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## Pharmaceutical interventions for emotionalism after stroke

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Key words: emotionalism, stroke, treatment, randomised controlled trial, meta-analysis

Correspondence to: Maree L. Hackett, PhD, The George Institute for Global Health, Faculty of Medicine, University of New South Wales, PO Box M201 Missenden Rd, NSW 2050, Australia. Email <u>mhackett@georgeinstitute.org.au</u> ; Tel +61 2 8052 4593 Antidepressants may be useful in the treatment of abnormal crying or laughing associated with stroke. This is an update of a Cochrane Review first published in 2004 and last updated in 2019.

#### Search methods

We searched the Cochrane Stroke Group Register, CENTRAL, MEDLINE, Embase, four other databases, and three trials registers (May 2022).

#### Selection criteria

Randomised controlled trials (RCTs) comparing psychotropic medication to placebo in people with stroke and emotionalism (emotional lability, pathological crying or laughing, emotional incontinence, involuntary emotional expression disorder, and pseudobulbar affect).

#### Results

Seven trials with 239 participants. Five trials were published >24 years ago. The most recent was published in 2006. Two trials had a cross-over design, but outcome data were unavailable from the pre-crossover phase in an appropriate format for inclusion as a parallel RCT. Results are based on five trials with 213 participants.

Antidepressants probably increase the number of people who experience a reduction in tearfulness (RR, 0.32 [95% CI 0.12 to 0.86]; 3 trials, 164 participants; moderate-certainty evidence). Fluoxetine possibly increases the number of people who experienced 50% reduction in emotionalism when compared to placebo (risk ratio [RR] 0.26 [95% CI 0.09 to 0.77]; 1 trial, 19 participants, Figure) but the certainty of evidence is very low. Sertraline may lead to little or no difference in Center for Neurologic Study-Lability Scale (CNS-LS) scores and Clinician Interview-Based Impression of Change (CIBIC) scores compared to placebo (RR, 0.20 [95% CI 0.03 to 1.50]; 1 trial, 28 participants; low-certainty evidence). No trials were found that evaluated other psychotropic interventions.

Two trials systematically recorded and reported adverse events, providing limited data on the potential harms of treatment. Six trials reported death as an adverse event and found no difference between antidepressants and placebo (RR, 0.59 [95% CI 0.08 to 4.50]; 172 participants; moderate-certainty evidence).

#### Discussion

This review provides very low- to moderate-certainty evidence that antidepressants reduce the frequency and severity of crying or laughing episodes when compared to placebo. The trials were small and had some degree of bias. The effect does not seem specific to one drug or class of drugs. More reliable data are required before conclusions can be made about who might benefit the most from treatment. Our conclusions must be interpreted with caution despite the effect being very large.

Large, well-designed trials are needed which: use a standardised method to diagnose emotionalism, determine severity, and assess change over time; provide treatment and follow-up for a sufficient duration to better assess rates of relapse or maintenance of remission; and include careful assessment and complete reporting of adverse events. People with emotionalism after stroke should be included in the design of future trials to ensure relevant outcomes are included. Sufficient participants are needed to allow for analysis of concomitant depression as a modifier or moderator of outcomes. The National Institute for Health and Care Research (NIHR), United Kingdom has recently funded a RCT of sertraline, daily, for six months, to reduce emotionalism after stroke (Evaluating Antidepressants for emotionaliSm after strokE, EASE NIHR152423) - starting in June 2023.

## Disclosures

The original review was supported by a travel grant from the Stroke Society of Australasia and nonfinancial support from the Academic Unit of Psychiatry, The University of Leeds, the Department of Clinical Neurosciences, University of Edinburgh.

Maree L Hackett is a coinvestigator on National Institute for Health Research Health Technology Assessment program grant NIHR152423; EASE: Evaluating Antidepressants for emotionaliSm after strokE: A multi-centre, randomised, double-blind, placebocontrolled trial to establish the effect(s) of administration of sertraline (50 mg once daily for Six Months) in people with a recent stroke and post-stroke emotionalism.

# Acknowledgement

This paper is based on a Cochrane Review published in The Cochrane Library 2022, Issue 11 (see <u>www.thecochranelibrary.com</u> for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and The Cochrane Library should be consulted for the most recent version of the review.

 Allida S, House AO, Hackett ML.Pharmaceutical interventions for emotionalism after stroke. *Cochrane Database of Systematic Reviews* 2022;11: CD003690. doi:10.1002/14651858.CD003690.pub5 <u>https://doi.org/10.1002/14651858.CD003690</u>

Study or Subgroup	Interve Events		Place Events	ebo Total		Risk ratio (Non-event) M-H, Random, 95% Cl	Risk ratio (Non M-H, Random,	
1.1.1 50% reduction	in emotio	nalism						
Brown 1998	7	9	0	10	100.0%	0.26 [0.09 , 0.77]		
Subtotal (95% CI)		9		10	100.0%	0.26 [0.09 , 0.77]		
Total events:	7		0				•	
Heterogeneity: Not ap	plicable							
Test for overall effect:	Z = 2.43 (	P = 0.02	)					
1.1.2 Improved sco	re on Cen	ter for N	leurologio	: Study -	Lability	Scale		
Burns 1999	13	14	. 9	14	100.0%	0.20 [0.03 , 1.50]		
Subtotal (95% CI)		14		14	100.0%	0.20 [0.03 , 1.50]		
Total events:	13		9					
Heterogeneity: Not ap	plicable							
Test for overall effect:	Z = 1.57 (	P = 0.12	)					
					•			
1.1.3 Clinician Inter		ea impre 14		•	•		_	
Burns 1999	13				100.0%			
Subtotal (95% CI)	40	14		14	100.0%	0.20 [0.03 , 1.50]		
otal events:	13		9					
Heterogeneity: Not ap	•	D - 0.40	<b>`</b>					
Test for overall effect:	Z = 1.57 (	P = 0.12	)					
1.1.4 Diminished tea	arfulness							
Burns 1999	14	14	9	14	10.0%	0.09 [0.01 , 1.50]		
Choi-Kwon 2006	37	44	14	48	42.3%	0.22 [0.11 , 0.45]		
Murray 2005	13	24	4	20	47.7%	0.57 [0.35 , 0.93]	-	
Subtotal (95% CI)		82		82	100.0%	0.32 [0.12 , 0.86]		
lotal events:	64		27				•	
-leterogeneity: Tau² =	0.46; Chi <sup>2</sup>	= 7.21,	df = 2 (P =	0.03); l²	= 72%			
Test for overall effect:	Z = 2.27 (	P = 0.02	)					
							0.002 0.1 1	10 50
								avours plac

# Figure

Effect of antidepressants versus placebo on emotionalism at the end of treatment, grouped by method used to determine emotionalism