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Are pharmacological interventions clinically useful to treat emotionalism after stroke? A Cochrane Review update summary with commentary

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Abstract.
BACKGROUND: Emotionalism, i.e. uncontrolled episodes of crying (or less commonly laughing) post stroke that are not triggered by situations that would have previously provoked such behavior occur in stroke survivors, may persist in some, and can be socially embarrassing.
OBJECTIVE: To evaluate whether pharmacological interventions are beneficial, acceptable, and safe in the treatment of emotionalism post stroke.
METHODS: A Cochrane review by Allida et al. was summarized with comments.
RESULTS: From a total of 7 eligible trials with a total of 239 participants included in the review, five with 213 participants could be used for data extraction. Very low to moderate quality evidence pointed to some beneficial effects of antidepressants in the treatment of emotionalism after stroke.
CONCLUSIONS: The available data suggest that antidepressants may reduce the frequency and severity of crying or laughing episodes in stroke survivors with emotionalism.

Keywords: Stroke, affective symptoms, antidepressive agents, crying, laughter, randomized controlled trial, review

The aim of this commentary is to discuss in a rehabilitation perspective the published Cochrane Review "Pharmaceutical interventions for emotionalism after stroke" by Allida, Patel, House, & Hackett.[1], under the direct supervision of the Cochrane Stroke Group. This Cochrane Corner is produced in agreement with *NeuroRehabilitation* by Cochrane Rehabilitation.

[1]This summary is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2019, Issue 3. Art. No.: CD003690. DOI: 10.1002/14651858.CD003690.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.

The views expressed in the summary with commentary are those of the Cochrane Corner author and do not represent the Cochrane Library or Wiley.

1. Background

Emotionalism, i.e. (1) episodes of crying (or less commonly laughing) post stroke that are (2) uncontrolled, and (3) not triggered by situations that would have previously provoked such behavior occurs not infrequently in stroke survivors. These episodes may or may not be triggered by a congruent emotion. Within the first month after stroke, emotionalism is observed in about 17% of stroke survivors, 20% between one and six months, and 12% thereafter (Gillespie et al., 2016), hence affecting a considerable proportion of stroke survivors. Clinically, emotionalism is distinct and needs to be distinguished from post stroke emotional disorders such as post stroke depression (PSD). It is important to inform those affected about the nature of the condition and to assess the presence or absence of co-morbid post stroke emotional disorders. Emotionalism with or without depression has traditionally been treated with antidepressants despite limited information on their effectiveness.

"Pharmaceutical interventions for emotionalism after stroke"

(Allida, Patel, House, & Hackett, 2019)

2. Objective

This Cochrane review is an update of the reviews published in 2004 first and updated in 2010 (Hackett et al., 2010) and sought evidence for clinical benefit, acceptability and harm when pharmacological interventions were used with the intention to treat emotionalism post stroke.

3. What was studied and methods

The population addressed in this review was people with a confirmed history of stroke and diagnosed as having emotionalism. The intervention studied was the use of pharmacological agents for the treatment of emotionalism following stroke. The intervention was compared to placebo treatment. The *primary outcome* studied was emotionalism. Emotionalism measures were as follows:

(1) The proportion of participants achieving at least a 50% reduction in abnormal emotional behaviour at the end of treatment;
(2) improved score on Center for Neurologic Study – Lability Scale (CNS-LS);
(3) Clinician Interview-Based Impression of Change (CIBIC); or
(4) diminished tearfulness.

Secondary outcomes included emotionalism at end of treatment, depression, cognitive functioning, activities of daily living (ADL), and disadvantages of treatment (adverse events, including death). A comprehensive search (up to May 2018) for randomized controlled trials (RCTs) or quasi-RCTs comparing psychotropic medication to placebo to treat stroke survivors with emotionalism was performed.

4. Results

From a total of 7 eligible trials with a total of 239 participants, five with 213 participants could be used for data extraction. Antidepressants used in the included trials were selective serotonine reuptake inhibitors (SSRIs), i.e. citalopram, fluoxetine, and sertraline, and tricyclic antidepressants (TCA), i.e. amitriptyline or nortriptyline.

Key results are:

- The review shows that emotionalism can be reduced by antidepressant treatment as indicated by an increase in the number of people who had 50% reduction with a risk ratio (RR) of 16.50 [95% CI (confidence interval) 1.07 to 253.40] in emotionalism (1 trial with 19 participants; very low quality evidence), improved scores on CNS-LS and for CIBIC (RR 1.44, 95%CI 0.95 to 2.19) (1 trial with 28 participants; low quality evidence), an increased number of people with reduced tearfulness (RR 2.18, 95% CI 1.29 to 3.71) (3 trials with 164 participants; moderate quality evidence), and improvement in scores on the Pathological Laughter and Crying Scale [MD (mean difference) –8.40, 95% CI –11.56 to –5.24] (1 trial with 28 participants; low quality evidence).
- Between group difference for change scores and end of treatment scores were not substantiated [SMD (standardized mean difference) –0.82, 95% CI –2.14 to –0.51] (2 trials with 72 participants).
- Pharmaceutical interventions had no effect on cognitive functioning (MD 0.30, 95% CI –3.27

to 2.67) or ADL (MD 1.40, 95% CI –5.22 to 2.42) (1 RCT, 28 participants).
- Concerning disadvantages of treatment, no differences between the groups were observed for central nervous system events such as tremor, sedation or confusion (RR 1.0, 95% CI 0.11 to 9.08) (2 trials with 56 participants) or death (RR 0.59, 95% CI 0.08 to 4.50) (6 trials with 172 participants; moderate quality evidence); however few trials systematically recorded or reported adverse events other than death.

5. Conclusions

The authors concluded that antidepressants may reduce the frequency and severity of outbursts of crying or laughing based on very low quality evidence. They further state that caution is needed to interpret the conclusions despite the very large effect due to several methodological deficiencies in the trials. While the effect does not seem specific to a particular drug or class of drugs, there were too few trials to assess this endpoint. There is a need for more reliable data to be able to make reliable conclusions about the treatment of post-stroke emotionalism.

6. Implications for practice in neurorehabilitation

Only a rather limited number of placebo-controlled RCTs (seven) that address the clinical benefit and risks associated with psychopharmacological treatment of emotionalism post stroke and included a limited overall number of participants (239) could be identified. Several factors limit our ability to draw conclusions for clinical practice in neurorehabilitation based on the Cochrane evidence presented. Overall, the data are rather limited with a few, mainly small studies with a risk for publication bias and imprecision of results which make the quality of evidence ranging from very low to moderate; risk of bias assessment was restricted by inadequate reporting in some of the included trials. Participants varied considerably with regard to time post stroke, and presumably co-morbid PSD. Across included trials, different types of antidepressants had been used for diverse periods of time ranging from 10 to 182 days. No sufficiently validated assessment tool for emotionalism exists as a "gold standard" that could have been used in those trials. Information on acceptability and harm is limited, adverse event reporting was poor. With all these weaknesses in mind, no clear recommendation can be deduced for clinical practice.

The review does, however, present some low quality evidence that antidepressants may reduce the frequency and severity of crying or laughing episodes in people experiencing emotionalism post stroke without an indication for associated clinically relevant harm. Accordingly, antidepressants may be used to treat emotionalism post stroke on an individual basis with careful evaluation of the clinical benefit and any adverse events. Based on their risk profile SSRIs might be preferable over TCA; the implications of such use as "off-label" need to be taken into consideration.

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Conflict of interest

The author declares no conflicts of interest.

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