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How effective and safe are non-drug treatments for spatial neglect following non-progressive brain injury? A Cochrane Review summary with commentary

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Abstract.
BACKGROUND: Around 30% of stroke survivors experience spatial neglect. Spatial neglect hinders rehabilitation outcomes and increases the risk of injury. Non-pharmacological interventions are available, yet their efficacy is unknown.
OBJECTIVE: To evaluate the effectiveness of non-pharmacological interventions for spatial neglect (inattention) following stroke and other non-progressive brain injuries.
METHODS: A summary of the Cochrane Review by Longley et al. 2020, with comments from a rehabilitation perspective.
RESULTS: A total of 43 studies were included in meta-analysis and the quality of evidence was very low for all analyses. The benefits or risks associated with each intervention for spatial neglect including visual treatment, prism adaptation training, body awareness, mental function, movement treatment, non-invasive brain stimulation, electrical stimulation, and acupuncture remain unclear.
CONCLUSIONS: Evidence in support or against the treatments is sparse and more rigorous studies are needed to evaluate their efficacy. Clinicians should continue to follow current guidelines when available to meet patients' rehabilitation goals.

Keywords: Stroke rehabilitation, perceptual disorders, activities of daily living, intervention, systematic review

The aim of this commentary is to discuss from a rehabilitation perspective the Cochrane Review "Non-pharmacological interventions for spatial neglect or inattention following stroke and other non-progressive brain injury" by Longley et al. (2021)[a], published by Cochrane Stroke Group. This Cochrane Corner is produced in agreement with NeuroRehabilitation by Cochrane Rehabilitation with

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[a]This summary is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2021, Issue 7, Art. No.:CD003586, DOI: 10.1002/14651858.CD003586.pub4 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

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views* of the review summary author in the "implications for practice" section.

1. Background

Non-progressive brain injuries are injuries caused by a discrete, one-time event and do not worsen or intensify with time. Common examples of non-progressive brain injuries include stroke and traumatic brain injury, which can result in long-lasting neuropsychological deficits, such as spatial neglect (SN). SN is common following a stroke, with an estimated prevalence of 30% after a unilateral stroke (Longley et al., 2021), and following severe traumatic brain injury (Chen et al., 2016). Individuals experiencing SN behave as if one side of the body or space does not exist, and thus fail to perceive and respond to stimuli coming from the contralesional part. SN negatively affects motor and cognitive rehabilitation outcomes and increases hospitalization and the risk of falls (Chen et al., 2016; Winstein et al., 2016). Non-pharmacological interventions are the main treatment options for SN; Longley et al. (2021) recently examined their effectiveness.

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

(Longley, V., Hazelton, C., Heal, C., Pollock, A., Woodward-Nutt, K., Mitchell, C., Pobric, G., Vail, A., & Bowen, A., 2021).

2. Objective

This Cochrane Review aimed to assess the effectiveness of currently available non-pharmacological interventions for SN following non-progressive brain injuries in adults.

3. What was studied and methods

This is an updated and broadened version of a previously published Cochrane review (Bowen et al., 2013). The review authors conducted a literature search across 14 databases to find randomized controlled trials (RCTs) from 1966 up to October 2020. The population addressed was adults with SN following non-progressive brain injury. The interventions examined comprises visual interventions, prism adaptation training, body awareness interventions, mental function interventions, movement interventions, non-invasive brain stimulation (NIBS), electrical stimulation, and acupuncture. Each intervention was compared either to an alternative form of intervention or no intervention at all. The primary outcome studied was functional ability in activities of daily living (ADL), measured at least one month after treatment completion. Secondary outcomes were: ADL at treatment completion, performance on a standardized neglect assessment, discharge destination, and adverse events (falls excluded).

4. Results

The review included 65 RCTs with a total of 1951 participants with SN following stroke; 43 studies were included in the meta-analysis. The quality of evidence of all meta-analyses were judged to be very low. Results on *ADL*, and *standardized neglect assessment* for both persistent and immediate effects (all versus any controls) and adverse events when available are reported below.

- Visual interventions
  ADL: No advantages or disadvantages were recorded from the interventions on persisting effects (2 studies, $n = 55$, SMD –0.04, 95% CI –0.57–0.49) or immediate effects (3 studies, $n = 75$, SMD –0.15, 95% CI –0.60–0.30).
  Standardized neglect assessment: No advantages or disadvantages from interventions were found on persisting effects (5 studies, $n = 98$) or immediate effects (7 studies, $n = 142$).
- Prism adaptation interventions
  ADL: Evidence shows no advantages or disadvantages from interventions on persisting effects (2 studies, $n = 39$, SMD –0.29, 95% CI –0.93–0.35) or immediate effects (5 studies, $n = 158$, SMD 0.20, 95% CI –0.12–0.51).
  Standardized neglect assessment: No advantages or disadvantages from prism adaptation interventions were found on persisting effects (1 study, $n = 16$) or immediate effects (5 studies, $n = 154$).
- Body awareness interventions
  ADL: Five studies ($n = 125$) found possible benefits for body awareness interventions (SMD 0.61, 95% CI 0.24–0.97) on persisting effects. No indication of advantages or disadvantages

*The views expressed in the summary with commentary are those of the Cochrane Corner author (different than the original Cochrane Review authors) and do not represent the Cochrane Library or Wiley.

was found on immediate effects (7 studies, $n = 221$, SMD 0.26, 95% CI –0.01–0.53).
Standardized neglect assessment: Possible benefits were found for interventions on persisting effects (5 studies, $n = 125$). No indication of advantages or disadvantages were found on immediate effects (10 studies, $n = 311$).
Adverse Events: Two studies ($n = 130$) reported adverse events with a total of three deaths in the control group and one death in the intervention groups. No indication of advantages or disadvantages were found from the interventions.

- Mental function interventions
  ADL: No evidence area was available for persisting effects. No advantages or disadvantages from mental function interventions were found on immediate effects (1 study, $n = 24$, SMD 0.32, 95% CI –0.49–1.12).
  Standardized neglect assessment: No evidence was available for persisting effects. No advantages or disadvantages from mental function interventions were found on immediate effects (3 study, $n = 60$).
- Movement interventions
  ADL: No evidence was available for persisting effects. Three studies found possible benefit on immediate effects ($n = 75$, SMD 0.57, 95% CI 0.09–1.04).
  Standardized neglect assessment: No evidence was available for persisting effects. Possible benefits from the interventions were found on immediate effects (2 studies, $n = 58$).
- Non-invasive brain stimulation
  ADL: No advantages or disadvantages were detected on persisting effects (3 studies, $n = 92$, SMD 0.35, 95% CI –0.08–0.77), but possible benefits were recorded on immediate effects (6 studies, $n = 160$, SMD 0.61, 95% CI 0.27–0.94)
  Standardized neglect assessment: Possible benefits from intervention were found on both persisting effects (3 studies, $n = 102$) and immediate effects (10 studies, $n = 244$).
- Electrical stimulation
  ADL: No evidence was available for persisting or immediate effects.
  Standardized neglect assessment: No evidence was available for persisting effects. Possible benefits from the intervention were found on immediate effects (2 studies, $n = 60$).
- Acupuncture versus any control
  ADL: No evidence was available for persisting effects. Possible advantages from the intervention were found on immediate effects (2 studies, $n = 104$, SMD 0.65, 95% CI 0.26–1.05).
  Standardized neglect assessment: No evidence was available for persisting effects. Possible benefits from the intervention were found on immediate effects (2 studies, $n = 104$).

5. Conclusions

Despite the array of currently available non-pharmacological interventions for SN following non-progressive brain injuries in adults, their effectiveness, benefits, and harms remain unclear. The authors identified a lack of evidence for ADL, an outcome that patients reported as important. Increasing the quality of methodology design and reporting in parallel with the adoption of patient-centered outcomes is critical to responding to this population's needs.

6. Implications for practice in neurorehabilitation

SN is common after non-progressive brain injuries, especially strokes. A heterogeneous set of interventions are available for patients with SN, aiming to help the individual learn to function using a single hemispace (Liu et al., 2019).

The very low quality of evidence found in this review prevents the formulation of new recommendations in favor of or against an intervention. Following Australian, Canadian, and American guidelines, when SN is suspected, patients should receive a full assessment with validated tools (*Stroke Foundation*, n.d.; Hebert et al., 2016; Winstein et al., 2016). Consensus-based recommendations encourage clinicians to foster patient-centered practice and explain the impairment and introduce compensatory strategies and cues to draw attention to impaired areas during rehabilitation (*Stroke Foundation*, n.d.).

When implementing a polytherapy regimen, other interventions may be offered to improve neglect symptoms, such as prism adaptation, visual scanning training, optokinetic stimulation, virtual reality, limb activation, mental imagery, and neck vibration combined with prism adaptation, as well as mirror therapy in cases of unilateral neglect (*Stroke Foundation*, n.d.; Hebert et al., 2016; Winstein et al., 2016). However, the recommendation for these interventions remains weak due to insufficient or conflicting evidence.

Conflict of interest

The author declares no conflicts of interest.

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