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Is there a role for SSRIs after FOCUS, AFFINITY and EFFECT?

5th European Stroke Science Workshop

Nov 28 – 30, 2019 Garmisch-Partenkirchen, Germany, Hotel Eibsee

Erik Lundström, MD, PhD, Associate Prof of Neurology
Inst of Neuroscience, Uppsala University, Sweden, and
Karolinska Institutet, Sweden

www.effects.se

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Presenting on behalf of *the* EFFECTS Trial Collaboration

Katharina Stibrand Sunnerhagen (chair), Bo Norrving, Per Wester, Per Näsman, Jörgen Borg, Håkan Wallén, Björn Mårtensson, Eva Isaksson, EL FOCUS (UK) Martin Dennis, Gillian Mead;
AFFINITY (Australia, NZ, Vietnam): Graeme Hankey and Maree Hacket

EFFECTS Efficacy oF Fluoxetine – a randomisEd Controlled Trial in Stroke

Disclosures

- Chief Investigator of EFFECTS
  - Swedish Research Council
  - Swedish Heart-Lung Foundation
  - Swedish Brain Foundation
  - King Gustav V and Queen Victoria's Foundation of Freemasons
  - Swedish Stroke Association (STROKE-Riksförbundet)
  - Swedish Society of Medicine
  - Karolinska Institutet

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Summery part 1

Stroke recovery – *I don't think so*

Depression – *I think so*

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SUMMERY part 2: The answer will be reviled in May

ESO EUROPEAN STROKE ORGANISATION

World Stroke Organization

VIENNA 12-15 MAY 2020

EFFECTS

AFFINITY

Individual **P**atient **D**ata Meta-analysis

20 mg Fluoxetine 6 months mRS

FOCUS

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Why SSRI?

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Possible mechanism SSRI

1. Neuro*genesis*

   Animal models; some parts of the brain

2. Neuro*protection*

   Linked to anti-inflammatory effects

3. Affect the adrenergic system

   Upregulation of beta-1 receptors

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Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial

François Chollet, Jean Tardy, Jean-François Albucher, Claire Thalamas, Emilie Berard, Catherine Lamy, Yannick Bejot, Sandrine Deltour, Assia Jaillard, Philippe Niclot, Benoit Guillon, Thierry Moulin, Philippe Marque, Jérémie Pariente, Catherine Arnaud, Isabelle Loubinoux

Summary

Background Hemiplegia and hemiparesis are the most common deficits caused by stroke. A few small clinical trials suggest that fluoxetine enhances motor recovery but its clinical efficacy is unknown. We therefore aimed to investigate whether fluoxetine would enhance motor recovery if given soon after an ischaemic stroke to patients who have motor deficits.

Lancet Neurol 2011; 10: 123–30

This online publication has been corrected. The corrected version first appeared at

* *118 ischemisk*
* *3 months*
* *Hemi paresis*

17% *more independant*

Chollet F et al. Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial. Lancet Neurol. 2011 Feb;10(2):123-30.

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Secondary outcome

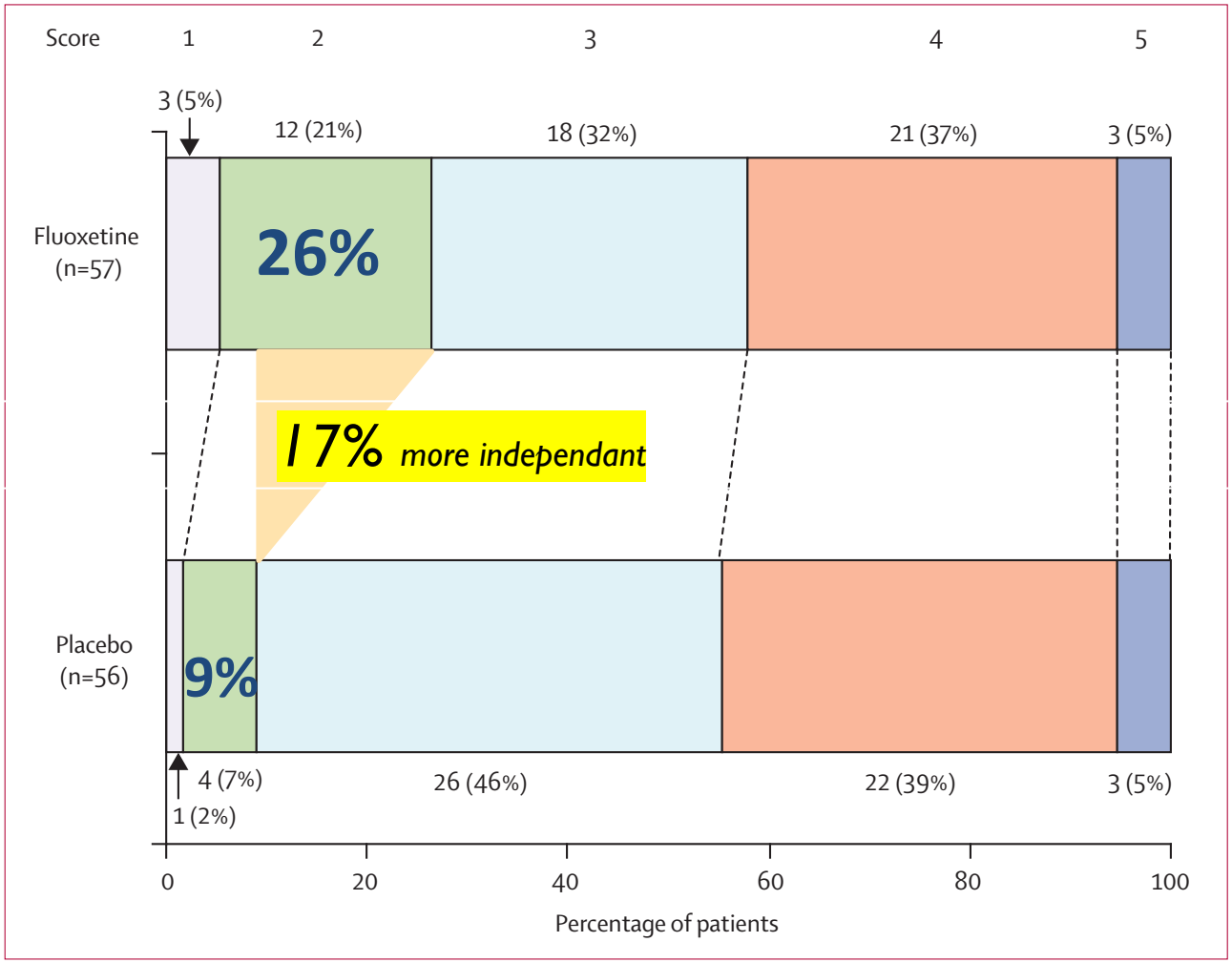

Figure 3: **Distribution of modified Rankin scale scores at day 90**
Data are number (%).

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	Fluoxetine (n=57)	Placebo (n=56)
Hyponatraemia	2 (4%)	2 (4%)
Nausea	5 (9%)	0
Diarrhoea	7 (12%)	4* (7%)
Abdominal pain	2 (4%)	2 (4%)
Hepatic enzyme disorders	5† (9%)	10 (18%)
Psychiatric disorders	3‡ (5%)	4 (7%)
Insomnia	19 (33%)	20 (36%)
Partial seizure	1 (2%)	0

Data are number (%). *Five adverse events in four patients. †Six adverse events in five patients. ‡Four adverse events in three patients.

Table 5: **Adverse events**

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Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery (Review)

Mead GE, Hsieh CF, Lee R, Kutlubaev MA, Claxton A, Hankey GJ, Hackett ML

THE COCHRANE COLLABORATION®

Cochrane Database of Systematic Reviews 2012, Issue 1, Updated 26 Nov 2019

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CONCLUSIO

REDUCES NEUROLOGICAL IMPAIRMENT, ANXIETY AND DEPRESSION AFTER STROKE

HETEROGENITY BETWEEN TRIALS

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CONCLUSIO

LARGE, WELL-DESIGNED TRIALS ARE NOW NEEDED TO DETERMINE WHETHER SSRI SHOULD BE GIVEN ROUTINELY TO PATIENTS WITH STROKE.

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Family of three trials

- FOCUS (UK) aimed to recruit > 3,000
- EFFECTS (Sweden) = 1,500
- AFFINITY (Australia, New Zealand & Vietnam) = 1,600

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If it works

- New mechanism *(for stroke recovery)*
- Simple – quickly implemented
- Inexpensive *(30 € for 6 months)*
- Safe *(used since 1988)*
- Both ischemic and haemorrhagic stroke

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FOCUS TRIAL
Fluoxetine Or Control Under Supervision

N = 3,127

EFFECTS

N = 1,500

AFFINITY
Assessment of fluoxetine in stroke recovery

N = 1,280

SUM = 5,907

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Effects of fluoxetine on functional outcomes after acute stroke (FOCUS): a pragmatic, double-blind, randomised, controlled trial

*FOCUS Trial Collaboration**

Writing group of the FOCUS Trial Collaboration
Martin Dennis (Chair), John Forbes, Catriona Graham, Maree Hackett, Graeme J Hankey, Allan House, Stephanie Lewis, Erik Lundström, Peter Sandercock, Gillian Mead.

Lancet, Volume 393, Issue 10168, 19–25 January 2019, Pages 265-274

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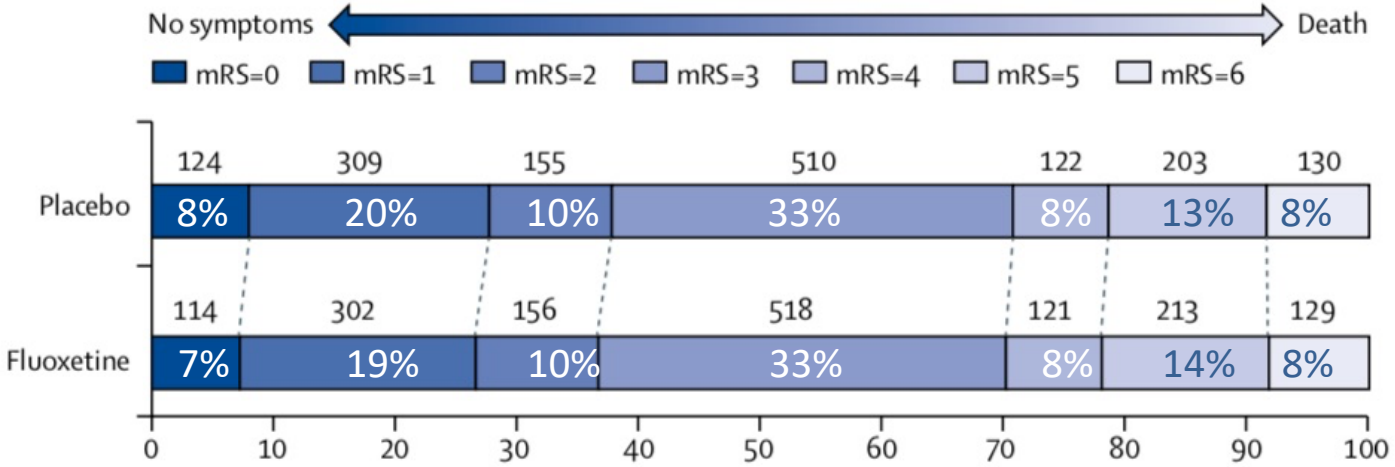
FOCUS



FLAME

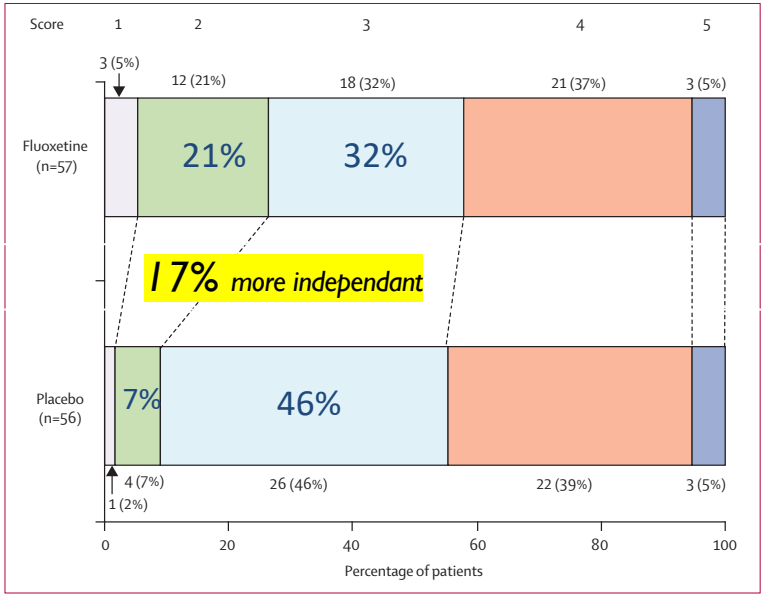


Figure 3: **Distribution of modified Rankin scale scores at day 90**
Data are number (%).

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Cochrane Library

Cochrane Database of Systematic Reviews

Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery (Review)

Legg LA, Tilney R, Hsieh CF, Wu S, Lundström E, Rudberg AS, Kutlubaev MA, Dennis M, Soleimani B, Barugh A, Hackett ML, Hankey GJ, Mead GE.
Published **26 November,** 2019. *Cochrane Database of Systematic Reviews* 2019, Issue 11. Art. No.: CD009286.
DOI: 10.1002/14651858.CD009286.pub3.

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Time line

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