Letter to the Editor

Stoke welcomes Letters to the Editor and will publish them, if suitable, as space permits. Letters must reference a Stroke published-ahead-of-print article or an article printed within the past 3 weeks. The maximum length is 750 words including no more than 5 references and 3 authors. Please submit letters typed double-spaced. Letters may be shortened or edited. Include a completed copyright transfer agreement form (available online at http://stroke.ahajournals.org and http://submit-stroke.ahajournals.org).

Letter by Mead et al Regarding Article, "Selective Serotonin Reuptake Inhibitors for Stroke: More Trials are Needed"

To the Editor:

We read with interest the recent Controversies in Stroke, in which 2 authors, Drs Marshall and Chollet, gave opposing views about whether selective serotonin reuptake inhibitors (SSRI) should be given routinely to people with stroke.1,2 Drs Marshall and Chollet both cite the Fluoxetine for Motor Recovery After Ischaemic Stroke (FLAME) trial, in which fluoxetine 20 mg daily given to 118 patients with motor deficits, who were not depressed, improved motor recovery and reduced disability measured with the modified Rankin scale at 3 months.3 A third author team reflected on the views expressed by Drs Chollet and Marshall and recommended the use of SSRI on a patient-by-patient basis, but taking particular account of their mood.4

Our Cochrane review of SSRI for stroke recovery identified 52 trials of SSRI in stroke recruiting 4059 patients.5 Twenty-eight of the trials used fluoxetine. Our meta-analyses demonstrated that at the end of treatment, patients allocated an SSRI were less likely to be dependent, disabled, neurologically impaired, depressed, or anxious. However, there was substantial clinical and methodological heterogeneity, and treatment effects were smaller when only high-quality trials were included. Furthermore, there seemed to be an excess of adverse events in those allocated an SSRI.

Although the results of our Cochrane review are promising, we do not believe there is sufficient evidence to change current clinical practice, which is to prescribe an SSRI to treat a moderate-to-severe poststroke depression. There were methodological weaknesses in some of the previous studies, the confidence intervals around estimates of treatment effects were wide, there was heterogeneity between trials, and there was an excess of adverse events associated with fluoxetine. The risk-benefit ratio is unknown. Importantly, we do not know whether any beneficial effects of fluoxetine persist after treatment is discontinued.

We are, therefore, establishing a family of multicenter randomized trials, Fluoxetine Or Control Under Supervision (FOCUS) in the United Kingdom (funded by the Stroke Association and now recruiting, www.focustrial.org.uk), Assessment Of FluoxetIne In s'Troke recovery (AFFINITY) in Australia (now recruiting, http://affinitytrial.org/), and Efficacy Of Fluoxetine, a randomizEd Controlled Trial in Stroke (EFFECTS) in Sweden (www.effects.se), to determine whether fluoxetine given for 6 months after stroke improves recovery at 6 months and whether any benefits persist to 12 months. These trials share broad eligibility criteria, methods of randomization, and outcome measures and will contribute data to a preplanned individual-patient meta-analysis. Together, these trials will aim to recruit several thousand patients. This will provide the power to identify even moderate-sized overall treatment effects, to examine differences in effect for subgroups based on types of impairment and mood and will hopefully confirm that the effects are generalizable across different populations and medical services (ie, those in United Kingdom, Australia, and Sweden).

Our view is that fluoxetine is a promising treatment that might improve recovery after stroke but that there is currently insufficient evidence for its routine use. Rather than treating patients routinely with fluoxetine, they should be offered, if possible, the opportunity to participate in a randomized trial. This will enable us to answer the burning clinical question about whether SSRIs given routinely after stroke will improve recovery and whether benefits apply to all types of stroke or just to some.

Disclosures

All authors have completed the Unified competing interest form at http://stroke.ahajournals.org/site/misc/conflictonlineform.pdf. Professors Mead and Dennis are coprincipal investigators of FOCUS trial. Professor Hankey and Dr Hackett are coprincipal investigators of AFFINITY Trial. Drs Murray and Lundstrom are coprincipal investigators of the EFFECTS trial. Professor Hankey has received consultancy fees from Bayer Health Care, Boehringer Ingelheim, and Johnson and Johnson.

Gillian E. Mead, MD, FRCP
Centre for Clinical Brain Sciences
Royal Infirmary, Little France Crescent
Edinburgh, United Kingdom

Martin Dennis, MD, FRCP
Centre for Clinical Brain Sciences
University of Edinburgh
Western General Hospital
Edinburgh, United Kingdom

Erik Lundström, MD, PhD
Department of Neurology
Academic Hospital
Upssala, Sweden

Veronica Murray, MD, PhD, FRCPE
Department of Clinical Sciences, Karolinska Institutet
Danderyd Hospital
Stockholm, Sweden

Maree Hackett, PhD
Neurological & Mental Health Division
George Institute for Global Health
Sydney, Australia

Graeme J. Hankey, MD, FRACGP
Stroke Unit, Department of Neurology
Royal Perth Hospital
Perth, Australia


Letter by Mead et al Regarding Article, "Selective Serotonin Reuptake Inhibitors for Stroke: More Trials are Needed"
Gillian E. Mead, Martin Dennis, Erik Lundström, Veronica Murray, Maree Hackett and Graeme J. Hankey

Stroke. 2013;44:e40-e41; originally published online January 22, 2013;
doi: 10.1161/STROKEAHA.112.681130
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/44/4/e40

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/