

Letter to the Editor Regarding “Fluoxetine May Enhance VEGF, BDNF and Cognition in Patients with Vascular Cognitive Impairment No Dementia: An Open-Label Randomized Clinical Study” [Letter]

Chiara C Brück 

Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands

Correspondence: Chiara C Brück, Email c.bruck@erasmusmc.nl

Dear editor

With great interest, I have read the article by Zhang et al,¹ who conducted an open-label randomized clinical study to assess the effects of fluoxetine on neurological markers and cognition in patients with vascular cognitive impairment no dementia (VCIND). The authors found that fluoxetine may enhance cognition in certain cognitive domains and serum concentration of BDNF and VEGF in patients with VCIND. I greatly appreciate the efforts of the authors on trying to improve the disease path of patients with VCIND. Nevertheless, there are several methodological limitations that I would like to communicate with the authors.

The authors correctly raised concerns about the open-label study design and small sample size but did not discuss their implications. The choice of an open-label study can introduce information bias, as participants are aware of their treatment. That knowledge can potentially influence their performance during the study (ie, on cognitive tests). The open-label choice is especially surprising since the drug that was tested, fluoxetine, is mostly prescribed as a pill and could therefore have been easily paired up with a placebo pill. A double-blind, placebo-controlled trial would have led to more convincing results and, I believe, would not have caused serious practical issues.

Furthermore, the authors calculated a sample size of 50 (25 treatment and 25 control) to detect a “clinically meaningful difference in cognition between the two groups”. This calculation is based on Serdar et al,² aiming at 80% statistical power and 5% significance level and assuming a standardized effect size of 0.8. I would argue that a standardized effect size of 0.8 is rather optimistic in the present study, and a more conservative effect size resulting in a larger sample size should be preferred. The authors also fail to discuss that due to loss of follow-up, the final sample size is effectively 47 instead of 50 and, thus, does not meet their required sample size at the 12-week follow-up. The study is therefore underpowered even with the optimistic sample size calculation of 50 participants.

While inclusion and exclusion criteria are discussed and the study was conducted at Xiangyang Central Hospital, it is not clear what the study population is. Clarifying whether the study participants entered the study from specific departments, ie, neurology, geriatric or memory clinic, or rather any hospital admission would give better insight into the generalizability of the results. If the study population was sampled from specific departments, this would greatly impair the generalizability of the results to the general VCIND population. Individuals with VCIND who do not seek help in the hospital might not benefit from the drug as individuals who have complaints and do seek help in hospitals for their condition. Hence, the study population should be clearly defined, and recommendations based on the results of this study should be formulated for the specific study population.

Disclosure

The author reports no conflicts of interest in this communication.

References

1. Zhang L, Liu X, Li T, et al. Fluoxetine may enhance VEGF, BDNF and cognition in patients with vascular cognitive impairment no dementia: an open-label randomized clinical study. *Neuropsychiatr Dis Treat*. 2021;17:3819–3825. doi:10.2147/NDT.S334647
2. Serdar CC, Cihan M, Yücel D, Serdar MA. Sample size, power and effect size revisited: simplified and practical approaches in pre-clinical, clinical and laboratory studies. *Biochemia Medica*. 2021;31(1):27–53. doi:10.11613/BM.2021.010502

Dove Medical Press encourages responsible, free and frank academic debate. The content of the Neuropsychiatric Disease and Treatment 'letters to the editor' section does not necessarily represent the views of Dove Medical Press, its officers, agents, employees, related entities or the Neuropsychiatric Disease and Treatment editors. While all reasonable steps have been taken to confirm the content of each letter, Dove Medical Press accepts no liability in respect of the content of any letter, nor is it responsible for the content and accuracy of any letter to the editor.

Neuropsychiatric Disease and Treatment

Dovepress

Publish your work in this journal

Neuropsychiatric Disease and Treatment is an international, peer-reviewed journal of clinical therapeutics and pharmacology focusing on concise rapid reporting of clinical or pre-clinical studies on a range of neuropsychiatric and neurological disorders. This journal is indexed on PubMed Central, the 'PsycINFO' database and CAS, and is the official journal of The International Neuropsychiatric Association (INA). The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/neuropsychiatric-disease-and-treatment-journal>

<https://doi.org/10.2147/NDT.S361484>