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Can pharmacological, psychological and non-invasive brain stimulation interventions prevent depression after stroke? A cochrane review summary with commentary

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Abstract.
BACKGROUND: Depression is very common in patients after a stroke and it can impact recovery.
OBJECTIVE: The Cochrane Review aimed to determine whether psychological therapy, pharmacological interventions, non-invasive brain stimulation, or their combination can prevent depression after stroke.
METHODS: The population addressed were patients who suffered from a stroke and had no previous diagnosis of depressive disorders. Studies comparing pharmacological intervention to placebo, psychological therapy to usual care, and non-invasive brain stimulation to sham stimulation or usual care were included.
RESULTS: Outcome information was available for nine pharmacological and two psychological trials, showing favorable treatment effects.
CONCLUSIONS: The available evidence suggests that pharmacological interventions and psychological therapy may prevent depression and improve mood after stroke. Although, the current evidence is of very low quality resulting in serious uncertainties about the estimates of effect observed.

Keywords: Depression, stroke, psychological therapy, antidepressant, non-invasive brain stimulation

The aim of this commentary is to discuss from a rehabilitation perspective the published Cochrane Review "Pharmacological, psychological and non-invasive brain stimulation interventions for preventing depression after stroke" (Allida et al., 2020) by Allida et al.[a], under the direct supervision of Cochrane Stroke Group. This Cochrane Corner is produced in agreement with *NeuroRehabilitation* by Cochrane Rehabilitation.

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[a]This summary is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2020, Issue 5, Art. No.: CD003689, DOI: 10.1002/14651858. CD003689.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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1. Background

Depression is a frequent consequence of stroke. It is reported that 33% of patients show symptoms of clinical depression at some time after the event, whether in the acute, medium, or longer term (Hackett et al., 2005). Depressive disorders can interfere with physical and cognitive rehabilitation and are associated with an increased risk of death (House et al., 2001). Although some research shows that antidepressant prophylaxis within the first few months after stroke could decrease the incidence of post-stroke depression (Gu et al., 2020; Salter et al., 2013), the role of early intervention to prevent the onset of depression and mood disorders after a stroke is still unclear.

Pharmacological, psychological and non-invasive brain stimulation interventions for preventing depression after stroke
(Allida, Cox, Hsieh, House, & Hackett, 2020)

2. Objective

The aim of this Cochrane Review was to determine whether pharmacological therapy, psychological interventions, non-invasive brain stimulation, or combinations of these interventions can prevent the incidence of diagnosable depression after stroke.

2.1. What was studied and methods

This review is an update of a previously published Cochrane Review updated in 2008 (Hackett et al., 2008). The first published review was in 2004 (Anderson et al., 2004). For this update, the authors searched all databases from inception until August 2018. The population addressed in this review were patients (average age range = 55 to 73 years) with a confirmed history of stroke and no previous diagnosis of depressive disorders. Studies comparing pharmacological intervention to placebo, psychological therapy to usual care, and non-invasive brain stimulation to sham stimulation or usual care were included. The primary outcome studied was the proportion of people meeting the diagnostic criteria of depression (e.g., depression, dysthymia, or minor depression) assessed by validated scales (e.g., Hamilton Depression Rating Scale, and the Hospital Anxiety Depression Scale), or by clinical or physician evaluation. Secondary outcomes studied were: psychological distress, general health, cognition, social activities, activities of daily living, disability, anxiety, and adverse events.

2.2. Results

The review included 19 RCTs (with 1771 participants). Twelve trials assessed pharmacological therapy compared to placebo, seven trials assessed psychological therapy compared to usual care and/or attention control. No trials investigated non-invasive brain stimulation compared to sham stimulation or usual care to prevent depression after stroke.

The results of the meta-analysis performed on the outcomes are the following:

2.2.1. Pharmacological interventions compared to placebo

- Depression: eight trials found favourable treatment effects (risk ratio (RR) 0.50, 95% confidence interval (CI) 0.37 to 0.68, 734 participants) at the end of treatment. Certainty of evidence: very-low.
- Cognition: two trials found no statistically significant difference in the average change in scores between baseline and end of treatment (MD 0.11, 95% CI –1.02 to 1.24, 159 participants). One trial revealed no statistically significant difference in the mean scores at the end of treatment (MD –0.42, 95% CI –2.60 to 1.76, 48 participants). Certainty of evidence: very-low.
- Activities of daily living: two trials found no statistically significant difference in the average change in scores between baseline and end of treatment (MD 1.18, 95% CI –7.77 to 10.14, 57 participants). Two trials revealed no statistically significant difference in the mean scores at the end of treatment (MD –3.86, 95% CI –9.48 to 1.77, 116 participants). Certainty of evidence: very-low.

2.2.2. Psychological therapy compared to usual care and/or attention control

- Depression: two trials of psychological therapy revealed favorable treatment effects (RR 0.68, 95% CI 0.49 to 0.94, 607 participants) at the end of treatment. Certainty of evidence: very-low.
- Psychological distress: two trials found favorable treatment effects in the average change in

psychological distress scores between baseline and the end of treatment (MD –1.37, 95% CI –2.27 to –0.48, 607 participants).
- Social activities: two trials found no statistically significant difference at the end of treatment (MD –0.39, 95% CI –3.81 to 3.03, 690 participants).
- Activities of daily living: three trials revealed no statistically significant difference in the average change in scores between baseline and end of treatment(MD 0.29, 95% CI –0.18 to 0.77, 847 participants). Certainty of evidence: very-low.

2.3. Adverse events

There was no statistically significant harm in the pharmacological interventions versus placebo (antidepressants) or psychological therapy versus usual care and/or attention control comparisons.

3. Conclusions

The author concluded pharmacological interventions and psychological therapy may prevent depression after stroke, but the evidence is insufficient to support the routine clinical use of these interventions. The current evidence is of very low quality resulting in serious uncertainties about the estimates of observed effects.

4. Implications for practice in neurorehabilitation

Depression is frequent after the loss of a major function, and its management is highly important. Does it improve spontaneously or should it be addressed with drugs or psychotherapy? These questions are highly relevant, but at this stage, we don't have yet a certain answer. Taken together, the evidence included in this review suggests that both pharmacological and psychological therapy may reduce the incidence of depression after stroke. However, all reported positive effects are assessed as very low-certainty. In such a situation, clinical expertise can still play a role while waiting for better evidence. Neither starting nor discontinuing current practicesis warranted. When interpreting these findings, clinicians should note that the studies in this field showed several limitations that can account for the uncertainty of the evidence. What we need most, are future trials of adequate power, and with patients enrolled early after the stroke onset.

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Conflict of interest

The authors declare no conflicts of interest.

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