2021

Critically appraised paper: Non-invasive brain stimulation does not enhance the effect of robotic-assisted upper limb training on arm motor recovery after stroke [commentary]

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10.1016/j.jphys.2021.05.007
Edwards, D. J. (2021). Critically appraised paper: Non-invasive brain stimulation does not enhance the effect of robotic-assisted upper limb training on arm motor recovery after stroke [Commentary]. *Journal of Physiotherapy, 67*(3), 218.https://doi.org/10.1016/j.jphys.2021.05.007

Journal of Physiotherapy 67 (2021) 218

AUSTRALIAN PHYSIOTHERAPY ASSOCIATION

Journal of PHYSIOTHERAPY

journal homepage: www.elsevier.com/locate/jphys

Appraisal

Critically appraised paper: Non-invasive brain stimulation does not enhance the effect of robotic-assisted upper limb training on arm motor recovery after stroke

Synopsis

Summary of: Reis SB, Bernardo WM, Oshiro CA, Krebs HI, Conforto AB. Effects of robotic therapy associated with noninvasive brain stimulation on upper-limb rehabilitation after stroke: systematic review and meta-analysis of randomized clinical trials. *Neurorehabil Neural Repair.* 2021;35:256–266.

Objective: To review the evidence as to whether adding non-invasive brain stimulation enhances the effects of robotic-assisted upper limb training on upper limb motor recovery in individuals with stroke. ***Data sources***: MEDLINE, EMBASE, CENTRAL, LILACS, CINAHL, DORIS, and PEDro were searched up to July 2019. This search was supplemented by searching online archives of theses and trial registries. ***Study selection***: Randomised controlled trials (parallel or crossover) involving people with upper limb paresis due to stroke, in which non-invasive brain stimulation before, during or after robotic-assisted upper limb rehabilitation was compared with sham non-invasive brain stimulation or robotic-assisted upper limb rehabilitation without non-invasive brain stimulation. Outcome measures were upper limb performance in either impairment-level and/or activity-level domains. ***Data extraction***: Two reviewers extracted data and discrepancies were resolved by consensus. For crossover designs, only the first-phase intervention data were extracted. Risk of bias for individual studies was assessed according to specified criteria by two reviewers and quality of the body of evidence was rated according to GRADEpro. ***Data synthesis***: Of 1,176 articles identified by the search, eight unique trials with a total of 324 participants (161 active, 163 control) met the selection criteria and were included in the review. The quality of evidence was high for both impairment-level and activity-level outcome measures. Based on the quantitative pooling of the available data, there was no effect of non-invasive brain stimulation on upper limb performance on the Fugl-Meyer Assessment (seven studies, MD 0.15, 95% CI −3.10 to 3.40) or on upper limb activity limitation (five studies, SMD 0.03, 95% CI −0.28 to 0.33). Planned subgroup analyses demonstrated similar results for both subacute and chronic stroke, robotic device characteristics (end-effector and exoskeleton), upper limb joints involved in training, and unimanual and bimanual training. There was no evidence that non-invasive brain stimulation paradigms (increased or decreased cortical excitability), timing of stimulation (before, after and during robotic-assisted therapy), or number of sessions influenced the results. ***Conclusion***: At present, there is high-quality evidence to suggest that the effects of robotic-assisted upper limb training on upper limb motor impairment or motor activity for individuals with stroke are not enhanced by existing non-invasive brain stimulation approaches.

Provenance: Invited. Not peer reviewed.

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https://doi.org/10.1016/j.jphys.2021.05.008

Commentary

In people with hemiparesis after stroke, intensive upper limb motor practice, such as robot-assisted training, can lead to clinically meaningful improvement, yet the benefit typically falls far short of full functional recovery. Supplemental therapies have the potential to enhance training effects, and non-invasive brain stimulation as a candidate add-on therapy has previously been reported; this literature was systematically reviewed by Reis and colleagues. The review found that there is no beneficial effect of non-invasive brain stimulation as a supplement to robot-assisted training. The eight reviewed trials used a variety of existing best non-invasive brain stimulation practices and available robotic technology.

The interpretation of these findings should consider the diversity of non-invasive brain stimulation methods in the reviewed studies. This included inhibitory or excitatory protocols, and stimulation by transcranial electric or magnetic stimulators, on a background of varied unilateral or bilateral robotic training of different doses and/or intensities. Taken together with the modest aggregate sample size, this challenges the ability to speak to all forms of non-invasive brain stimulation being ineffective. Modifying non-invasive brain stimulation parameters or methods has been likened to manipulating a drug's chemical composition,[1] fundamentally changing the action and effect. Thus, the forms of non-invasive brain stimulation across trials were fundamentally different.

A clinical benefit of supplemental non-invasive brain stimulation has been demonstrated in individual studies of non-robotic upper limb training.[2,3] One consideration here may be ceiling effects with robotic training, which by nature is more intensive than traditional motor therapies. Future trials may evaluate whether non-invasive brain stimulation alters the recovery rate across a training regimen, in addition to the more commonly assessed effect magnitude or number of clinical responders.

This work makes an important and timely contribution to the literature in an area of continued scientific and clinical interest. Understanding intervention features that are ineffective helps limit premature clinical adoption and shape future trials.

Provenance: Invited. Not peer reviewed.

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https://doi.org/10.1016/j.jphys.2021.05.007

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