1	Kang et al., 2009

GLOBAL COGNITION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Visual perception motion tracking programmes** may not have a difference in efficacy compared to **cognitive rehabilitation** for improving global cognition.	1	Kang et al., 2009

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Mirror therapy** may not have a difference in efficacy compared to **conventional rehabilitation** for improving motor rehabilitation.	2	Thieme et al., 2013; Dhole et al., 2009
1b	**Individual mirror therapy** may not have a difference in efficacy compared to **group mirror therapy** for improving motor rehabilitation.	1	Thieme et al., 2013
1b	**Visuomotor imagery therapy** may not have a difference in efficacy compared to **standard care** for improving motor rehabilitation.	1	Welfringer et al., 2011

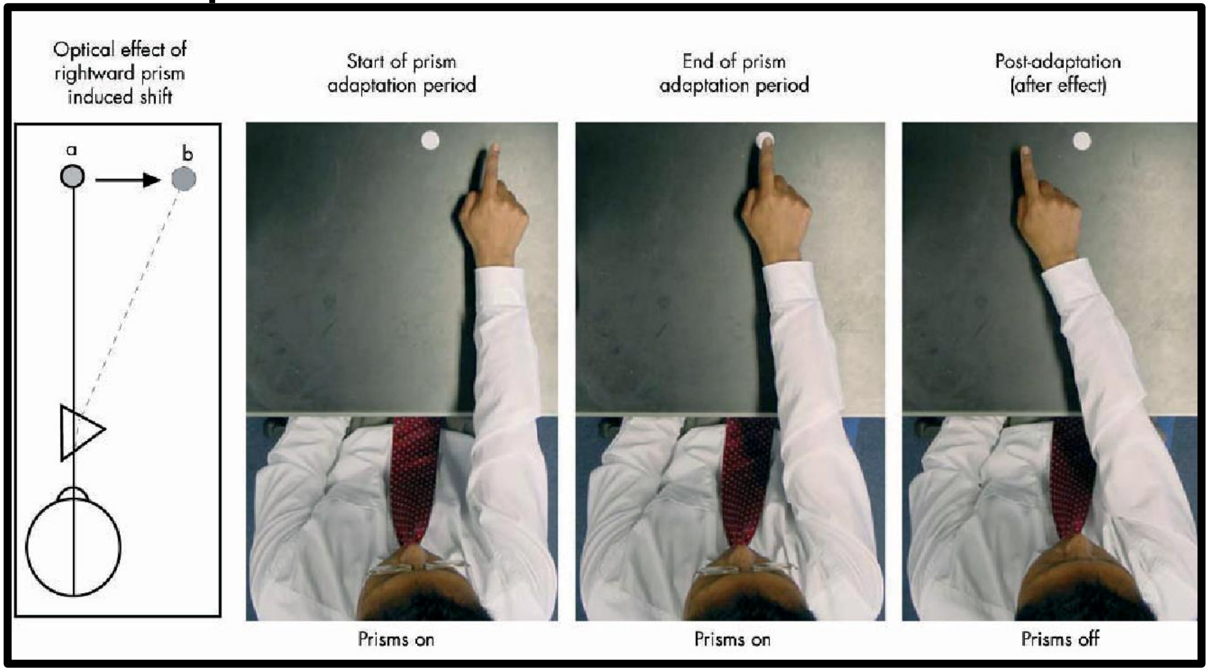
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Kinesthetic ability training** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	1	Kutlay et al., 2018
1a	**Mirror training** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	1	Thieme et al., 2013; Dhole et al., 2009
1b	**Individual mirror therapy** may not have a difference in efficacy compared to **group mirror therapy** for improving activities of daily living.	1	Thieme et al., 2013
1b	**Visual perception motion tracking programmes** may not have a difference in efficacy compared to **cognitive rehabilitation** for improving activities of daily living.	1	Kang et al., 2009

Key Points

Visuomotor feedback strategies may be beneficial for improving neglect.

Visuomotor feedback strategies may not be beneficial for improving motor rehabilitation or activities of daily living.

Prism Adaptation Treatment



Adopted from: https://www.semanticscholar.org/paper/Hemispatial-neglect.-Parton-Malhotra/36a38a9a06727477354cdb0b6cbb5c43178365ff/figure/2

Prisms affect spatial representation by causing an optical deviation of the visual field to either the left or the right. One of the most common low vision interventions for stroke induced hemianopia is the incorporation of binocular sector prisms in the person's habitual spectacle lenses. These may be Fresnel membrane lenses or prisms that are cemented onto the lens surface. While wearing the prisms, an individual's visual field will be shifted in one direction. Importantly, the visuomotor system will adapt to this new deviation over time, understanding that the true location of the objects are not as they appear in the goggles. Once the prisms are removed, the participants will still be adapted to the visual deviation and will show a bias to one side for visuomotor behaviour. This forced deviation can help individuals with neglect attend better to the contralesional visual hemisphere.

17 RCTs were found that evaluated prism adaptation interventions for neglect rehabilitation. 14 RCTs evaluated prism adaptation compared to conventional rehabilitation or sham prisms (Goedert et al., 2020; Vaes et al., 2018; Rowe et al., 2017; Ten Brink et al., 2017; Rode et al., 2015; Bowers et al., 2014; Mancuso et al., 2012; Mizuno et al., 2011; Jacquin-Courtois et al., 2010; Turton et al., 2010; Serino et al., 2009; Nys et al., 2008; Rossetti et al., 1998; Rossi et al., 1990). One RCT compared prims adaptation plus methylphenidate to prism adaptation with a placebo (Luate et al., 2018). One RCT compared prism adaptation to visual scanning as well as to limb activation (Prifitis et al., 2013). One RCT compared prism adaptation paired with functional electrical stimulation to prism adaptation alone and to functional electrical stimulation alone (Choi et al., 2019).

The methodological details and results of all 17 RCTs are presented in Table 6.

Table 6. RCTs evaluating prismatic adaptation interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Prism Adaptation vs Sham Prism/Conventional Rehabilitation		
Goedert et al. (2020) RCT (7) N_{Start}=19 N_{End}=17 TPS=Subacute	E: Prism Adaptation Treatment C: Standard Care Duration: 1 session/d, 10d	• Catherine Bergego Scale (+exp) • Behavioural Inattention Test (-)
Vaes et al. 2018 RCT (5) N_{start}=54 N_{end}=43 TPS=Subacute	E: Prism Adaptation (10°) C: Placebo Prism Adaptation Duration: 30min/d, 5d/wk for 2wk Statistical Analysis: Mann-Whitney U Test	• Bell's Cancelation (-) • Diamond Cancelation (-) • Schenkenberg Line Bisection (-) • Rectangles Bisection (+exp) • Search Time Task (-) • Drawing Task A (clock) (-) • Drawing B (butterfly) (+exp) Extinction task: • Index of Neglect (+exp) • Index of Extinction (+exp) • Spatial Memory Task (+exp) Visuospatial Navigation task (maze) • Endpoint (mm) (+exp) • Centre of Neglect (+exp)
Rowe et al. (2017) RCT (5) N_{Start}=87 N_{End}=71 TPS=Subacute	E1: Fresnel Prism Glasses E2: Visual Search Training C: Standard Care Duration: min 2hr/d, 5d/wk, 6wks for E1; min 30min/d, 5d/wk, 6wks for E2	<u>E1 vs C</u> • Visual Field Assessment (-) • Reading Ability (-) • Visual Function Questionnaire (-) • Rivermead Mobility Index (-) • Nottingham Extended Activities of Daily Living Assessment (-) • Euro Qual 5D (-) • Euro Qual VAS Score (-) • Short Form-12 Physical Component (-) • Short Form-12 Mental Component (-) <u>E2 vs C</u> • Visual Field Assessment (-) • Reading Ability (-) • Visual Function Questionnaire (+exp2) • Rivermead Mobility Index (-) • Nottingham Extended Activities of Daily Living Assessment (-) • Euro Qual 5D (-) • Euro Qual VAS Score (-) • Short Form-12 Physical Component (-) • Short Form-12 Mental Component (-) <u>E1 vs E2</u> • Visual Field Assessment (-) • Reading Ability (-) • Visual Function Questionnaire (+exp2) • Rivermead Mobility Index (-) • Nottingham Extended Activities of Daily Living Assessment (-) • Euro Qual 5D (-), Euro Qual VAS Score (-) • Short Form-12 Physical Component (-) • Short Form-12 Mental Component (-)
Ten Brink et al. 2017	E: Prism Adaptation	• Catherine Bergego Scale (-)

RCT (8) N_{start}=69 N_{end}=69 TPS=Subacute	C: Placebo Prism Adaptation Duration: 30min/d, 5d/wk for 2wk Statistical Analysis: Mann-Whitney U Test	• Mobility Assessment Course (-) • Shape Cancelation Task (-)
Rode et al. (2015) RCT (7) N_{Start}=20 N_{End}=18 TPS=Subacute	E: Prism Adaptation Glasses Training C: Placebo Prism Adaptation Training Glasses Duration: 6-10min, 1session/wk, 4wks	• Functional Independence Measure (-) • Behavioural Inattention Test (-)
Bowers et al. (2014) Crossover RCT (7) N_{Start}=73 N_{End}=61 TPS=Chronic	E: 57 Prism Diopter C: Sham Prism Diopter Duration: 4wks, no washout period	• Preference for Prism Glasses (-) • Overall Mobility Improvement Score (-)
Mancuso et al. (2012) RCT (7) N_{start}=29 N_{end}=22 TPS=Chronic	E: Pointing Intervention with Prismatic Goggles with a Rightward Shift of 5° C: Pointing Intervention with Neutral Goggles Duration: 30min/d, 5d/wk for 1wk Statistical Analysis: ANOVA	• Albert Test (-) • Bell's Cancellation Test (-) • Orientation Lines Test (-) Behavioural Inattention Test • Object Drawing Test (-) • Line Bisection Test (-) • Dealing Playing Card Test (-) • Objects Searching Test (-)
Mizuno et al. (2011) RCT (7) N_{start}=38 N_{end}=34 TPS=Subacute	E: Pointing Intervention with Prismatic Goggles (12°) C: Pointing intervention with neutral goggles Duration 20min, 2x/d, 5d/wk for 2wk Statistical Analysis: Mann-Whitney	• Functional Independence Measure (-) Behavioural Inattention Test: • Conventional Subtest (-) • Behavioural Subtest (-) • Catherine Bergego Scale (-)
Jacquin-Courtois et al. (2010) RCT (6) N_{Start}=12 N_{End}=12 TPS=Subacute ** auditory neglect	E: Prism Adaptation Treatment C: Sham Prism Adaptation (10°) Duration: 10min Statistical Analysis: ANOVA	Dichotic Listening Task: • Number of Correct Responses (-); • Lateralization (+exp) • Number of Fusion Errors (+exp) • *double check these outcomes
Turton et al. (2010) RCT (6) N_{start}=36 N_{end}=34 TPS=Subacute	E: Pointing Intervention with Prismatic Goggles (6°) C: Pointing Intervention with Neutral Goggles Duration: 5d/wk for 2wk Statistical Analysis: ANOVA	• Behavioural Inattention Test (-) • Catherine Bergego Scale (-) • Rate of Change in Pointing Bias (+exp)
Serino et al. (2009) RCT (7) N_{start}=20 N_{end}=20 TPS=Subacute	E: Pointing Intervention with Prismatic Goggles (10°) C: Pointing Intervention with Neutral Goggles Duration: 30min/d, 5d/wk for 2wk Statistical Analysis: ANOVA	• Behavioural Inattention Test (+exp) • Bell's Cancellation Test (exp) • Star Cancellation Test (exp) • Letter Cancellation Test (+exp) • Reading Accuracy (+exp)
Nys et al. (2008) RCT (6) N_{start}=16 N_{end}=16 TPS=Acute	E: Prismatic Adaptation Treatment (10°) C: Sham Prismatic Adaptation Treatment Duration: 30min/d, 4d Statistical Analysis: ANOVA	• Line Bisection Test (-) • Letter Cancellation (-) • Scene Copying task (-)
Rossetti et al. (1998) RCT (5) N_{start}=12 N_{end}=16 TPS=Subacute *note, two exp in one	E: Prismatic Adaptation (10°) C: Sham Prismatic Adaptation Duration: 2-5min Statistical Analysis: A two-way repeated measure of variance	• Line Bisection (+exp) • Line Cancellation (+exp) • Simple Figure Copying (+exp) • Drawing (+exp) • Reading (+exp)
Rossi et al. (1990) RCT (4)	E: Prismatic Adaptation Treatment (8.5°, 15-diopter)	• Barthel Index (-) • Motor-free Visual Perceptual Test (+exp)

N_{start}=39 N_{end}=35 TPS=Subacute	C: No Treatment Duration: 4wks Statistical Analysis: ANOVA	• Line Bisection Test (+exp) • Line Cancellation Test (+exp) • Tangent Screen Examination (+exp) • Harrington Flocks Visual Screener (+exp)
Prism Adaptation + Methylphenidate vs Prism Adaptation + Placebo		
Luate et al. 2018 RCT (9) N_{start}=24 N_{end}=21 TPS=Subacute	E: Prism Adaptation + Methylphenidate (10mg) C: Prism Adaptation + Placebo (10mg) Duration: 30min/d, 5d/wk for 2wk (prism adaptation) + 10mg methylphenidate (or placebo) 2x/d for 2wk Statistical Analysis: Mann-Whitney U-Test	• Line Bisection Test (-) • Line Cancellation Test (-) • Reproduction of a Scene Test (-) • Star Cancellation Test (+exp) • Balloon Test (-) • Functional Independence Measure (+exp) • Catherine Bergego Scale (+exp)
Prism Adaptation vs Visual Scanning vs Limb Activation		
Priftis et al. (2013) RCT (5) N_{Start}=33 N_{End}=31 TPS=Subacute	E1: Visual Scanning Training E2: Limb Activation Treatment E3: Prism Adaptation (10°) Duration: 20min, 2x/d 5d/wk for 2wk Statistical Analysis: Mann-Whitney U Test	E3 vs E1 • Fluff Test (-) • Comb and Razor Test (-) • Semi-structured Scale for the Functional Evaluation of Hemi-Inattention (-) • Room Description (-) • Picture Scanning (-) • Menu Reading (-) • Coin Sorting (-) • Catherine Bergego Scale (-) E3 vs E2 • Fluff Test (-) • Comb and Razor Test (-) • Semi-structured Scale for the Functional Evaluation of Hemi-Inattention (-) • Room Description (-) • Picture Scanning (-) • Menu Reading (-) • Coin Sorting (-) • Catherine Bergego Scale (-)
Prism Adaptation + Functional Electrical Stimulation vs Prism Adaptation vs Functional Electrical Stimulation		
Choi et al. (2019) RCT (6) N_{Start}=30 N_{End}=30 TPS=Subacute	E1: Prism Adaptation + Functional Electrical Stimulation E2: Prism Adaptation E3: Functional Electrical Stimulation Duration: 50min/d, 5d/wk, 3wks	E1 vs E2 • Albert Test (+exp1) • Motor-Free Visual Perception Test (+exp1) • Catherine Bergego Scale (+exp1) E1 vs E3 • Albert Test (+exp1) • Motor-free Visual Perception Test (+exp1) • Catherine Bergego Scale (+exp1)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Prism Adaptation Treatment

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the use of **prism adaptation** for improving neglect when compared to **conventional rehabilitation**.	14	Goedert et al., 2020; Vaes et al., 2018; Rowe et al., 2017; Ten Brink et al., 2017; Rode et al., 2015; Bowers et al., 2014; Mancuso et al., 2012; Mizuno et al., 2011; Jacquin-Courtois et al., 2010; Turton et al., 2010; Serino et al., 2009; Nys et al., 2008; Rossetti et al., 1998; Rossi et al., 1990
1b	**Prism adaptation with methylphenidate** may not have a difference in efficacy compared to **prism adaptation alone** for improving neglect.	1	Luate et al., 2018
2	**Prism adaptation** may not have a difference in efficacy compared to **visual scanning** or **limb activation** for improving neglect.	1	Prifitis et al., 2013
1b	**Prism adaptation with functional electrical stimulation** may produce greater improvements in neglect than **prism adaptation alone.**	1	Choi et al., 2019
1b	**Prism adaptation with functional electrical stimulation** may produce greater improvements in neglect than **functional electrical stimulation alone.**	1	Choi et al., 2019

LEARNING AND MEMORY			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Prism adaptation** may produce greater improvements in learning and memory than **conventional rehabilitation/sham**.	1	Vaes et al., 2018

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Prism adaptation** may not have a difference in efficacy compared to **conventional rehabilitation/sham** for improving motor rehabilitation.	2	Rowe et al., 2017; Bowers et a., 2014

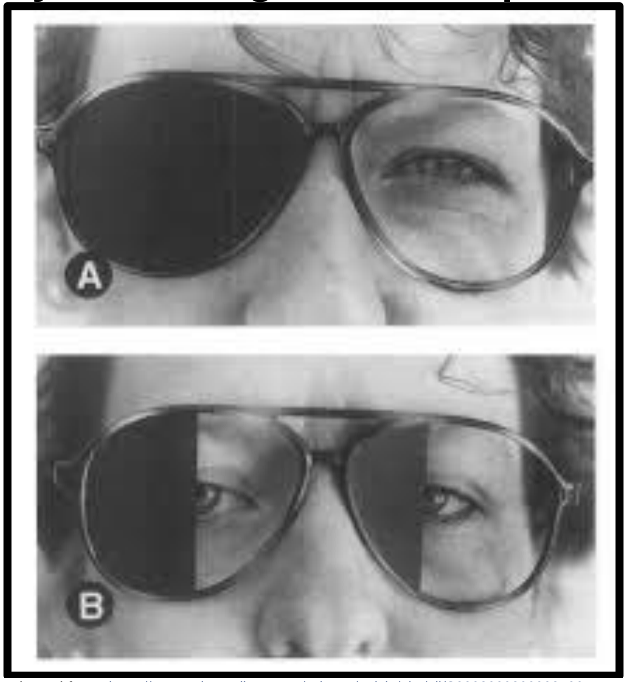
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Prism adaptation** may not have a difference in efficacy compared to **conventional rehabilitation/sham** for improving activities of daily living.	4	Rowe et al., 2017; Rode et al., 2015; Mizuno et al., 2011; Rossi et al., 1990
1b	**Prism adaptation with methylphenidate** may produce greater improvements in activities of daily living than **prism adaptation alone**.	1	Luate et al., 2018

Key Points

The literature is mixed regarding prism adaptation training for improving neglect.

Prism adaptation may not be beneficial for improving motor rehabilitation or activities of daily living.

Eye-Patching and Hemispatial Glasses



Adapted from: https://www.sciencedirect.com/science/article/abs/pii/S0003999399903106

Eye-patching is an interesting approach to hemispatial neglect rehabilitation that has been proposed since the early 1990s as a method to improve visual-scanning and attend to the neglected field (Butter & Kirsch, 1992). Beis et al. (1999) stated that their "*hypothesis was that eye patches can be used to alter the processing of visual information by affecting the information processing structures of the central nervous system"*. Shulman noted that in healthy subjects, eye patches should increase eye movements towards the contralateral space (Shulman, 1984). Thus, eye patching of the eye ipsilateral to the lesion causes patients to look toward contralateral space by either moving their eye or by movement of the head. In turn these effects, as cited by Beis et al. (1999), *"encourage the development of voluntary, deliberate control of attention in the short term and the development of automatic shifts of attention over the longer term,"* (Beis et al., 1999; Seron et al., 1989).

Nine RCTs were found evaluating eye patching interventions for neglect rehabilitation. Four RCTs compared eye patching to conventional rehabilitation (Machner et al., 2014; Tsang et al., 2009; Zeloni et al., 2002; Beis et al., 1999). One RCT compared eye patching to visual scanning (Ianes et al., 2012). Two RCTs compared eye patching with cognitive rehabilitation training to cognitive rehabilitation training alone (Aparicio-Lopez et al., 2016; Aparicio-Lopez et al., 2015). One RCT compare eye patching with constraint induced movement therapy to constraint induced movement therapy alone (Wu et al., 2013). One RCT compared eye patching with trunk rotation therapy to conventional rehabilitation (Fong et al., 2007).

The methodological details and results of all nine RCTs are presented in Table 7.

Table 7. RCTs evaluating eye-patching and hemispatial glasses interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Eye Patching vs Conventional Rehabilitation		
Machner et al. (2014) RCT (5) N_{Start}=23 N_{End}=21 TPS=Acute	E: Hemifield Eye Patching and Repetitive Optokinetics Stimulation (15min/d) + Usual Care C: Usual Care Duration: 7d	• Catherine Bergego Scale (-) • Barthel Index (-) • Modified Rankin scale (-) • National Institutes of Health Stroke Scale (-) • Bell's Cancellations Test (-) • Star Cancellation Test (-) • Line Bisection Test (-) • Ogden Figure Copying Task (-) • Reading Errors (-)
Tsang et al. (2009) RCT (7) N_{start}=35 N_{end}=34 TPS=Acute	E: Conventional Occupational Therapy + Right Half-field Eye Patching C: Occupational Therapy Duration: 3hr/d, 5d/wk for 4wk	• Behavioural Inattention Test - Conventional Subtest (+exp) • Functional Independence Measure (-)
Zeloni et al. (2002) RCT (3) N_{start}=11 N_{end}=11 TPS=Subacute	E: Goggles with Right Hemisphere Occlusion C: Standard Rehabilitation Duration: 1wk	• Albert's Test (+exp) • Letter Cancellation (-) • Bell's Cancellation (-) • Line Bisection (-) • Figure Drawing 1 (-) • Figure Drawing 2 (-)
Beis et al. (1999) Cross-over RCT (5) N_{start}=22 N_{end}=22 TPS=Subacute	E: Right Half-field Patches Over Both Eyes C: No Patch Duration: 3mo	Eye movement: • Time in Left Hemifield (-) • Leftward Eye Movements (+exp) • Functional Independence Measure: (+exp)
Eye Patching vs Visual Scanning Training		
Ianes et al. (2012) RCT (7) N_{start}=18 N_{end}=18 TPS=Acute	E: Right Half-field Eye Patching (8hr/d) C: Visual Scanning Training (40min/d) Duration: 5d/wk for 3wk	• Line Bisection Test (-) • Line Crossing Test (-) • Bell's Cancellation Test (-)
Eye Patching + Cognitive Rehabilitation vs Cognitive Rehabilitation Alone		
Aparicio-Lopez et al. (2016) RCT (4) N_{Start}=28 N_{End}=22 TPS= Chronic	E: Right Hemifield Eye Patching + Computerized Cognitive Rehabilitation C: Computerized Cognitive Rehabilitation Duration: 15 one-hour sessions, mean 2.71 sessions/wk	Neuropsychological exploration (-) • Bell Cancellation test (-) • Figure Copying of Ogden (-) • Line Bisection percent positively for rightward deviations (-) • Line Bisection percent negatively for leftward deviations (-) • Line Bisection lines omitted (-) • Baking Tray Task-Left (-) • Baking Tray Task-Right (-)

		• Reading Task (-) • Catherine Bergego Scale-Self (-) • Catherine Bergego Scale-Rater (-)
Aparicio-Lopez et al. (2015) RCT (6) N_{Start}=12 N_{End}=12 TPS=Subacute	E: Computer-based Cognitive Rehabilitation + Right Hemifield Eye Patching C: Computer-based Cognitive Rehabilitation Duration: 1hr/d, 5d/wk for 3wk	• Line Bisection Test (-) • Bell's Cancellation Test (-) • Figure Copying of Ogden (-) • Baking Tray Task (-) • Catherine Bergego Scale (-) • Reading Test (+exp)
Eye Patching + Constraint Induced Therapy vs Constraint Induced Therapy Alone		
Wu et al. (2013) RCT (7) N_{Start}=27 N_{End}=24 TPS = Chronic	E1: Constraint Induced Therapy (6hr/d) + Right Monocular Occlusion E2: Constraint Induced Therapy C: Conventional Rehabilitation (2hr/d) Duration:5d/wk for 3wk	E1 vs E2 • Catherine Bergego Scale (-) Eye Movement Variables: • Number of Left Fixation Points (+exp_2) • Fixation Amplitude (-) • Left Fixation Time (-) Arm-trunk Movement Variables: • Reaction Time (-) • Time of Peak Velocity (+exp_1) • Movement Time (-) • Total Distance (-) • Trunk Lateral Shift: (+exp_1) E1/E2 vs C • Catherine Bergego Scale (+exp_1,+exp_2) Eye Movement Variables: • Number of Left Fixation Points (+exp_2,+con), • Fixation Amplitude (-) • Left Fixation Time (-) Arm-trunk Movement Variables: • Reaction Time (+exp_2) • Time of Peak Velocity (+exp_1) • Movement Time (-) • Total Distance (-) • Trunk Lateral Shift (-)
Eye Patching + Trunk Rotation Therapy vs Conventional rehabilitation		
Fong et al. (2007) RCT (6) N_{start}=60 N_{end}=54 TPS=Acute	E1: Voluntary Trunk Rotation + Right Hemifield Eye Patching E2: Voluntary Trunk Rotation C: Conventional Rehabilitation Duration: 1hr/d, 5d/wk for 4wk Statistical Analysis: ANOVA	E1 vs C Behavioural Inattention Test: • Conventional (-) • Behavioural (-) • Clock Drawing Test (-) Functional Independence Measure – Motor: • Total (-) • Self-care (-) • Sphincter (-) • Transfer (-) • Locomotion (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Eye Patching and Hemispatial Glasses

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Eye patching** may not have a difference in efficacy compared to **conventional rehabilitation** for improving neglect.	4	Machner et al., 2014; Tsang et al., 2009; Zeloni et al., 2002; Beis et al., 1999
1b	**Eye patching** may not have a difference in efficacy compared to **visual scanning** for improving neglect.	1	Ianes et al., 2012
1b	**Eye patching with cognitive rehabilitation** may not have a difference in efficacy compared to **cognitive rehabilitation alone** for improving neglect.	2	Aparicio-Lopez et al., 2015; Aparicio-Lopez et al., 2015
1b	**Constraint induced therapy with eye patching** may not have a difference in efficacy compared to **conventional rehabilitation or** constraint induced **therapy alone** for improving neglect.	1	Wu et al., 2013
1b	**Eye patching with trunk rotation therapy** may not have a difference in efficacy compared to **conventional rehabilitation** for improving neglect.	1	Fong et al., 2007

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Constraint induced therapy** may not have a difference in efficacy compared to **conventional rehabilitation or constraint induced therapy alone** for improving motor rehabilitation.	1	Wu et al., 2013

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Eye patching** may not have a difference in efficacy compared to **conventional rehabilitation** for improving stroke severity.	1	Machner et al., 2014

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Eye patching** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	3	Machner et al., 2014; Tsang et al., 2009; Beis et al., 1999
1b	**Eye patching with trunk rotation therapy** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	1	Fong et al., 2007

Key Points

Eye patching may not be beneficial for neglect and activities of daily living.

Trunk Rotation Therapy

Adapted from: https://journals.sagepub.com/doi/abs/10.1177/0269215507076391?journalCode=crea and https://www.archives-pmr.org/article/S0003-9993(97)90236-7/pdf

Trunk impairment is common after stroke and is directly associated with balance and gait (Jijimol et al. 2013; Verheyden et al. 2006). It has been proposed that the orientation of the trunk midline in space functions as the dividing line between our personal representation of left versus right space and acts as an anchor for the calculation of body position (Karnath et al., 1991). Karnath et al. (1993) demonstrated that turning only the trunk of the patient to the left such that both right and left stimuli were projected to the right side of the trunk could compensate for deficits in reaction times to stimuli in the left visual field. By shifting the midline, the individual is artificially manipulating their internal reference point, and modifying their egocentric reference frames.

Three RCTs were found evaluating trunk rotation therapy interventions for neglect rehabilitation. One RCT compared trunk rotation therapy to trunk rotation therapy with eye patching, and to conventional rehabilitation (Fong et al., 2007). One RCT compared trunk rotation therapy and visual scanning to conventional rehabilitation (Wiart et al., 1997). One compared the use of a Bon Saint Come Device to conventional neurorehabilitation (DeSeze et al., 2001).

The methodological details and results of the three RCTs are presented in Table 8.

Table 8. RCTs evaluating trunk rotation therapy interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Trunk Rotation Therapy + Eye Patching vs Trunk Rotation Therapy vs Conventional Rehabilitation		
Fong et al. (2007) RCT (6) N_{start}=60 N_{end}=54 TPS=Acute	E1: Voluntary Trunk Rotation + Right Hemifield Eye Patching E2: Voluntary Trunk Rotation C: Conventional Rehabilitation Duration: 1hr/d, 5d/wk for 4wk Statistical Analysis: ANOVA	E2 vs C Behavioural Inattention Test: • Conventional (-) • Behavioural (-) • Clock Drawing Test (-) Functional Independence Measure – Motor: • Total (-) • Self-care (-) • Sphincter (-) • Transfer (-) • Locomotion (-) E1 vs E2 Behavioural Inattention Test: • Conventional (-) • Behavioural (-) • Clock Drawing Test (-) Functional Independence Measure – Motor: • Total (-) • Self-care (-) • Sphincter (-) • Transfer (-) • Locomotion (-)
Trunk Rotation Therapy + Visual Scanning vs Conventional Rehabilitation		
Wiart et al. (1997) RCT (4) N_{start}=22 N_{end}=22 TPS=Chronic	E: Bon Saint Come Trunk Training (Trunk Rotation + Visual Scanning) + Traditional Rehabilitation C: Traditional Rehabilitation Duration: 1hr/d, 5d/wk for 4wk Statistical Analysis: ANOVA	• Schekenberg Test (+exp) • Bell's Cancellation Test (+exp) • Albert Test (+exp) • Functional Independence Measure (+exp)
Bon Saint Come Device vs Conventional Neurorehabilitation		
DeSeze et al. (2001) RCT (6) NStart=20 NEnd=20 TPS=Subacute	E: Saint Come Device + Conventional Neurorehabilitation C: Conventional Neurorehabilitation Duration: Device 1hr/d 2mo Conventional Neurorehabilitation - 1 hr/d, 2mo	• Static Postural Status (-) • Trunk Control Test (+exp) • Upright Equilibrium Index (+exp) • Sitting Equilibrium Index (+exp) • Improvement in Neglect (+exp) • Gait Recovery (+exp) • Average Functional Ambulation Classification (+exp) • Functional Independence Measure (-) • Bells Test (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Trunk Rotation Therapy

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Trunk rotation and eye patching** may not have a difference in efficacy compared to **conventional rehabilitation** for improving neglect.	1	Fong et al., 2007
1b	**Trunk rotation and eye patching** may not have a difference in efficacy compared to **trunk rotation alone** for improving neglect.	1	Fong et al., 2007
2	**Trunk rotation and visual scanning** may produce greater improvements in neglect than **conventional rehabilitation**.	1	Wiart et al., 1997
1b	There is conflicting evidence about the use of the **Bon Saint Come Device** for improving neglect when compared to **conventional neurorehabilitation.**	1	DeSeze et al., 2001

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**The Bon Saint Come Device** may produce greater improvements in neglect than **conventional neurorehabilitation.**	1	DeSeze et al., 2001

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Trunk rotation and eye patching** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	1	Fong et al., 2007
1b	**Trunk rotation and eye patching** may not have a difference in efficacy compared to **trunk rotation alone** for improving activities of daily living.	1	Fong et al., 2007
2	**Trunk rotation and visual scanning** may produce greater improvements in activities of daily living than **conventional rehabilitation**.	1	Wiart et al., 1997
1b	**The Bon Saint Come Device** may not have a difference in efficacy compared to **conventional neurorehabilitation.**	1	DeSeze et al., 2001

Key Points

Trunk rotation therapy may not be beneficial for neglect and activities of daily living

Trunk rotation therapy may be beneficial for motor rehabilitation

General Cognitive and Perceptual Training

Adapted from: https://www.rehabmart.com/post/25-tools-every-occupational-therapist-needs

Neglect is frequently associated with multiple deficits including problems with sustained attention and arousal, as well as motor and sensory impairments (Barrett et al., 2006). General cognitive and perceptual training interventions consist of treatments that target deficits associated with neglect such as selective attention, perceptual training, cueing therapy and music therapy. These interventions train aspects of cognition and perception that are affected by hemispatial neglect caused by stroke. It is thought that by training these aspects of cognition and perception there will be improvements in neglect outcomes as well.

13 RCTs were found evaluating general cognitive and perceptual training interventions for neglect rehabilitation. Five RCTs compared general visuospatial/perceptual training to conventional (Peers et al., 2021; Svaerke et al., 2019; Aimola et al., 2014; Lincoln et al., 1985; Weinberg et al., 1982). Two RCTs examined general cognitive training compared to standard care/sham (Barker-Collo et al., 2009; Carter et al., 1983). Five RCTs examined cueing compared to standard care/sham (Cavanaugh et al., 2021; Sukumaran et al., 2020; Karner et al., 2019; Turgut et al., 2018; Toglia et al., 2009). One RCT examined music therapy compared to language therapy and to usual care (Särkämö et al., 2008).

The methodological details and results of the 13 RCTs are presented in Table 9.

Table 9. RCTs evaluating general cognitive and perceptual training interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
General Visuospatial/Perceptual Training vs Conventional Therapy		
Peers et al. (2021) RCT (8) N_{Start}=80 N_{End}=80 TPS=Chronic	E1: Selective Attention Training E2: Working Memory Training C: Waitlist Duration: 20min/day, 4wks (20 sessions)	<u>E1 vs C</u> • Spatial Bias Score (-) • Self-Reported Changes in Functioning (+exp1) • Oxford Cognitive Screen (OCS-BRIDGE) - Visual Extinction Absolute Bias (-) • OCS-BRIDGE Hearts Cancellation Absolute Bias (-) • OCS-BRIDGE SALT Reaction Time Absolute Bias (-) • TVA VSTM Capacity (-) • TVA K Variability (-) • OCS-BRIDGE FINS Forward Span (-) • OCS-BRIDGE FINS Backward Span (-) • AWMA Dot Matrix (-) • AWMA Spatial Recall (Memory) (-) • AWMA Spatial Recall (Processing) (-) • EBIQ Core Patient (-) • EBIQ Core Carer (-) • Cognitive Failures Questionnaire (-) • Subjective Neglect Questionnaire (-) <u>E2 vs C</u> • Spatial Bias Score (-) • Self-Reported Changes in Functioning (-) • OCS-BRIDGE Visual Extinction Absolute Bias (-) • OCS-BRIDGE Hearts Cancellation Absolute Bias (-) • OCS-BRIDGE SALT Reaction Time Absolute Bias (-) • TVA VSTM Capacity (-) • TVA K Variability (-) • OCS-BRIDGE FINS Forward Span (-) • OCS-BRIDGE FINS Backward Span (-) • AWMA Dot Matrix (-) • AWMA Spatial Recall (Memory) (-) • AWMA Spatial Recall (Processing) (-) • EBIQ Core Patient (-) • EBIQ Core Carer (-) • Cognitive Failures Questionnaire (-) • Subjective Neglect Questionnaire (-) <u>E1 vs E2</u> • Spatial Bias Score (-) • Self-Reported Changes in Functioning (+exp1) • OCS-BRIDGE Visual Extinction Absolute Bias (-) • OCS-BRIDGE Hearts Cancellation Absolute Bias (-) • OCS-BRIDGE SALT Reaction Time Absolute Bias (-) • TVA VSTM Capacity (-) • TVA K Variability (-) • OCS-BRIDGE FINS Forward Span (-) • OCS-BRIDGE FINS Backward Span (-)

		• AWMA Dot Matrix (-) • AWMA Spatial Recall (Memory) (-) • AWMA Spatial Recall (Processing) (-) • EBIQ Core Patient (-) • EBIQ Core Carer (-) • Cognitive Failures Questionnaire (-) • Subjective Neglect Questionnaire (-)
Svaerke et al. (2019) RCT (5) N_{Start}=18 N_{End}=14 TPS=Acute	E1: 3wks of Computer-based Cognitive Rehabilitation followed by 3 wks of Usual Care E2: 3 wks of Usual Care followed by 3wks of Computer-based Cognitive Rehabilitation Duration: 30-45 min/session, 1 session every other day, 3wks	E1 vs E2 • Cognitive Assessment at Bedside with iPad (-) • Street Test (-) • Drawing Test (-) • Block Design (-) • SCL-90-R (+exp2)
Aimola et al. (2014) RCT (5) N_{Start}=70 N_{End}=50 TPS=Chronic	E: Supervised Reading and Exploration Training C: Unsupervised Control Training Duration: 14 blocks/d 120 trials/block, 294 exploration and 196 reading blocks Controls: 10 blocks/d, 1hr, total 350 blocks	• Visual Search (+exp) • Reading (+exp) • Tasks Stimulating ADL (-) • Obstacle Avoidance (-) • Attention Tasks (no stats) • Sustained Attention to Response Test (SART) (-) • Test of Everyday Attention - Visual Elevator (-) • TEA - Auditory Elevator without Distraction (-)
Lincoln et al. (1985) RCT (6) N_{Start}=33 N_{End}=33 TPS=Chronic	E: Perceptual Training C: Conventional Therapy Duration: 4hrs/wk, 4wks	• Rivermead Perceptual Assessment Battery (-) • Activities of Daily Living (-)
Weinberg et al. (1982) RCT (5) N_{Start}=35 N_{End}=33 TPS=Acute	E: Cognitive Training Program for Neglect C: Visuo-Cognitive Tasks Duration: 20hrs (1hr/d, 4wks)	• Visuo-Cognitive Tests (no stats) • Embedded Figures (+exp) • Visual Simultaneity (+exp) • Conditional Cancellation (+exp) • WAIS Digit Symbol (+exp) • WAIS Picture Completion (+exp) • WAIS Block Design (+exp) • WAIS Object Assembly (+exp) • Knox Cubes (+exp)
General Cognitive Training vs Standard Care		
Barker-Collo et al. (2009) RCT (7) N_{Start}=78 N_{End}=66 TPS=Chronic	E: Attention Process Training C: Standard Care Duration: 1 hr/weekday, 4wks, up to 30hrs total	• Full Attention (+exp) • Auditory Attention (+exp) • Visual Attention (-) • Trail-Making Test A (-) • Trail-Making Test B (-) • PASAT 2.4 sec (-) • PASAT 2.0 sec (-) • Bell Left (-) • Bell Right (-) • Bell Center (-) • SF-36 Physical Component Score (-) • SF-36 Mental Component Score (-)
Carter et al. (1983) RCT (8) N_{Start}=33 N_{End}=33 TPS=Not Reported	E: Cognitive Retraining C: Conventional Therapies Duration: 30 min/d, 3d/wk, 3wks	• Scanning (+exp) • Visual-Spatial (+exp) • Time-Judgement (+exp)
Cueing vs Standard Care/Sham		
Cavanaugh et al. (2021) RCT (8) N_{Start}=48	E: Feature-Based Attention Training in the eye with a deficit	• Humphrey Visual Field Changes (-) • Macular Integrity Assessment Microperimetry (-)

N_{End}=46 TPS=Chronic	C: Feature-Based Attention Training in the intact eye (Sham) Duration: 300 discriminations/session, 1 session/d, 5d/wk, 6mo	• Quality of Life (-)
Sukumaran et al. (2020) RCT (6) N_{Start}=14 N_{End}=12 TPS=Acute	E: Visual and Auditory Stimulation and Motor Tasking + Standard Post-Stroke Physiotherapy and Gait Training C: Standard Post-Stroke Physiotherapy and Gait Training Duration: 20-30min/session, 2seesions/d, 1mo	• Star Cancellation Test (+exp) • Line Bisection Test (-) • Picture Identification Task (-) • National Institutes of Health Stroke Scale (-) • Modified Rankin Scale Score (-)
Karner et al. (2019) RCT (6) N_{Start}=47 N_{End}=39 TPS=Subacute	E: Cueing Training with the Personal Robot (PARO) C: Patients were read aloud to Duration: 30 min/session, 3 sessions/wk, 2wks	• Cats Test (+exp) • Line Bisection Test (-) • Scores of Independence Index for Neurological and Geriatric Rehabilitation (SINGER) - Self-Care (-) • SINGER - Mobility (-) • SINGER - Communication (-) • SINGER - Cognitive Abilities (+exp)
Turgut et al. (2018) RCT (6) N_{Start}=29 N_{End}=21 TPS=Subacute	E: Daily reading task + Endogenous and Exogenous cues C: Neuropsychological treatment of the same length, not targeting visuospatial attention Duration: min/session, 5 d/wk, 3wks	• Text Reading (+exp) • Word Reading (+exp) • Catherine Bergego Scale (+exp) • Clock Drawing Test (+exp) • Line Bisection (+exp) • Apples Cancellation Task (+exp)

Toglia et al. (2009)
RCT (7)
N_{Start}=40
N_{End}=40
TPS=NR (Reported, but 6 participants were >45 days post stroke)
	E: Dynamic Cueing and Feedback during an Object Search Task
	C: No Cueing or Feedback during an Object Search Task
	Duration: 1 60 min session including interventions, pre- and post-tests, and an interview
		• Object Search Task (+exp)
		  • Object Detection Score (+exp)
		  • Laterality Index (+exp)

Music Therapy vs Language Therapy vs Usual Care		
Sarkamo et al. (2008) RCT (6) N_{Start}=60 N_{End}=55 TPS=Acute	E1: Music Group + Usual Care E2: Language Group + Usual Care C: Usual Care Duration: 2mo	E1 vs C • Rivermead Behavioural Memory Test (+exp1) • Wechsler Memory Scale (-) • Language (Boston Aphasia Examination & CERAD Battery) (-) • Visuospatial Cognition (Clock Task, Copying Task, Benton Visual Retention Test & the Balloons Test) (-) • Focused Attention-Correct Responses (Mental Subtraction & Stroop Tests) (+exp1) • Focused Attention-Reaction Times (Mental Subtraction & Stroop Tests) (-) • Sustained Attention-CR (Vigilance & Simple Reaction Time Subtests) (-) • Sustained Attention-RT (Vigilance & Simple Reaction Time Subtests) (-) • Music Cognition (Scale & Rhythm Subtests of Montreal Battery of Evaluation of Amusia) (-) • Frontal Assessment Battery (-) E1 vs E2 • Rivermead Behavioural Memory Test (+exp1) • Wechsler Memory Scale (-) • Language (Boston Aphasia Examination & CERAD Battery) (-) • Visuospatial Cognition (Clock Task, Copying Task, Benton Visual Retention Test & the Balloons Test) (-)

		• Focused Attention-Correct Responses (Mental Subtraction & Stroop Tests) (+exp1) • Focused Attention-Reaction Times (Mental Subtraction & Stroop Tests) (-) • Sustained Attention-CR (Vigilance & Simple Reaction Time Subtests) (-) • Sustained Attention-RT (Vigilance & Simple Reaction Time Subtests) (-) • Music Cognition (Scale & Rhythm Subtests of Montreal Battery of Evaluation of Amusia) (-) • Frontal Assessment Battery (-) E2 vs C • Rivermead Behavioural Memory Test (-) • Wechsler Memory Scale (-) • Language (Boston Aphasia Examination & CERAD Battery) (-) • Visuospatial Cognition (Clock Task, Copying Task, Benton Visual Retention Test & the Balloons Test) (-) • Focused Attention-Correct Responses (Mental Subtraction & Stroop Tests) (-) • Focused Attention-Reaction Times (Mental Subtraction & Stroop Tests) (-) • Sustained Attention-CR (Vigilance & Simple Reaction Time Subtests) (-) • Sustained Attention-RT (Vigilance & Simple Reaction Time Subtests) (-) • Music Cognition (Scale & Rhythm Subtests of Montreal Battery of Evaluation of Amusia) (-) • Frontal Assessment Battery (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about General Cognitive and Perceptual Training

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**General visuospatial/perceptual training** may not have a difference in efficacy compared to **conventional therapy** for improving neglect.	5	Peers et al., 2021; Svaerke et al., 2019; Aimola et al., 2014; Lincoln et al., 1985; Weinberg et al., 1982
1a	There is conflicting evidence about the use of **general cognitive training** for improving neglect when compared to **standard care.**	2	Barker-Collo et al., 2009; Cater et al., 1983
1a	There is conflicting evidence about the use of **cueing** for improving neglect when compared to **standard care/sham.**	5	Cavanaugh et al., 2021; Sukumaran et al., 2020; Karner et al., 2019; Turgut et al., 2018; Toglia et al., 2009
1b	**Music therapy** may not have a difference in efficacy compared to **standard care** for improving neglect.	1	Sarkamo et al., 2008

1b	**Music therapy** may not have a difference in efficacy compared to **language therapy** for improving neglect.	1	Sarkamo et al., 2008

LEARNING & MEMORY			
LoE	Conclusion Statement	RCTs	References
1b	**General visuospatial/perceptual training** may not have a difference in efficacy compared to **conventional therapy** for improving learning and memory.	2	Peers et al., 2021; Weinberg et al., 1982
1b	**General cognitive training** may not have a difference in efficacy compared to **standard care** for improving learning and memory.	1	Barker-Collo et al., 2009
1b	There is conflicting evidence about the use of **music therapy** for improving learning and memory when compared to **standard care.**	1	Sarkamo et al., 2009
1b	There is conflicting evidence about the use of **music therapy** for improving learning and memory when compared to **language therapy.**	1	Sarkamo et al., 2009

GLOBAL COGNITION			
LoE	Conclusion Statement	RCTs	References
1b	**General visuospatial/perceptual training** may not have a difference in efficacy compared to **conventional therapy** for improving general cognition.	2	Peers et al., 2021; Weinberg et al., 1982
1a	There is conflicting evidence about the use of **general cognitive training** for improving global cognition when compared to **standard care.**	2	Barker-Collo et al., 2009; Cater et al., 1983
1b	**Music therapy** may not have a difference in efficacy compared to **standard care** for improving global cognition.	1	Sarkamo et al., 2008
1b	**Music therapy** may not have a difference in efficacy compared to **language therapy** for improving global cognition.	1	Sarkamo et al., 2008

MOTOR REHABILITATION			
LoE	Conclusion Statement	RCTs	References
1b	**General visuospatial/perceptual training** may not have a difference in efficacy compared to **conventional therapy** for improving motor rehabilitation.	2	Peers et al., 2021; Aimola et al., 2014

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**General visuospatial/perceptual training** may not have a difference in efficacy compared to **conventional therapy** for improving motor rehabilitation.	2	Aimola et al., 2014; Lincoln et al., 1985
1b	**Cueing** may not have a difference in efficacy compared to **standard care/sham** for improving stroke severity.	1	Sukumaran et al., 2020

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Cueing** may not have a difference in efficacy compared to **standard care/sham** for improving activities of daily living.	1	Karner et al., 2019

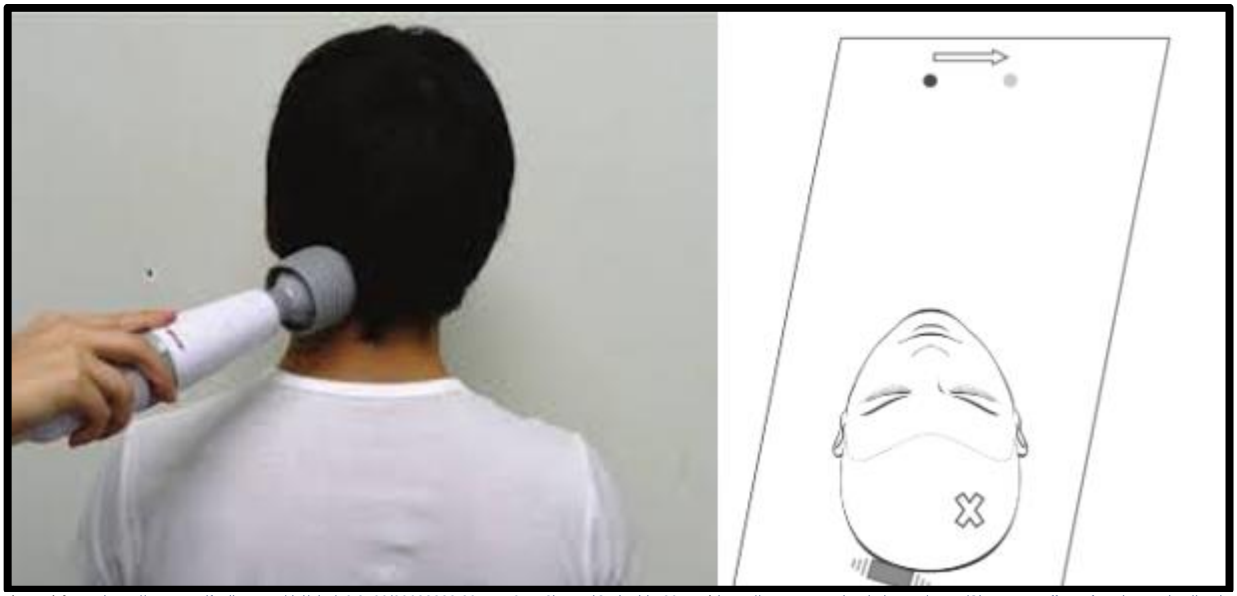
Key Points

General visuospatial/perceptual training may not be beneficial for neglect.

The literature is mixed concerning cueing for improving neglect.

Stimulation Interventions

Neck Stimulation



Adapted from: https://www.tandfonline.com/doi/abs/10.3109/09638288.2011.570411?journalCode=idre20 and https://www.semanticscholar.org/paper/Short-term-effect-of-neck-muscle-vibration-on-in-Leplaideur-Leblong/f07328c742e1f2a5e2451b4d4aac5e3231e22ef5/figure/0

Karnath et al. (1993) demonstrated that the detection and identification of stimuli in the left visual field in patients with neglect could be improved by trunk rotation, resulting in the lengthening of left posterior neck muscles, or by somatosensory stimulation applied to the left posterior neck muscles in the form of neck muscle vibration. Neck muscle vibration is thought to improve neglect by creating a kinaesthetic illusion, whereby a spot of light will appear to move in the opposite direction of stimulation (Leplaideur et al., 2016). It is non-invasive, has no side-effects and is easy to apply (Schindler et al., 2002). This somatosensory stimulation can also increase awareness of the neglected hemifield, providing a cue of sorts to attend more to that side of the body.

Two RCTs was found evaluating neck muscle vibration interventions for neglect rehabilitation. It compared visual exploration training and neck muscle vibration to visual exploration alone (Schindler et al., 2002). One RCT was found evaluating neck muscle taping for neglect rehabilitation and compared it to placebo (Varaltra et al. 2019).

The methodological details and results of the single RCT are presented in Table 10.

Table 10. RCTs evaluating neck muscle vibration therapy interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Schindler et al. (2002) Cross-over RCT (5) N_{Start}=20 N_{End}=20 TPS=Subacute	E: Visual Exploration Training + Neck Muscle Vibration C: Visual Exploration Training Duration: 40min/d, 5d/wk for 3wk Statistical Analysis: ANOVA	• Visual Subjective Straight-ahead Judgements (+exp) • Cancellation Test (+exp) • Tactile Search (+exp) • Indented Text Reading (+exp) • Visual Size Discrimination (-) Activities of Daily Living Questionnaire: • Personal Care (+exp) • Reaching and Grasping (+exp) • Spatial Orientation (+exp) • Time Orientation (-) • Awareness of Deficit (-)
Neck Taping vs Sham		
Varalta et al. (2019) RCT (9) N_{Start}=12 N_{End}=12 TPS=Chronic	E: Neck Taping using Kenzo Kase's KinesioTaping Method C: Sham Neck Taping Duration: Tape replaced every 4d, total of 30d of treatment	• Star Cancellation Test (-) • Letters Cancellation Test (-) • Comb and Razor Test (-) • Active Range of Motion - Rotation Right (+exp) • Active Range of Motion - Rotation Left (-) • Active Range of Motion - Inclination Right (-) • Active Range of Motion - Inclination Left (-) • Active Range of Motion - Flexion (-) • Active Range of Motion - Extension (-) • Cervical Joint Position Error Test (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about neck Muscle Vibration

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Visual exploration with neck muscle vibration** may produce greater improvements in neglect than **visual exploration alone**.	1	Schindler et al., 2002
1b	**Neck muscle taping** may not have a difference in efficacy compared to **placebo** for improving neglect.	1	Varaltra et al. 2019

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about **neck taping** for improving motor rehabilitation when compared to **sham alone**.	1	Varaltra et al. 2019

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	There is conflicting evidence about the use of **visual exploration with neck muscle vibration** for improving activities of daily living when compared to **visual exploration alone**.	1	Schindler et al., 2002

Key Points

The literature is mixed concerning visual exploration with neck muscle vibration for improving neglect, motor rehabilitation and activities of daily living.

Transcutaneous Electrical Nerve Stimulation

Adapted from: https://flspinalsurgeon.com/transcutaneous-electrical-nerve-stimulation-tens/

Transcutaneous electrical nerve stimulation (TENS) involves the application of electrical current through surface electrodes on the skin to facilitate activation of nerves (Teoli et al. 2019). The application of afferent electrical stimulation at the sensory level may help to enhance neuroplasticity of the brain, through increased activation and recruitment of cortical networks involved in information processing of the contralesional hemifield. It is an alternative form of somatosensory stimulation, whereby the stimulation on the neglected side will also increase attention to the neglected side.

Four RCTs were found evaluating TENS interventions for neglect rehabilitation. Three RCTs compared TENS with visual scanning training to visual scanning training alone (Seniow et al., 2016; Polanowska et al., 2009; Schroder et al., 2008). One RCT compared TENS with cueing and feedback, along with cognitive rehabilitation to TENS with cognitive rehabilitation and no cueing/feedback, as well as to cognitive rehabilitation alone (Rusconi et al., 2002).

The methodological details and results of all 4 RCTs are presented in Table 11.

Table 11. RCTs evaluating transcutaneous electrical nerve stimulation interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
TENS + Visual Scanning Training vs Visual Scanning Training		
Seniow et al. (2016) RCT (6) N_{Start}=29 N_{End}=29 TPS=Subacute	E: Transcutaneous Electrical Nerve Stimulation (TENS) + Visual Scanning Training C: Sham Transcutaneous Electrical Nerve Stimulation + Visual Scanning Training Duration: 45min/d, 5d/wk for 3wk Statistical Analysis: Mann-Whitney U Test	• Behavioural Inattention Test (-)
Polanowska et al. (2009) RCT (7) N_{start}=40 N_{end}=35 TPS=Subacute	E: Computerized Visual Scanning Training + Electrical Somatosensory Stimulation C: Computerized Visual Scanning Training + Sham Stimulation Duration: 30min/d, 2d/wk for 6wk Statistical Analysis: ANOVA	• Barthel Index (-) • Functional Independence Measure (-) • Visual Scanning Accuracy (+exp) • Visual Scanning Range (+exp)
Schroder et al. (2008) RCT (6) N_{start}=30 N_{end}=30 TPS=Subacute	E1: Transcutaneous Electrical Nerve Stimulation + Computerized Scanning Training E2: Optokinetic Stimulation + Computerized Scanning Training C: Computerized Scanning Training Duration: 20-40min/d, 5d/wk for 4wk Statistical Analysis: ANOVA	E1 vs C • Reading and Writing Tasks (+exp$_1$) • Line Bisection (+exp$_1$) • Figure Copying (+exp$_1$) • Free Drawing (+exp$_1$) • Star Cancellation (+exp$_1$) • Line Cancellation (+exp$_1$) • Test Battery of Attentional Performance (+exp$_1$) E1 vs E2 • Reading and Writing tasks (-) • Line Bisection (-) • Figure Copying (-) • Free Drawing (-) • Star Cancellation (-) • Line Cancellation (-) • Test Battery of Attentional Performance (-)
Cueing/Feedback + Cognitive Rehabilitation vs TENS + Cognitive Rehabilitation vs Cognitive Rehabilitation		
Rusconi et al. (2002) RCT (3) N_{start}=20 N_{end}=20 TPS=Subacute	E1: Cognitive Rehabilitation + Cueing and Feedback E2: Cognitive Rehabilitation with Feedback + Transcutaneous Electrical Nerve Stimulation E3: Cognitive Rehabilitation + TENS with No Feedback E4: Cognitive Rehabilitation Duration: 1hr/d, 5d/wk for 8wk Statistical Analysis: ANOVA	E1/E2/E3/E4/C • Line Cancellation Test (-) • Letter Cancellation Test (-) • Line Bisection Test (-) • Sentence Reading (-) • Facial Recognition (-) • Position Sense (-) • Clock Test (-) • Drawing of 2 Houses (-) • Raven's Coloured Matrices (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Transcutaneous Electrical Nerve Stimulation

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**TENS + visual scanning training** may produce greater improvements in neglect than **visual scanning training alone**.	3	Seniow et al., 2016; Polanowska et al., 2009; Schroder et al., 2008
1b	**TENS + computerized scanning training** may not have a difference in efficacy compared to **optokinetic stimulation + computerized scanning training** for improving neglect.	1	Schroder et al., 2008
2	**TENS + cognitive rehabilitation with feedback** may not have a difference in efficacy compared to **TENS + cognitive rehabilitation without feedback, cognitive rehabilitation with cueing and feedback and cognitive rehabilitation alone** for improving neglect.	1	Rusconi et al., 2002

GLOBAL COGNITION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**TENS + cognitive rehabilitation with feedback** may not have a difference in efficacy compared to **TENS + cognitive rehabilitation without feedback, cognitive rehabilitation with cueing and feedback and cognitive rehabilitation alone** for improving global cognition.	1	Rusconi et al., 2002

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Visual scanning training with electrical somatosensory stimulation** may not have a difference in efficacy compared to **visual scanning training alone** for improving activities of daily living.	1	Polanowska et al., 2009

Key Points

TENS may be beneficial for improving neglect.

Repetitive Transcranial Magnetic Stimulation

Adapted from: https://www.technologynetworks.com/neuroscience/news/rtms-study-claims-to-improve-working-memory-319448

Transcranial magnetic stimulation is a painless and non-invasive method of affecting neural activity through the exogenous generation of an electromagnetic field through a coil placed on the scalp, that consequently induces a change in the electrical fields of the brain (Peterchev et al. 2012). The voltage and current of the electromagnetic field generated are dependent on the parameters of the stimulation device, which is not distorted by the biological tissues in which it is applied in (Peterchev et al. 2012). The neuromodulatory effects of transcranial magnetic stimulation are attributed largely to neural membrane polarization shifts that can lead to changes in neuron activity, synaptic transmission, and activation of neural networks (Peterchev et al. 2012). Repetitive transcranial magnetic stimulation (rTMS) is the application of repetitive trains of transcranial magnetic stimulation at regular intervals.

After a stroke, interhemispheric competition is altered; with cortical excitability increasing in the unaffected hemisphere increasing and decreasing in the affected hemisphere (Zhang et al. 2017). rTMS can be used to help modulate this interhemispheric competition, with low stimulation frequencies (≤1Hz) decreasing cortical excitability and inhibiting activity of the contralesional hemisphere, while high frequency (>1Hz) stimulation increases excitability and have a facilitatory effect on activity of the ipsilesional hemisphere (Dionisio et al. 2018).

Eight RCTs were found evaluating TMS interventions for neglect rehabilitation. Six RCTs compared rTMS to sham stimulation (Iwanski et al., 2020; Cha et al., 2017; Yang et al., 2017; Cha & Kim, 2016; Cha & Kim, 2015; Kim et al., 2013). One RCT compared a high volume of rTMS therapy to a low volume of rTMS therapy (Kim et al., 2013). One RCT compared transcranial noise stimulation therapy to sham stimulation (Herpich et al., 2019).

The methodological details and results of all six RCTs are presented in Table 12.

Table 12. RCTs evaluating rTMS interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
rTMS vs Sham Stimulation		
Iwanski et al. (2020) RCT (7) N_{Start}=28 N_{End}=27 TPS=Subacute	E: Low-Frequency rTMS, 1800 Pulses to the Left Angular Gyrus C: Sham Low-Frequency rTMS, same procedure as experimental group Duration: 30 min/session, 5d/wk, 3wks	• Behavioural Inattention Test - Conventional (-) • Star Cancellation (-) • Letter Cancellation (-) • Behavioural Inattention Test - Behavioural (-) • Functional Independence Measure and Functional Assessment Measure (-) • Visuospatial Scale (-)
Cha, 2017 RCT (10) N_{start}=25 N_{end}=25 TPS=Subacute	E: Standard Therapy + Real rTMS C: Standard Therapy + Sham rTMS Duration: 30min/d, 5d/wk for 4wk (standard therapy) + 20min/d, 5d/wk for 4wk Statistical Analysis: ANOVA	• Fugl-Meyer Assesment (+exp) • Box and Block Test (-) • Albert Test (+exp) • Grip Strength (+exp)
Yang et al. 2017 RCT (7) N_{start}=60 N_{end}=60 TPS=Subacute	E1: rTMS Alone E2: rTMS + Sensory Cueing C: Sham rTMS Duration: 3hr/d, 5d/wk for 2wk Statistical Analysis: ANOVA	E1/E2 vs C Behavioural Inattention Test • Cancellation (+exp$_2$) • Drawing (-) • Bergego Scale (-) • Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Modified Barthel Index (-) E1 vs E2 • Behavioural Inattention Test (-) • Bergego Scale (-) • Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Modified Barthel Index (-)
Cha & Kim (2016) RCT (6) N_{Start}=30 N_{End}=30 TPS=Subacute	E: rTMS C: Sham rTMS Duration: 50min/d, 5d/wk for 4wk Statistical Analysis: Independent T-Test	• Line Bisection Test (+exp) • Albert Test (+exp) • Box and Block Test (+exp) • Grip Strength (+exp)
Cha & Kim (2015) RCT (6) N_{Start}=22 N_{End}=20 TPS=Subacute	E: rTMS (10min) C: Sham rTMS Duration: 40min/d, 5d/wk for 4wk Statistical Analysis: Independent T-Test	• Motor Free Visual Perceptual Test (+exp) • Line Bisection Test (+exp) • Albert Test (+exp) • Star Cancellation Test (+exp)
Kim et al. (2013) RCT (7) N_{start}=33 N_{end}=27 TPS=Acute	E1: High Frequency rTMS E2: Low Frequency rTMS C: Sham Stimulation Duration: 20min/d, 5d/wk for 2wk Statistical Analysis: ANOVA	E1/E2 vs C • Line Bisection Test: (+exp$_1$, +exp$_2$) • Motor-Free Visual Perception Test (-) • Star Cancellation (-) • Catherine Bergego Scale (-) • Korean-Modified Barthel Index: (+exp$_1$, +exp$_2$) E1 vs E2 • Line Bisection Test: (-) • Motor-Free Visual Perception Test (-) • Star Cancellation (-) • Catherine Bergego Scale (-) • Korean-Modified Barthel Index: (-)
High Volume of rTMS vs Low Volume of rTMS		
Kim et al. (2015)	E: 10 Sessions of Daily rTMS	• Letter Cancellation Test (+exp)

RCT (5) N_{Start}=34 N_{End}=34 TPS=Chronic	C: A Single Session of rTMS Duration: 20min/d, 5d/wk for 2wk Statistical Analysis: ANOVA	• Line Bisection Test (+exp) • Ota's Task (+exp)
Visual training and Transcranial Random Noise stimulation vs Visual training and sham stimulation		
Herpich et al. (2019) RCT (6) N_{Start}=5 N_{End}=5 TPS=Chronic	E: Visual Training coupled with Transcranial Random Noise Stimulation (tRNS) C: Visual Training coupled with Sham tRNS Duration: 20min/d, 350 trials/d, 10d	• Normalized direction range Score (-) • Learning Index (-) • Amount of Learning (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Repetitive Transcranial Magnetic Stimulation

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the use of **rTMS** for improving neglect when compared to **sham stimulation**.	6	Iwanski et al., 2020; Cha et al., 2017; Yang et al., 2017; Cha & Kim, 2016; Cha & Kim, 2015; Kim et al., 2013
1b	**Visual Training and Transcranial Random Noise Stimulation** may not have a difference in efficacy as compared to **Visual Training and Transcranial Sham Stimulation** for improving neglect	1	Herpich et al., 2019
1b	**rTMS with sensory cueing** may not have a difference in efficacy compared to **rTMS alone** for improving neglect.	1	Yang et al., 2017
1b	**High frequency rTMS** may not have a difference in efficacy compared to **low frequency rTMS** for improving neglect.	1	Kim et al., 2013
2	**A higher volume of rTMS therapy** may produce greater improvements in neglect than **a lower volume of rTMS therapy**.	1	Kim et al., 2015

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the use of **rTMS** for improving motor rehabilitation when compared to **sham stimulation**.	3	Cha et al., 2017; Yang et al., 2017; Cha & Kim et al., 2016
1b	**rTMS with sensory cueing** may not have a difference in efficacy compared to **rTMS alone** for improving motor rehabilitation.	1	Yang et al., 2017
1b	**Visual Training and Transcranial Random Noise Stimulation** may not have a difference in efficacy as compared to **Visual Training and Transcranial Sham Stimulation** for improving motor rehablitation	1	Herpich et al., 2019

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**rTMS** may not have a difference in efficacy compared to **sham stimulation** for improving activities of daily living.	3	Iwanski et al. 2020; Yang et al., 2017; Kim et al. 2013
1b	**rTMS with sensory cueing** may not have a difference in efficacy compared to **rTMS alone** for improving activities of daily living.	1	Yang et al., 2017
1b	**High frequency rTMS** may not have a difference in efficacy compared to **low frequency rTMS** for improving activities of daily living.	1	Kim et al., 2013

LEARNING AND MEMORY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Visual Training and Transcranial Random Noise Stimulation** may not have a difference in efficacy as compared to **Visual Training and Transcranial Sham Stimulation** for improving learning and memory.	1	Herpich et al., 2019

Key Points

The literature is mixed regarding rTMS for improving neglect and motor rehabilitation.

rTMS may not be beneficial for improving activities of daily living

Theta Burst Stimulation

Adapted from: https://www.psychiatryadvisor.com/home/depression-advisor/intermittent-theta-burst-stimulation-for-major-depressive-disorder-treatment/

Theta Burst Stimulation (TBS) is an emerging treatment modality that is a patterned form of rTMS where stimulation pulses are delivered in triplets or bursts at a high frequency (50Hz), and in a short interval (200ms), intending to mimic naturally occurring theta brain oscillations (Schwippel et al. 2019). TBS can also be used to adjust interhemispheric rivalry after a stroke through the delivery of continuous TBS (cTBS) to reduce cortical excitability in the contralesional hemisphere (600 pulses over 40 seconds); or intermittent TBS (iTBS) to increase cortical excitability in the ipsilesional hemisphere (600 pulses over 190 seconds) (Schwippel et al. 2019; Cotoi et al. 2019).

Ten RCTs were found evaluating theta burst stimulation (TBS) interventions for neglect rehabilitation. Seven RCTs compared theta burst stimulation (TBS) rTMS to sham stimulation (Nyffeler et al., 2019; Vatanparasti et al., 2019; Cazzoli et al., 2015; Fu et al., 2015; Hopfner et al., 2015; Cazzoli et al., 2012; Koch et al., 2012). Two RCTs compared TBS at 80% of resting motor threshold to TBS at 40% resting motor threshold (Fu et al., 2017; Cao et al., 2016). One RCT compared continuous TBS to high frequency TBS to low frequency TBS (Yang et al., 2015).

The methodological details and results of all seven RCTs are presented in Table 13.

Table 13. RCTs evaluating TBS interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Theta Burst Stimulation vs Sham		
Nyffeler et al. (2019) RCT (8) N_{Start}=30 N_{End}=30 TPS=Acute	E1: 8 Trains of Continuous Theta Burst Stimulation E2: 16 Trains of Continuous Theta Burst Stimulation C: Sham Continuous Theta Burst Stimulation Duration: 44 sec/ Continuous Theta Burst Stimulation, 4 Continuous Theta Burst Stimulation trains/d, 2d in E1, 4d in E2	E1 vs C • Composite Score (Fluff Test, Two-Part Picture Test, Bird Cancellation Task) (+exp1) • Functional Independence Measure (+exp1) • Lucerne ICF-based Multidisciplinary Observation Scale (LIMOS) (+exp1) • LIMOS - Upper Limb (+exp1) E2 vs C • Catherine Bergego Scale (+exp2) • Composite Score (Fluff Test, Two-Part Picture Test, Bird Cancellation Task) (+exp2) • Functional Independence Measure (+exp2) • LIMOS (+exp2) • LIMOS - Upper Limb (-) E1vs E2 • Catherine Bergego Scale (-) • Composite Score (Fluff Test, Two-Part Picture Test, Bird Cancellation Task) (-) • Functional Independence Measure (-) • LIMOS (-) LIMOS - Upper Limb (-)
Vatanparasti et al. (2019) RCT (6) N_{Start}=15 M_{End}=14 TPS=NR	E: Prism Adaptation (PA) + Continuous Theta Burst Stimulation (cTBS) C: PA + Sham cTBS Duration: 5 sessions/wk, 2wks	• Start Cancellation Test (-) • Line Bisection Test (-) • Number of Lines on the Left Side (-) • Figure Copying Test (-) • Clock Drawing (-)
Cazzoli et al. (2015) RCT (5) N_{Start}=13 N_{End}=13 TPS=Subacute Note: 3 subjects participated in both conditions.	E: Continuous Theta Burst Stimulation (cTBS) C: Sham Continuous Theta Burst Stimulation (cTBS) Duration: NR Statistical Analysis: ANOVA	• Computer Balloon Search Test (+exp) • Star Cancellation (+exp) • Random Shape Cancellation Test (+exp)
Fu et al. (2015) RCT (8) N_{Start}=22 N_{End}=20 TPS=Subacute	E: Continuous Theta Burst Stimulation C: Sham Stimulation Duration: 1hr/d, 14d (consecutive) Statistical Analysis: ANOVA	• Star Cancellation Test (+exp) • Line Bisection Test (-)
Hopfner et al., (2015) Cross-Over RCT (7) N_{Start}=12 N_{End}=12 TPS=Subacute	E: Smooth pursuit training + cTBS (20min) C: Smooth Pursuit Training + sham Duration: 1 session/condition, separated by 1wk	• Cancellation Test (+exp)
Cazzoli et al. (2012) Cross-Over RCT (8) N_{start}=24 N_{end}=24 TPS=Acute	E1: Continuous TBS (1min) E2: Sham Stimulation C: No Stimulation Duration: 8x/d, 2d (consecutive) Statistical Analysis: ANOVA	E1 vs E2 • Catherine Bergego Scale (+exp_1) • Vienna Test System – Peripheral Perception (+exp_1) • Random Shape Cancellation Test (+exp_1) • Two Part Picture Scanning Test (+exp_1) • Munich Reading Texts (-)

Koch et al. (2012) RCT (9) N_{start}=20 N_{end}=18 TPS=Subacute	E: Continuous TBS + Conventional Therapy C: Sham TBS + Conventional Therapy Duration: 45min/d, 5d/wk for 2wk Statistical Analysis: ANOVA	• Behavioural Inattention Test (+exp) • Letter Cancellation Task (+exp) • Drawing Task (+exp) • Behavioral Inattention Test-B Scale (+exp) • Picture Scanning Task (+exp) • Menu Reading Task (+exp) • Behavioral Inattention Test-C Scores (+exp)
Theta Bursts at 80% Resting Motor Threshold vs Theta Bursts at 40% Resting Motor Threshold		
Fu et al. 2017 RCT (6) N_{start}=12 N_{end}=12 TPS=Subacute	E: rTMS Theta Bursts at 80% Resting Motor Threshold C: rTMS Theta Bursts at 40% Resting Motor Threshold Duration: 15min (4x/d) for 10d (consecutive) Statistical Analysis: Mann-Whitney U Test	• Line Bisection Test (+exp) • Star Cancelation Test (+exp)
Cao et al. (2016) RCT (5) N_{Start}=13 N_{End}=13 TPS=Subacute	E: 80% Resting Motor Threshold Intermittent Theta Burst Stimulation (iTBS) C: 40% Resting Motor Threshold Intermittent Theta Burst Stimulation (iTBS) Duration: 1x/d, 10d Statistical Analysis: ANOVA	• Line Bisection Task (+exp) • Star Cancellation Test (+exp)
Low Frequency TBS vs High Frequency TBS vs Continuous TBS vs Sham		
Yang et al. (2015) RCT (5) N_{Start}=38 N_{End}=38 TPS=Subacute	E1: Theta Burst Stimulation (TBS) at 1Hz E2: Theta Burst Stimulation (TBS) at 10Hz E3: Continuous Theta Burst Stimulation (cTBS) C: Sham Theta Burst Stimulation (TBS) Duration: 30min/d, 2wks Statistical Analysis: ANOVA	E1/E2/E3 vs C • Star Cancellation Test (+exp_1 ,+exp_2, +exp_3) • Line Bisection Test (+exp_1, +exp_2 +exp_3) E2 vs E3/E1 • Star Cancellation Test (+exp_3) • Line Bisection Test (+exp_1, +exp_3)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Theta Burst Stimulation

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Theta burst stimulation** may produce greater improvements in neglect than **sham stimulation**.	8	Nyffeler et al, 2019; Vatanparasti et al, 2019; Cazzoli et al., 2015; Fu et al., 2015; Yang et al., 2015; Hopfner et al., 2014; Cazzoli et al., 2012; Koch et al., 2012
1b	**Theta burst stimulation at 80% of resting motor threshold** may produce greater improvements in neglect than **theta burst stimulation at 40% resting motor threshold**.	2	Fu et al., 2017; Cao et al., 2016
2	**Continuous theta burst stimulation** may produce greater improvements in neglect than **1Hz or 10Hz theta burst stimulation**.	1	Yang et al., 2015

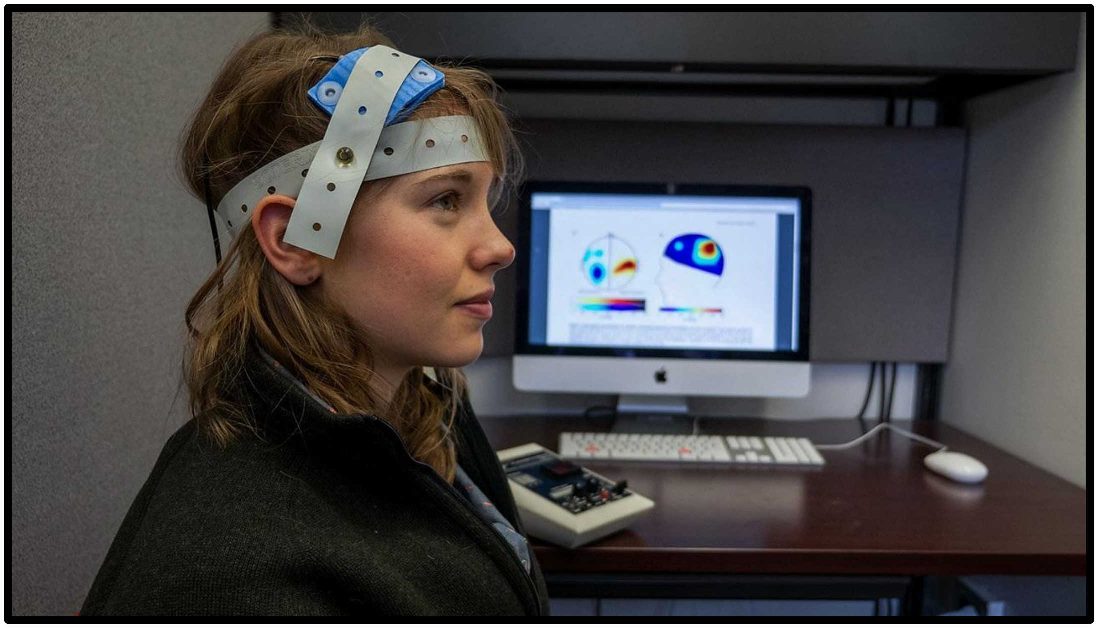
1b	**Eight Trains of continuous theta burst stimulation** may not have a difference in efficacy compared to **sixteen trains of continuous theta burst stimulation** for improving neglect.	1	Nyffeler et al, 2019

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Theta burst stimulation** may produce greater improvements in activities of daily living than **sham stimulation**.	1	Nyffeler et al., 2019
1b	**Eight Trains of continuous theta burst stimulation** may not have a difference in efficacy compared to **sixteen trains of continuous theta burst stimulation** for improving activities of daily living.	1	Nyffeler et al., 2019

Key Points

Continuous TBS may be beneficial for improving neglect.

Transcranial Direct Current Stimulation



Adapted from: https://www.sciencemag.org/news/2016/02/brain-zapping-therapies-might-be-hitting-lefties-wrong-side-head

Another form of non-invasive brain stimulation is transcranial direct-current stimulation (tDCS). This procedure involves the application of mild electrical currents (1-2 mA) conducted through two saline-soaked, surface electrodes applied to the scalp, overlaying the area of interest and the contralateral forehead above the orbit. Anodal stimulation is performed over the affected hemisphere and increases cortical excitability, while cathodal stimulation is performed over the unaffected hemisphere and decreases cortical excitability (Alonso-Alonso et al. 2007). Additionally, tDCS can be applied on both hemispheres concurrently, this is known as dual tDCS. In contrast to transcranial magnetic stimulation, tDCS does not induce action potentials, but instead modulates the resting membrane potential of the neurons (Alonso-Alonso et al. 2007).

Five RCTs were found evaluating transcranial direct current stimulation (tDCS) interventions for neglect rehabilitation. One RCT evaluated cathodal tDCS compared to anodal tDCS as well as to a sham condition (Ladavas et al., 2015). One RCT examined dual tDCS compared to anodal tDCS with a third group consisting of sham tDCS (Sunwoo et al., 2013). Two RCTs compared active anodal tDCS to sham tDCS (Plow et al., 2012; Ko et al., 2008). One study conducted three separate RCTs: one evaluated repetitive transorbital alternating current stimulation (rtACS) compared with cathodal tDCS plus rtACS as well as to sham rtACS/tDCS; one compared rtACS with sham rtACS; and one compared dual tDCS with sham tDCS (Raty et al., 2021).

The methodological details and results of the five RCTs are presented in Table 14.

Table 14. RCTs evaluating transcranial direct current stimulation (tDCS) interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Ladavas et al. (2015) RCT (8) N_{Start}=30 N_{End}=30 TPS=Acute	E1: Cathodal Transcranial Direct Current Stimulation (tDCS) E2: Anodal tDCS C: Sham tDCS Duration: 30 min/session, 5d/wk, 2wks	E1 vs C • Conventional Battery from the Behavioural Inattention Test (+exp1) E2 vs C • Conventional Battery from the Behavioural Inattention Test (+exp2) E1 vs E2 • Conventional Battery from the Behavioural Inattention Test (no stats)
Sunwoo et al. (2013) RCT (8) N_{Start}=10 N_{End}=10 TPS=Chronic	E1: Dual tDCS, Anode over Right Posterior Parietal Cortex (PPC), Cathode over Left PPC E2: Anodal tDCS over Right PPC C: Sham tDCS Duration: 1 session of each condition, 20min each	E1 vs C • Line Bisection Test (+exp1) E2 vs C • Line Bisection Test (+exp2) E1 vs E2 • Line Bisection Test (+exp1)
Plow et al. (2012) RCT (6) N_{Start}=12 N_{End}=8 TPS=Chronic	E: Vision Restoration Therapy + Active Anodal transcranial direct current stimulation C: Vision Restoration Therapy + Sham transcranial direct current stimulation Duration: 1 hr/session, 3 sessions/wk, 3wks	• Visual Field Border (+exp) • Stimulus Detection Accuracy (+exp) • Subjective Affected Field Area (+con) • Recovery of Ability to Perform ADLs (-) • Veterans Affairs Low Vision-Visual Functional Questionnaire (+exp)
Ko et al. (2008) Cross-over RCT (8) N_{start}=15 N_{end}=15 TPS=Subacute	E: Active Anodal tDCS C: Sham Stimulation Duration: 20min, 48hr washout period Statistical Analysis: ANOVA	• Line Bisection Test (+exp) • Shape Cancellation Test (+exp) • Letter Cancellation Test (-)
Repetitive Transorbital Alternating Current Stimulation		
Raty et al. (2021) RCT (8) N_{Start}=57 N_{End}=50 TPS=Chronic	Experiment 1 (NEnd=21) E1: Repetitive Transorbital Alternating Current Stimulation (rtACS) E2: Cathodal Transcranial Direct Current Stiulation (tDCS) + rtACS C: Sham rtACS/tDCS Experiment 2 (NEnd=17) E1: rtACS C: Sham rtACS Experiment 3 (NEnd=13) E1: Dual tDCS C: Sham tDCS Duration (same amongst all experiments): 20-40min/session/d, 5d/wk, 2wks	Experiment 1 E1 vs C • Detection Accuracy (-) • Mean Stimulus Detection Sensitivity Ipsilesional Eye (-) • Mean Stimulus Detection Sensitivity Contralesional Eye (+con) E2 vs C • Detection Accuracy (-) • Mean Stimulus Detection Sensitivity Ipsilesional Eye (-) • Mean Stimulus Detection Sensitivity Contralesional Eye (-) E1 vs E2 • Detection Accuracy (-) • Mean Stimulus Detection Sensitivity Ipsilesional Eye (-) • Mean Stimulus Detection Sensitivity Contralesional Eye (-) Experiment 2 • Detection Accuracy (-) • Mean Stimulus Detection Sensitivity Ipsilesional Eye (-)

		• Mean Stimulus Detection Sensitivity Contralesional Eye (-) Experiment 3 • Detection Accuracy (-) • Mean Stimulus Detection Sensitivity Ipsilesional Eye (-) • Mean Stimulus Detection Sensitivity Contralesional Eye (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Transcranial Direct Current Stimulation

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Anodal tDCS** may produce greater improvements in neglect than **sham stimulation**.	4	Ladavas et al., 2015; Sunwoo et al., 2013; Plow et al., 2012 Ko et al., 2008
1b	**Cathodal tDCS** may produce greater improvements in neglect than **sham stimulation.**	1	Ladavas et al., 2015
1b	There is conflicting evidence about the use of **dual tDCS** for improving neglect when compared to **sham stimulation**.	2	Raty et al., 2021; Sunwoo et al., 2013
1b	**Cathodal tDCS + rtACS** may not have a difference in efficacy compared to **sham** for improving neglect.	1	Raty et al., 2021
1b	**Active rtACS** may not have a difference in efficacy compared to **sham rtACS** for improving neglect.	1	Raty et al., 2021
1b	There is conflicting evidence about the use of dual **active rtACS** for improving neglect when compared to **sham rtACS + sham tDCS**.	1	Raty et al., 2021
1b	**Dual tDCS** may produce greater improvements in neglect than **anodal tDCS.**	1	Sunwoo et al., 2013

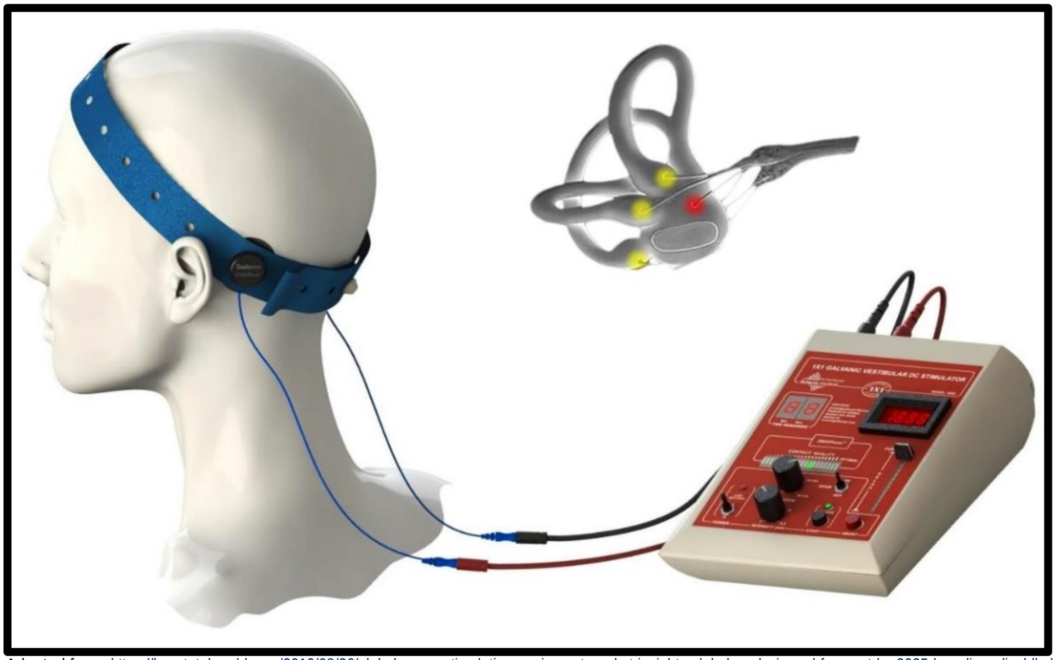
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the use of **anodal tDCS** for improving activities of daily living when compared to **sham stimulation**.	1	Plow et al., 2012

Key Points

Anodal tDCS may be beneficial for improving neglect.

The literature is mixed regarding dual tDCS for improving neglect.

Vestibular Stimulation



Adapted from: https://baystateherald.com/2019/08/26/global-neuro-stimulation-equipment-market-insights-global-analysis-and-forecast-by-2025-by-ndi-medical-llc-boston-scientific-corporation-neuronetics-medtronic/

Vestibular stimulation is a variant of transcranial direct current stimulation (tDCS). It is a non-invasive neuromodulation technique that involves placing electrodes directly over the vestibular nerve (which is responsible for the patient's sense of balance) and sending electrical signals through the skull (Krewer et al. 2013a). Spatial perception and exploration is a multisensory task requiring the integration of signals from visual, auditory, proprioceptive and vestibular cortices (Barra et al., 2010). If neglect is assumed to be an error in the perceptual integration and transformation of this information, manipulating input (vestibular) could ameliorate the impact of neglect.

Six RCTs were found evaluating vestibular stimulation interventions for neglect rehabilitation. Four RCTs compared galvanic vestibular stimulation (GVS) to sham stimulation (Volkening et al., 2018; 2014; Ruet et al., 2014; Schmidt et al., 2013; Utz et al., 2011). One RCT compared a high volume of GVS treatment to a medium and low volume of GVS treatment (Wilkinson et al., 2014). One RCTs compared manual vestibular stimulation to conventional rehabilitation (Dai et al., 2013).

The methodological details and results of all six RCTs are presented in Table 15.

Table 15. RCTs evaluating of vestibular stimulation interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Galvanic Vestibular Stimulation vs Sham		
Volkening et al. (2018) RCT (9) N_{start}=29 N_{end}=24 TPS=Acute	E1: Galvanic Vestibular Stimulation (GVS) with the Cathode on the Left + Conventional Treatment E2: GVS with the Cathode on the Right + Conventional Treatment C: Sham Stimulation + Conventional Treatment Duration: 20min/session, 10-12 sessions daily, 5d/wk	E1 vs C • Visuo-tactile Search Task (-) • Line Cancellation (-) • Letter Cancellation (-) • Line Bisection (-) • Star Cancellation (-) • Star Copying (-) • Diamond Copying (-) • Flower Copying (-) • Address Copying (-) E2 vs C • Visuo-tactile Search Task (-) • Line Cancellation (-) • Letter Cancellation (-) • Line Bisection (-) • Star Cancellation (-) • Star Copying (-) • Diamond Copying (-) • Flower Copying (-) • Address Copying (-) E1 vs E2 • Visuo-tactile Search Task (-) • Line Cancellation (-) • Letter Cancellation (-) • Line Bisection (-) • Star Cancellation (-) • Star Copying (-) • Diamond Copying (-) • Flower Copying (-) • Address Copying (-)
Ruet et al. (2014) Cross-over RCT (6) N_{Start}=4 N_{End}=4 TPS=Subacute	E1: Right Cathodal GVS E2: Left Cathodal GVS C: Sham GVS Duration: 20min sessions, 48hr washout Statistical Analysis: Mann-Whitney Test	E1/E2 vs C • Line Bisection Test (-) • Star Cancellation Test (-) E1/E2 vs C • Line Bisection Test (-) • Star Cancellation Test (-)
Schmidt et al. (2013) Cross-over RCT (7) N_{Start}=7 N_{End}=7 TPS=Chronic	E1: Right Cathodal GVS E2: Left Cathodal GVS C: Sham GVS Duration: 20min sessions, 48hr washout Statistical Analysis: ANOVA	E1 vs E2 • Arm Position Sense - Left Arm: (-) E1 vs C • Arm Position Sense - Left Arm: (-) E2 vs C • Arm Position Sense - Left Arm: (+exp$_2$)
Utz et al. (2011) Cross-over RCT (7) N_{Start}=6 N_{End}=6 TPS=Subacute	E1: Right Cathodal GVS E2: Left Cathodal GVS C: Sham GVS Duration: 20min sessions, 24hr washout Statistical Analysis: ANOVA	E1 vs C • Line Bisection Test (+exp$_1$) E2 vs C • Line Bisection Test (-) E1 vs E2 • Line Bisection Test (-)
High Volume GVS vs Low Volume GVS vs Medium Volume GVS		
Wilkinson et al. (2014) RCT (6) N_{Start}=52 N_{End}=49 TPS=Subacute	E1: Active Sessions on Right GVS only E2: 1 Active Session + 9 Sham Vestibular Galvanic Stimulations E3: 5 Active Sessions + 5 Sham Vestibular Galvanic Stimulations	E1 vs E2 vs E3 • Behavioural Inattention Test - Conventional Subtest (-)

	Duration: 25min/d, 5d/wk for 2wk Statistical Analysis: ANOVA	
Manual Vestibular Stimulation vs Conventional Rehabilitation		
Dai et al. (2013) RCT (4) N_{Start}=55 N_{End}=48 TPS=Subacute	E: Vestibular Rehabilitation C: Conventional Rehabilitation Duration: 30min	• Behavioral Inattention Test Conventional Score (-) • Functional Independence Measure Score (-) • Postural Assessment Scale for Stroke Patients Score (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Vestibular Stimulation

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**A right cathodal GVS stimulation** may not have a difference in efficacy compared to **a left cathodal GVS stimulation** for improving neglect.	3	Volkening et al., 2018; Schmidt et al., 2013; Utz et al. 2011
1a	**A right cathodal GVS stimulation** may not have a difference in efficacy compared to **sham GVS stimulation** for improving neglect.	4	Volkenining et al., Ruet et al., 2014; 2018; Schmidt et al., 2013; Utz et al. 2011
1a	**A left cathodal GVS stimulation** may not have a difference in efficacy compared to **sham GVS stimulation** for improving neglect.	3	Volkenining et al., 2018; Schmidt et al., 2013; Utz et al. 2011
1b	**A high volume of overall GVS stimulation** may not have a difference in efficacy compared to **a lower volume of overall GVS stimulation** for improving neglect.	1	Wilkinson et al., 2014
2	**Manual vestibular stimulation** may not have a difference in efficacy compared to **conventional rehabilitation** for improving neglect.	1	Dai et al., 2013

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Manual vestibular stimulation** may not have a difference in efficacy compared to **conventional rehabilitation** for improving motor rehabilitation.	1	Dai et al., 2013

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Manual vestibular stimulation** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	1	Dai et al., 2013

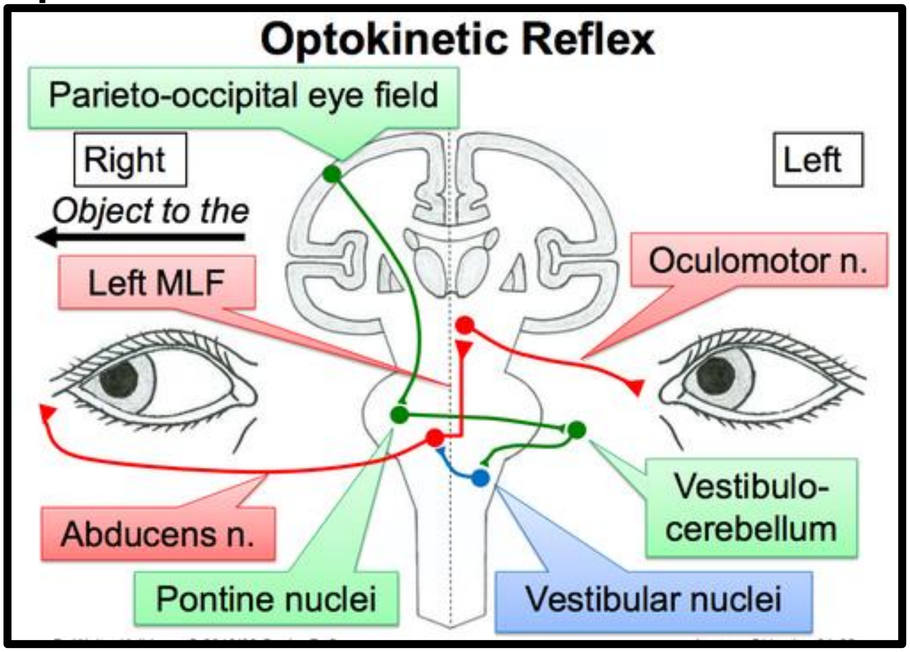
Key Points

Galvanic vestibular stimulation (GVS) may not be beneficial for improving neglect

There does not appear to be a difference in efficacy between left, right or sham GVS, and high or low volume GVS

Manual vestibular stimulation may not be beneficial for improving neglect, activities of daily living and motor rehabilitation.

Optokinetic Stimulation



Adapted from: https://www.cram.com/flashcards/neuroanatomy-lecture-31-ocular-reflexes-1481121

Optokinetic stimulation (OKS) uses a visual stimulus moving linearly from right to left to induce the optokinetic reflex and nystagmus in the contralesional direction (Pierce & Buxbaum, 2002). By inducing the slow phase of nystagmus, a patient is 'forced' to spend more time focusing in the neglected hemifield. Like vestibular stimulation, optokinetic stimulation is also believed to function by modulating sensory input to the representation of personal space, and egocentric reference frames (Karnath, 1996).

Ten RCTs were found evaluating optokinetic stimulation interventions for neglect rehabilitation. Two RCTs compared optokinetic stimulation and eye patching to conventional rehabilitation (Wang et al., 2015; Machner et al., 2014). One RCT compared optokinetic stimulation to sham (Kerkhoff et al., 2012a). Four RCTs compared optokinetic stimulation to visual scanning (Kerkhoff et al., 2014; Kerkhoff et al., 2013; Kerkhoff et al., 2012b; Pizzamiglio et al., 2004). One RCT compared optokinetic stimulation with computerized cognitive rehabilitation, to transcutaneous electrical nerve stimulation with computerized cognitive rehabilitation, and to computerized cognitive rehabilitation alone (Schroder et al., 2008). One RCT compared computer-based Optic Flow training to Covert Attention Training (Elshout et al., 2016). One RCT compared optokinetic stimulation with sensory cueing to standard post-stroke physiotherapy and gait training (Sukumaran et al., 2020).

The methodological details and results of all seven RCTs are presented in Table 16.

Table 16. RCTs evaluating optokinetic stimulation interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Optokinetic Stimulation + Eye Patch vs Usual Care		

Wang et al. (2015)
RCT (4)
N_{Start}=9
N_{End}=9
TPS=Acute
	E: Optokinetic Stimulation Training with eye patching + Conventional Treatment
	C: Conventional Treatment
	Duration: 20min/d, 4wks
		• Behavioural Inattention Test (+exp)
		  • Conventional (+exp)
		  • Behavioural (+exp)
		• Fugl-Meyer (+exp)
		  • Upper Extremity (+exp)
		  • Lower Extremity (-)
		• Equilibrium Coordination Test (-)
		• Nonequilibrium Coordination Test (+exp)

Machner et al. (2014) RCT (5) N_{Start}=23 N_{End}=21 TPS=Acute	E: Hemifield Eye Patching and Repetitive Optokinetics Stimulation + Usual Care C: Usual Care Duration: 1hr/d, 7d (consecutive) Statistical Analysis: ANOVA (with post hoc T-test)	• Catherine Bergego Scale (-) • Barthel Index (-) • Modified Rankin scale (-) • National Institutes of Health Stroke Scale (-) • Bell's Cancellations Test (-) • Star Cancellation Test (-) • Line Bisection Test (-) • Ogden Figure Copying Task (-) • Reading Errors (-)
Optokinetic Stimulation vs Visual Scanning Training or Sham		
Kerkhoff et al. (2014) RCT (8) N_{Start}=24 N_{End}=24 TPS=Acute/Subacute	E: Smooth Pursuit Eye Movement Training C: Visual Scanning Training Duration: 30min/d, 5d/wk for 4wk Statistical Analysis: ANOVA (with Holm's Procedure)	• Functional Neglect Index (+exp) • Unawareness and Behavioural Neglect Scale (+exp) • Barthel Index (-) • Help Scale (-)
Kerkhoff et al. (2013) RCT (6) N_{Start}=50 N_{End}=45 TPS=Subacute	E: Smooth Pursuit Eye Movement Training C: Visual Scanning Training Duration: 1hr/d for 5d (consecutive) Statistical Analysis: ANOVA	• Auditory Subjective Midline Test (+exp) • Paragraph Reading Task (+exp) • Line Bisection (-) • Single Digit Cancellation (+exp) • Double Digit Cancellation (+exp)
Kerkhoff et al. (2012a) RCT (7) N_{start}=20 N_{end}=20 TPS=Subacute Note: auditory neglect	E: Optokinetic Stimulation C: Sham Optokinetic Stimulation Duration: 50min/d, 5d/wk for 4wk Statistical Analysis: ANOVA (with Holm's Procedure)	• Auditory Subjective Median Plane - Mean Deviation (+exp)
Kerkhoff et al. (2012b) RCT (7) N_{start}=20 N_{end}=20 TPS=Subacute Note: auditory neglect	E: Optokinetic Stimulation C: Visual Scanning Duration: 50min/d, 5d/wk for 4wk Statistical Analysis: ANOVA (with Holm's Procedure)	• Auditory Subjective Median Plane - Mean Deviation (+exp) • Digit Cancellation (+exp) • Reading (+exp) • Horizontal Line Bisection (+exp)

Pizzamiglio et al. (2004)
RCT (5)
N_{start}=22
N_{end}=22
TPS=Subacute
	E: Optokinetic Stimulation + Standard Neglect Rehabilitation
	C: Standard Neglect Rehabilitation (Visual Scanning Training + Practice of Tasks)
	Duration: 1hr/d, 5d/wk for 6wk
	Statistical Analysis: ANOVA
		• Line Cancellation (-)
		• Letter Cancellation (-)
		• Wundt-Jastrow Illusion (-)
		• Reading (-)
		Semi-structured Scale for the Functional Evaluation of Hemi-Inattention
		  • Extrapersonal Neglect (-)
		  • Personal Neglect (-)
		• Line Bisection Test (-)

TENS + Computerized Training vs Optokinetic Stimulation + Computerized Training vs Computerized Training Alone		

Schroder et al. (2008) RCT (6) N_{start}=30 N_{end}=30 TPS=Subacute	E1: Transcutaneous Electrical Nerve Stimulation + Computerized Scanning Training E2: Optokinetic Stimulation + Computerized Scanning Training C: Computerized Scanning Training Duration: 20-40min/d, 5d/wk for 4wk Statistical Analysis: ANOVA	E2 vs C • Reading and Writing Tasks (+exp_2) • Line Bisection (+exp_2) • Figure Copying (+exp_2) • Free Drawing (+exp_2) • Star Cancellation (+exp_2) • Line Cancellation (+exp_2) • Test Battery of Attentional Performance (+exp_2) E1 vs E2 • Reading and Writing tasks (-) • Line Bisection (-) • Figure Copying (-) • Free Drawing (-) • Star Cancellation (-) • Line Cancellation (-) • Test Battery of Attentional Performance (-)
Computer-based Optic Flow Training vs Covert Attention Training		
Elshout et al. (2016) RCT (4) N_{Start}=30 N_{End}=27 TPS=Chronic	E: Computer-based Optic Flow Training C: Covert Attention Training Duration: 1hr/d, 5d/wk, 8wks	• Goldmann Perimetry (+exp) • Humphrey Perimetry (-) • Reading (-)
Optokinetic Stimulation + Sensory Cueing vs Standard Post-Stroke Physiotherapy + Gait Training		
Sukumaran et al. (2020) RCT (6) N_{Start}=14 N_{End}=12 TPS=Acute	E: Optic Flow and Auditory Stimulation + Sensory Limb Cueing C: Standard Post-Stroke Physiotherapy and Gait Training Duration: 20-30min/session, 2seesions/d, 1mo	• Star Cancellation Test (+exp) • Line Bisection Test (-) • Picture Identification Task (-) • National Institutes of Health Stroke Scale (-) • Modified Rankin Scale Score (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

\Conclusions about Optokinetic Stimulation

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the use of **optokinetic stimulation** for improving neglect when compared to **visual scanning**.	4	Kerkhoff et al., 2014; Kerkhoff et al., 2013; Kerkhoff et al., 2012b; Pizzamiglio et al., 2004
1b	**Optokinetic stimulation** may produce greater improvements in neglect than **sham stimulation**.	1	Kerkhoff et al., 2012a
1b	**Optokinetic stimulation + computerized scanning training** may produce greater improvements in neglect than **computerized scanning training alone**.	1	Schroder et al., 2008
1b	**Optokinetic stimulation + computerized scanning training** may not have a difference in efficacy compared to **TENS + computerized scanning training** for improving neglect.	1	Schroder et al., 2008
2	There is conflicting evidence about the use of **Optokinetic stimulation + eye patching** for	2	Wang et al., 2015; Machner et al., 2014

	improving neglect when compared to **conventional rehabilitation.**		
2	There is conflicting evidence about the use of **Computer-based Optic Flow Training** for improving neglect when compared to **Covert Attention Training**.	1	Elshout et al., 2016
1b	**Optokinetic stimulation + sensory cueing** may not have a difference in efficacy compared to **Standard Post-Stroke Physiotherapy + Gait Training** for improving neglect.	1	Sukumaran et al., 2020

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Optokinetic stimulation + eye patching** may produce greater improvements in motor rehabilitation than **conventional rehabilitation alone**.	1	Wang et al., 2015

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Optokinetic stimulation + eye patching** may not have a difference in efficacy compared to **conventional rehabilitation** for improving stroke severity.	1	Machner et al., 2014
1b	**Optokinetic stimulation + sensory cueing** may not have a difference in efficacy compared to **Standard Post-Stroke Physiotherapy + Gait Training** for improving stroke severity.	1	Sukumaran et al., 2020

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Optokinetic stimulation** may not have a difference in efficacy compared to **visual scanning** for improving activities of daily living.	1	Kerkhoff et al., 2014
2	**Optokinetic stimulation + eye patching** may not have a difference in efficacy compared to **conventional rehabilitation** for improving activities of daily living.	1	Machner et al., 2014

Key Points

The literature is mixed regarding optokinetic stimulation training for improving neglect.

Functional Electric Stimulation

Adapted from: https://www.researchgate.net/figure/Contralaterally-controlled-functional-electrical-stimulation-system-Volitional-opening_fig1_51603829

Functional Electric Stimulation (FES) is a motor rehabilitation technique that has been used to improve motor control of neurologically impaired motor systems, and to facilitate the return to voluntary movement in individuals with conditions such as hemiplegia, spinal cord, multiple sclerosis, etc. (Singer, 1987). Previous research found that passive movement to the contralesional limb in the contralesional hemispace may be beneficial for individuals with spatial neglect (Robertson & North, 1993). Passive movement of the affected limb can be induced through FES, allowing the individual to observe the flexion and extension of the limb during the application of the technique (Harding & Riddoch, 2009). During FES, electrical stimulation applied to the muscles that, when contracted, produce a functional movement, such as lifting or holding an object (Marquez-Chin & Popovic, 2020). The use of FES facilitates the generation of passive movement, and it is potentially viable to treat spatial neglect (Eskes & Butler, 2006). However, the benefit of electrical stimulation for spatial neglect post stroke should be approached with caution given the small number of participants and risk of bias (Longley et al., 2021).

One RCT was found to evaluate FES compared to prism adaptation (Choi et al. 2019).

The methodological details and results the RCT is presented in Table 17.

Table 17. RCTs evaluating functional electrical stimulation interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Choi et al. (2019) RCT (6) N_{Start}=30 N_{End}=30 TPS=Subacute	E1: Prism Adaptation + Functional Electrical Stimulation E2: Prism Adaptation E3: Functional Electrical Stimulation Duration: 50min/d, 5d/wk, 3 wks	E1 vs E2 • Albert Test (+exp1) • Motor-Free Visual Perception Test (+exp1) • Catherine Bergego Scale (+exp1) E1 vs E3 • Albert Test (+exp1) • Motor-free Visual Perception Test (+exp1) • Catherine Bergego Scale (+exp1)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Functional Electric Stimulation

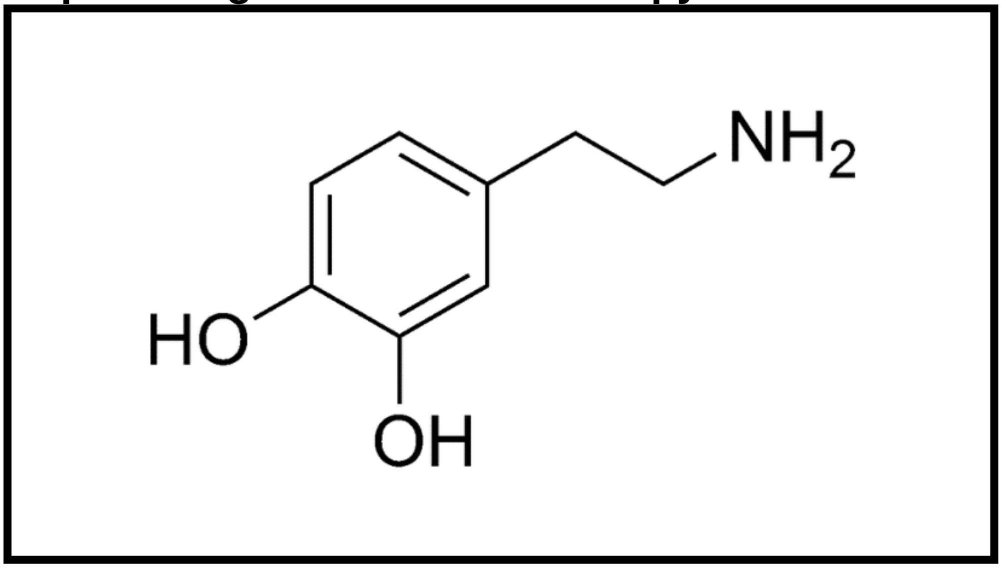
NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Prism Adaptation + Functional Electrical Stimulation** may produce greater improvements in neglect than **Prism Adaptation alone.**	1	Choi et al., 2019
1b	**Prism Adaptation + Functional Electrical Stimulation** may produce greater improvements in neglect than **Functional Electrical Stimulation alone.**	1	Choi et al., 2019

Key Points

Functional electric stimulation may be beneficial for improving neglect.

Pharmacological Interventions

Dopaminergic Medication Therapy



Adapted from: https://examinedexistence.com/what-is-dopamine-and-what-is-its-function/

Marshall & Gotthelf (1979), as cited in (Pierce & Buxbaum, 2002), reported that a reduced level of dopamine, a neurotransmitter, has been identified as playing a role in the arousal and orientation to stimuli. Hurford et al. (1998) reported a single case study of a patient with unilateral spatial neglect who received two consecutive treatments; methylphenidate followed by bromocriptine. While treatment with methylphenidate resulted in some improvement of neglect symptoms, bromocriptine, a dopamine agonist, was associated with greater improvement. While being treated with bromocriptine (5 mg, 3 times daily), performance on line bisection, letter cancellation and star cancellation tests improved such that results fell within the range of normal scores (Hurford et al., 1998). Improvements in performance were sustained or increased following cessation the medication regime and anecdotal reports were provided of improvements in everyday function (Hurford et al., 1998).

Two RCs were found evaluating dopaminergic medication interventions for neglect rehabilitation. One compared rotigotine to a placebo (Gorgoraptis et al., 2012). One compared levodopa to placebo (Li et al. 2020).

The methodological details and results of these RCTs are presented in Table 18.

Table 18. RCTs evaluating dopaminergic medication interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Rorigotine versus Placebo		
Gorgoraptis et al. (2012) RCT (9) N_{Start}=16 N_{End}=16 TPS=Chronic	E: Rotigotine (9.0mg skin patch) C: Placebo Duration: (rotigone), 24hr, 3x during 6wk Statistical Analysis: Replicated Randomized N-of-1 design	• Mesulam Cancellation Task (+exp) • Bell's Cancellation Test (-) • Line Bisection Test (-) • Touch Screen Visual Search Task (-) • Visual Vigilance and Salience Task (-) • Corsi Vertical Span Test (-) • Motricity Index (-) • Nine-hole Peg Test (-) • Box and Blocks Test (-)
Levadopa versus Placebo		
Li et al. (2020) **RCT (8)** **N_{Start}=9** **N_{End}=9** **TPS=Acute**	E1: Levodopa Followed by Reward E2: Placebo Followed by Reward E3: Levodopa Followed by No Reward E4: Placebo Followed by No Reward Duration: 1hr	E1 vs E2 • Total Cancellation Performance (-) E1 vs E3 • Total Cancellation Performance (-) E2 vs E3 • Total Cancellation Performance (-) E3 vs E4 • Total Cancellation Performance (+exp3) E1 vs E4 • Total Cancellation Performance (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Dopaminergic Medications

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Rotigotine** may not have a difference in efficacy compared to a **placebo** for improving neglect.	1	Gorgoraptis et al., 2012
1b	**Levodopa followed by Reward** may not have a difference in efficacy compared to **Placebo followed by Reward** for improving neglect.	1	Enderby et al., 1994
1b	**Levodopa followed by No Reward** may produce greater improvements in neglect than **Placebo followed by No Reward.**	1	Enderby et al., 1994
1b	**Levodopa followed by Reward** may not have a difference in efficacy compared to **Levodopa followed by No Reward** for improving neglect.	1	Enderby et al., 1994

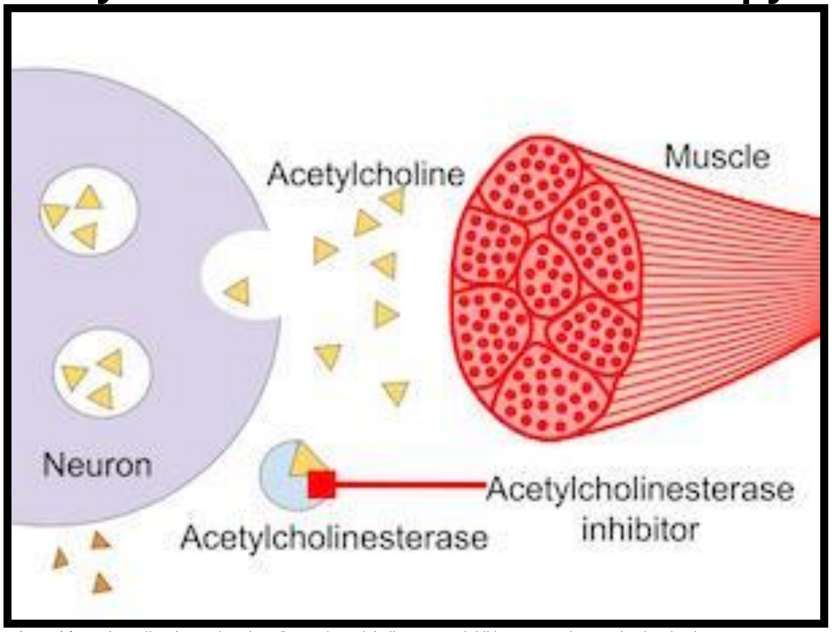
LEARNING AND MEMORY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Rotigotine** may not have a difference in efficacy compared to a **placebo** for improving learning and memory.	1	Gorgoraptis et al., 2012

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Rotigotine** may not have a difference in efficacy compared to a **placebo** for improving motor rehabilitation.	1	Gorgoraptis et al., 2012

Key Points

Dopaminergic medications may not be beneficial for improving neglect, learning and memory, and motor rehabilitation.

Acetylcholinesterase Inhibitor Therapy



Adapted from: https://study.com/academy/lesson/acetylcholinesterase-inhibitors-examples-mechanism.html

Acetylcholinesterase inhibitors, (rivastigmine, donepezil and galantamine) which have been used in the treatment of Alzheimer's disease, act by preventing the breakdown of acetylcholine, therefore causing levels to increase (Narasimhalu et al., 2010). These drugs have been used in association with treatments for cognitive disorders and may help improve cognitive functioning (Narasimhalu et al., 2010; Whyte et al., 2008).

Treatment with the acetylcholinesterase inhibitor rivastigmine in conjunction with cognitive training was associated with significant improvement on assessments of unilateral spatial neglect (Paolucci et al., 2010). Gains appeared to be maintained one-month following treatment, while individuals in the control group continued to improve over time to reach comparable levels. Further study is required to determine if acetylcholinesterase inhibitors are an effective method of rehabilitation for neglect.

One RCT was found evaluating acetylcholinesterase inhibitors for neglect rehabilitation. It compared rivastigmine with physical therapy and cognitive training to cognitive training alone (Paolucci et al 2010).

The methodological details and results of the single RCT are presented in Table 19.

Table 19. RCTs evaluating acetylcholinesterase Inhibitor interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Paolucci et al. (2010) RCT (7) N_{start}=20 N_{end}=20 TPS=Acute	E: Rivastigmine Therapy + Physical Therapy + Cognitive Training C: Cognitive Training (1hr/d, 5d/wk) Duration: 3mg, 2x/d (orally) for 8wk Statistical Analysis: ANOVA	• Letter Cancellation Test (+exp) • Wundt-Jastrow Area Illusion Test (+exp) • Albert's Barrage Test (-) • Sentence Reading Test (-) • Barthel Index (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Acetylcholinesterase Inhibitors

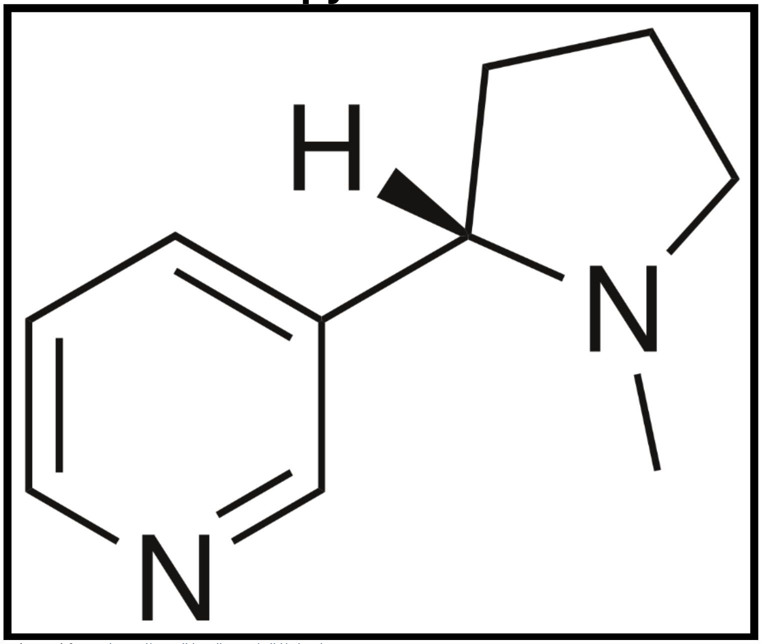
NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the use **rivastigmine, physical therapy and cognitive training** for improving neglect when compared to **cognitive training alone**.	1	Paolucci et al., 2010

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Rivastigmine, physical therapy and cognitive training** may not have a difference in efficacy compared to **cognitive training alone** for improving activities of daily living.	1	Paolucci et al., 2010

Key Points

The literature is mixed concerning rivastigmine therapy for improving neglect.

Nicotine Therapy



Adapted from: https://en.wikipedia.org/wiki/Nicotine

Nicotine therapies are based around the same principles as acetylcholinesterase inhibitors. Findings from neuroimaging and behavioural studies in animals and healthy humans suggest that the cholinergic system may be involved in selective and focused attention (Lucas et al., 2013). Nicotine, a powerful cholinergic agonist, could potentially modulate activity in frontal and parietal areas and lead to improvements in unilateral spatial neglect.

One RCT was found evaluating nicotine for neglect rehabilitation. It compared nicotine to a placebo (Lucas et al., 2013).

The methodological details and results of the single RCT are presented in Table 20.

Table 20. RCTs evaluating nicotine interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Lucas et al. (2013) Cross-over RCT (7) N_{Start}=10 N_{End}=10 TPS=Chronic	E: Nicotine (10mg nicotine patch) C: Placebo Duration: 3d/wk for 12hr during 1wk Statistical Analysis: ANOVA	• Letter Cancellation Test (+exp) • Shape Cancellation Test (+exp) • Bell's Cancellation Test (+exp) • Cued Detection Task (Posner's paradigm) (+exp) • Line Bisection Test (-) • Quadruplet Detection Task (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

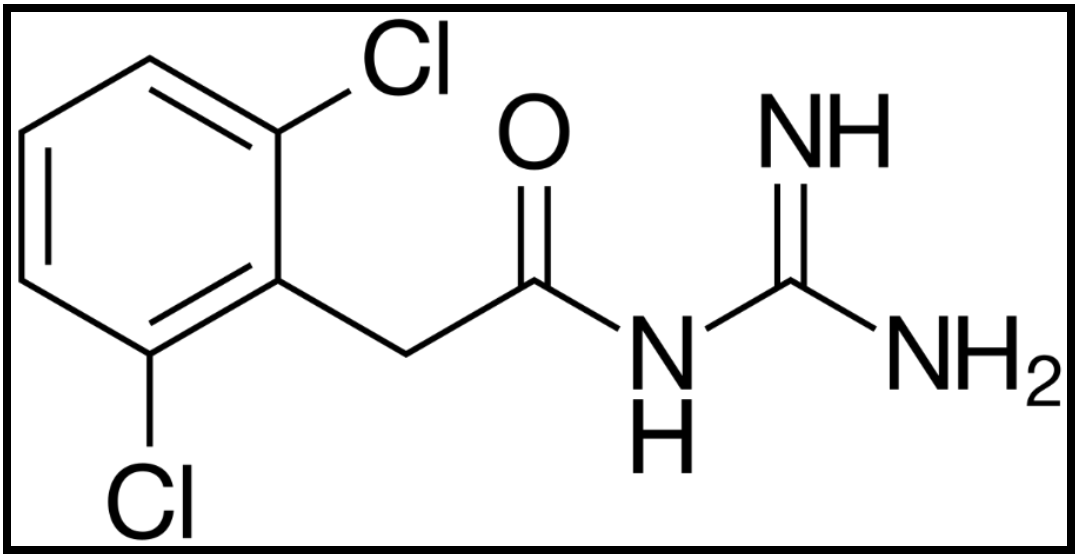
Conclusions about Nicotine Therapy

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Nicotine** may produce greater improvements in neglect than **conventional rehabilitation**.	1	Lucas et al., 2013

Key Points

Nicotine may be beneficial for improving neglect.

Guanfacine



Adapted from: https://en.wikipedia.org/wiki/Guanfacine

Guanfacine (Tenex) is a drug used to treat attention deficit hyperactivity disorder (ADHD) and high blood pressure. It is an adrenergic alpha-2A receptor agonist, increasing parasympathetic activity. Vigilance as a cognitive function has been linked to the adrenergic system (Smith & Nutt, 1996; Aston-Jones et al., 1994). The dug has been shown to increase attention, and working memory in healthy humans (Biederman et al., 2008; Jäkälä et al., 1999). Because of this, it has the potential to be a successful pharmacological intervention for treating neglect post-stroke.

One RCT was found evaluating guanfacine for neglect rehabilitation. It compared guanfacine to a placebo (Dalmaijer et al., 2018).

The methodological details and results of the single RCT are presented in Table 21.

Table 21. RCTs evaluating guanfacine interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Dalmaijer et al. 2018 RCT Crossover (9) N_{start}=13 N_{end}=13 TPS=Variable	E: Oral guanfacine (2mg) C: Oral placebo (2mg) Duration: One-time dose Statistical Analysis: ANOVA	• Cancellation Task (+exp) • Directional Attention Bias (-) • Vertical Corsi Span Task (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Guanfacine

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the use of **guanfacine** for improving neglect when compared to **a placebo.**	1	Dalmaijer et al., 2018

LEARNING AND MEMORY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Guanfacine** may not have a difference in efficacy compared to **a placebo** for improving learning and memory.	1	Dalmaijer et al., 2018

Key Points

> The literature is mixed regarding guanfacine for improving neglect.

Citicoline

Adopted from: https://www.mims.com/philippines/drug/info/citxl?type=full

Citicoline, the abbreviation of cytidine-5'-diphosphocholine (CDP-choline), is an endogenous chemical compound that has neuroprotective effects, and it has been used as a dietary supplement to facilitate the regeneration of neurons, to increase levels of neurotransmitters, and to improve cognitive functions, as well as to treat depression and regulate mood (Jasielski et al., 2020). Citicoline is crucial for the synthesis of phosphatidylcholine, a component of the cell membrane that degrades during cerebral ischemia (Fioravanti & Yanagi, 2005). Citicoline increases the levels of sirtuin-1, a protein that regulates metabolic homeostasis and neuronal aging; additionally, citicoline increases the dopamine, norepinephrine, and serotonin levels in the central nervous system, promoting neuroprotective effects (Jasielski et al., 2020). Citicoline may serve as a cognitive enhancer, resulting in improvements in memory and learning deficits in individuals with dementia and other age-related disorders (Kuryata et al. 2021). Citicoline has also been used to treat vascular cognitive impairment (Alvarez-Sabin, et al. 2011), as well as acute ischemic stroke, with a substantial treatment effect (Secades et al., 2016).

One RCT was found evaluating citicoline for neglect rehabilitation. It compared citicoline to no treatment (Alvarez-Sabin et al. 2013).

The methodological details and results of the single RCT are presented in Table 22.

Table 22. RCTs evaluating optokinetic stimulation interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Alvarez-Sabin et al. (2013) RCT (6) N$_{Start}$=347 N$_{End}$=199 TPS=Subacute	E: Citicoline Treatment C: No Citicoline Treatment Duration: 12mo	• Attention and Executive Function (Stroop Colour Word Interference Test, Trails A and B and Symbol digits Modalities Test, Mental Control, Digit Span Backward and Forward) (+exp) • Language (Boston Naming Test (Naming), Verbal Fluency for Animals and Controlled Oral Word Association test, Pseudowords and Sentences Repetition and Token Test) • Memory (Auditory Verbal learning Test and Visual Reproduction (WMS-III) (-) • Spatial Perception (Judgement of Line Orientation) (-) • Motor Speed (Grooved Pegboard for Dominant and Nondominant Hand) (-) • Temporal Orientation (Benton's Temporal Orientation) (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Citicoline

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Citicoline** may not have a difference in efficacy compared to **no treatment** for improving neglect.	1	Alvarez-Sabin et al. 2013

LEARNING AND MEMORY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Citicoline** may not have a difference in efficacy compared to **no treatment** for improving learning and memory	1	Alvarez-Sabin et al. 2013

GLOBAL COGNITION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Citicoline** may produce greater improvements in global cognition than **no treatment**.	1	Alvarez-Sabin et al. 2013

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**

1b	**Citicoline** may not have a difference in efficacy compared to **no treatment** for improving motor rehabilitation.	1	Alvarez-Sabin et al. 2013

Key Points

Citicoline may be beneficial for improving global cognition.
Citicoline may not be beneficial for improving neglect, learning and memory, and motor rehabilitation.

Selegiline

Adopted from: https://namanpharma.com/product/namanegelin-5mg/

Selegiline, also known as L-Deprenyl, is a selective inhibitor of MAO-B (monoamine oxidase), a mitochondrial enzyme that preserves endogenous and exogenous dopamine, and it has been used in the treatment of Parkinson's disease (Fabbrini et al. 2012; Heinonen & Rinne, 1989), as well as in the treatment of Alzheimer's disease and major depressive disorder (Miklya, 2016). The inhibition of MAO-B offers protection against the effects of various neurotoxins, such as the DA-ergic agents MPTP and 6-hydroxydopamine (6-OHDA) (Gerlach et al. 1996). In addition, selegiline may reduce the production of oxidative radicals (Ebadi, 2002). Selegiline has been used to improve recovery in individuals with stroke (Sivenius et al. 2001).

One RCT was found evaluating Selegiline for neglect rehabilitation. It compared Selegiline to placebo (Bartolo et al. 2015).

The methodological details and results of the single RCT are presented in Table 23.

Table 23. RCTs evaluating optokinetic stimulation interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Bartolo et al. (2015) RCT (7) N_{Start}=47 N_{End}=44 TPS=Acute	E: Selegiline C: Placebo Duration: Once/ day, 6wks	• Mini-Mental State Examination (-) • Frontal Assessment Battery (-) • Montreal Cognitive Assessment (+exp) • Rey Auditory Verbal Learning Test Immediate Recall (-) • Rey Auditory Verbal Learning Test Delayed Recall (-) • Logical Memory Immediate Recall (+exp) • Logical Memory Delayed Recall (-) • Digit Span (+exp) • Corsi's Test (-) • Attentive Matrices (+exp) • Trail-Making Test A (+exp) • Trail-Making Test B (+exp) • Stroop Test-T (+exp) • Stroop Test-E (+exp) • Symbol Digit (-) • Rey-Osterrieth Figure, Copy (-) • Progressive Matrices 47 (-) • Phonological Fluency (-) • Semantic Fluency (-) • Functional Independence Measure (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Selegiline

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the use of **Selegiline** for improving neglect when compared to **placebo**.	1	Bartolo et al., 2015

LEARNING AND MEMORY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Selegiline** may not have a difference in efficacy compared to **placebo** for improving learning and memory	1	Bartolo et al., 2015

GLOBAL COGNITION			
LoE	**Conclusion Statement**	**RCTs**	**References**

1b	There is conflicting evidence about the use of **Selegiline** for improving global cognition when compared to **placebo**.	1	Bartolo et al., 2015

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Selegiline** may not have a difference in efficacy compared to **placebo** for improving activities of daily living.	1	Bartolo et al., 2015

Key Points

The literature is mixed regarding Selegiline for improving neglect and global cognition. Selegiline may not be beneficial for improving learning and memory, and activities of daily living.

Piracetam

Adopted from: https://www.nootrokick.com/piracetam-al-1200-30-pills/

Piracetam is a cyclic derivative of gamma-aminobutyric acid, and the most common nootropic drug; frequently used in the treatment of dementia, vertigo, anemia, Alzheimer's disease, and stroke (Winnicka et al., 2005). Piracetam was found to increase cerebral blood flow and the utilization of oxygen in the brain, protecting the brain from neuron death or cell damage on animal models (Chen et al., 2019). This medication was approved in Europe in the 70s to treat vertigo and disorders related to older age (Malykh & Sadaie, 2010), and it has been used in the treatment of stroke given its neuroprotective effects, such as restoration of neurotransmission, and an antithrombotic effect (Ricci et al., 2000). Vascular effects have also been linked to the use of piracetam, such as the effects on blood circulation, on the movement of erythrocytes, on blood coagulation, and on cerebral blood flow (Winbald, 2005).

One RCT was found evaluating piracetam for neglect rehabilitation. It compared piracetam to placebo (Enderby et al. 1994).

The methodological details and results of the single RCT are presented in Table 24.

Table 24. RCTs evaluating optokinetic stimulation interventions for neglect rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)

Enderby et al. (1994)
RCT (6)
N_{Start}=158
N_{End}=137
TPS=Subacute
	E: Piracetam
	C: Placebo
	Duration: 12wks
		• Barthel Index (-)
		• Kurian-Sky Performance Test (-)
		• Rivermead Perceptual Assessment Battery (+exp)
		  • Body Image-Self (+exp)
		  • Sequencing Pictures (+exp)
		  • Figure Ground Discrimination (+exp)
		• Walking Ability (+exp)
		• Motricity Index (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Piracetam

NEGLECT			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Piracetam** may produce greater improvements in motor rehabilitation than **placebo**.	1	Enderby et al., 1994

MOTOR REHABILITATION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the use of **Piracetam** for improving motor rehabilitation when compared to **placebo**.	1	Enderby et al., 1994

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Piracetam** may not have a difference in efficacy compared to **placebo** for improving activities of daily living.	1	Enderby et al., 1994

Key Points

Piracetam may be beneficial for improving global cognition.
The literature is mixed regarding Piracetam for improving motor rehabilitation.
Piracetam may not be beneficial for improving activities of daily living.

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