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[Intervention Review]

Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke

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ABSTRACT

Background

Depression is an important morbidity associated with stroke that impacts on recovery yet often undetected or inadequately treated. This is an update and expansion of a Cochrane Review first published in 2004 and updated in 2008.

Objectives

Primary objective

• To determine whether pharmacological therapy, non-invasive brain stimulation, psychological therapy, or combinations of these interventions reduce the prevalence of diagnosable depression after stroke

Secondary objectives

• To determine whether pharmacological therapy, non-invasive brain stimulation, psychological therapy, or combinations of these interventions reduce levels of depressive symptoms, improve physical and neurological function and health-related quality of life, and reduce dependency after stroke

• To assess the safety of and adherence to such treatments

Search methods

We searched the Specialised Registers of Cochrane Stroke and Cochrane Depression Anxiety and Neurosis (last searched August 2018), the Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 1), in the Cochrane Library, MEDLINE (1966 to August 2018), Embase (1980 to August 2018), the Cumulative Index to Nursing and Alllied Health Literature (CINAHL) (1982 to August 2018), PsycINFO (1967 to August 2018), and Web of Science (2002 to August 2018). We also searched reference lists, clinical trial registers (World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) to August 2018; ClinicalTrials.gov to August 2018), and conference proceedings, and we contacted study authors.

Selection criteria

Randomised controlled trials comparing (1) pharmacological interventions with placebo; (2) one of various forms of non-invasive brain stimulation with sham stimulation or usual care; (3) one of various forms of psychological therapy with usual care and/or attention control; (4) pharmacological intervention and various forms of psychological therapy with pharmacological intervention and usual care and/or attention control; (5) non-invasive brain stimulation and pharmacological intervention with pharmacological intervention and sham stimulation or usual care; (6) pharmacological intervention and one of various forms of psychological therapy with placebo and psychological therapy; (7) pharmacological intervention and non-invasive brain stimulation with placebo plus non-invasive brain stimulation; (8) non-invasive brain stimulation and one of various forms of psychological therapy versus non-invasive brain stimulation plus usual care and/or attention control; and (9) non-invasive brain stimulation and one of various forms of psychological therapy versus sham brain stimulation or usual care plus psychological therapy, with the intention of treating depression after stroke.

Data collection and analysis

Two review authors independently selected studies, assessed risk of bias, and extracted data from all included studies. We calculated mean difference (MD) or standardised mean difference (SMD) for continuous data, and risk ratio (RR) for dichotomous data, with 95% confidence intervals (CIs). We assessed heterogeneity using the I^2 statistic and certainty of the evidence according to GRADE.

Main results

We included 49 trials (56 comparisons) with 3342 participants. Data were available for: (1) pharmacological interventions with placebo (with 20 pharmacological comparisons); (2) one of various forms of non-invasive brain stimulation with sham stimulation or usual care (with eight non-invasive brain stimulation comparisons); (3) one of various forms of psychological therapy with usual care and/or attention control (with 16 psychological therapy comparisons); (4) pharmacological intervention and various forms of psychological therapy with pharmacological intervention and usual care and/or attention control (with two comparisons); and (5) non-invasive brain stimulation and pharmacological intervention with pharmacological intervention and sham stimulation or usual care (with 10 comparisons). We found no trials for the following comparisons: (6) pharmacological intervention and various forms of psychological therapy interventions versus placebo and psychological therapy; (7) pharmacological intervention and non-invasive brain stimulation versus placebo plus non-invasive brain stimulation; (8) non-invasive brain stimulation and one of various forms of psychological therapy versus non-invasive brain stimulation plus usual care and/or attention control; and (9) non-invasive brain stimulation and one of various forms of psychological therapy versus sham brain stimulation or usual care plus psychological therapy.

Treatment effects observed: very low-certainty evidence from eight trials suggests that pharmacological interventions decreased the number of people meeting study criteria for depression (RR 0.70, 95% CI 0.55 to 0.88; 1025 participants) at end of treatment, and very low-certainty evidence from six trials suggests that pharmacological interventions decreased the number of people with less than 50% reduction in depression scale scores at end of treatment (RR 0.47, 95% CI 0.32 to 0.69; 511 participants) compared to placebo. No trials of non-invasive brain stimulation reported on meeting study criteria for depression at end of treatment. Only one trial of non-invasive brain stimulation reported on the outcome <50% reduction in depression scale scores; thus, we were unable to perform a meta-analysis for this outcome. Very low-certainty evidence from six trials suggests that psychological therapy decreased the number of people meeting the study criteria for depression at end of treatment (RR 0.77, 95% CI 0.62 to 0.95; 521 participants) compared to usual care/attention control. No trials of combination therapies reported on the number of people meeting the study criteria for depression at end of treatment. Only one trial of combination (non-invasive brain stimulation and pharmacological intervention) therapy reported <50% reduction in depression scale scores at end of treatment. Thus, we were unable to perform a meta-analysis for this outcome.

Five trials reported adverse events related to the central nervous system (CNS) and noted significant harm in the pharmacological interventions group (RR 1.55, 95% CI 1.12 to 2.15; 488 participants; very low-certainty evidence). Four trials found significant gastrointestinal adverse events in the pharmacological interventions group (RR 1.62, 95% CI 1.19 to 2.19; 473 participants; very low-certainty evidence) compared to the placebo group. No significant deaths or adverse events were found in the psychological therapy group compared to the usual care/attention control group. Non-invasive brain stimulation interventions and combination therapies resulted in no deaths.

Authors' conclusions

Very low-certainty evidence suggests that pharmacological or psychological therapies can reduce the prevalence of depression. This very low-certainty evidence suggests that pharmacological therapy, psychological therapy, non-invasive brain stimulation, and combined interventions can reduce depressive symptoms. Pharmacological intervention was associated with adverse events related to the CNS and the gastrointestinal tract. More research is required before recommendations can be made about the routine use of such treatments.

PLAIN LANGUAGE SUMMARY

Pharmacological, psychological, and brain stimulation treatments for depression after stroke

Review question

Do pharmacological treatments, non-invasive brain stimulation, psychological treatments, or combination treatments reduce the proportion of people with depression or the extent of depressive symptoms after stroke?

Background

Depression is common after stroke yet often is not detected or inadequately treated.

Search date

We identified studies by searches conducted on 13 August 2018.

Study characteristics

We included trials that reported on the use of pharmacological, non-invasive brain stimulation, psychological, and combination therapy interventions to treat depression after stroke. Mean age of participants ranged from 54 to 78 years. Studies were from Asia (30), Europe (11), North America (6), and Australia (2).

Key results

We included 49 trials (56 treatments) involving 3342 participants. Pharmacological treatments resulted in fewer people meeting the study criteria for depression and less than 50% reduction in depression scale scores at end of treatment. Psychological therapy reduced the number of people meeting the study criteria for depression at end of treatment. More people in the pharmacological treatment group reported central nervous system (in five trials) and gastrointestinal side effects (in four trials) than in the placebo groups. Information on side effects of other treatments was not provided.

Certainty of the evidence

Estimates of treatment effects were imprecise due to small numbers in most studies and recruitment of people with very different baseline characteristics. We rated the certainty of evidence as very low due to these and other limitations in study design.

Conclusion

Antidepressant drugs may benefit people with persistent depressive symptoms after stroke, but care is required in their use, as little is known about their side effects. Psychological therapy may offer a treatment option. Future research should include a broader group of people with stroke.