

Format for ANSWERING REVIEWERS

October 6, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 20975-review.doc).

Title: Transcranial magnetic stimulation as a new tool to control pain perception

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Name of Journal: *World Journal of Anesthesiology*

ESPS Manuscript NO: 20975

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers

Answers to Reviewed by 00503225

We thank the Reviewer for his/her comments on the paper and provide answers to the raised issues below. Changes to the paper requested by the Reviewer are indicated as underlined and bold text in the manuscript.

1. The authors have done a great job reviewing discussing THE TRANSCRANIAL MAGNETIC STIMULATION. The article however is too long and needs to be edited by a native as it contains some grammatical errors.

Admittedly, the article is too long. We have shortened the article as suggested, reducing also the bibliography.

Moreover, we also carefully reviewed the language of the manuscript in the attempt to improve the readability of the paper with the support of a native speaker.

2. Moreover, the authors have not provided any information on the quality of the studies that they have assessed nor their search strategy. I believe adding these information could be of great interest.



We have improved the description of the search strategy and the information about the quality of the studies as was suggested on page 6. We wrote that “*a search of literature on the analgesic effect of rTMS in chronic pain published from 1991 to May 2015 was performed using PubMed and the Cochrane Library. Keywords included chronic pain and neurostimulation, chronic pain and transcranial magnetic stimulation, neuropathic pain and neurostimulation, neuropathic pain and transcranial magnetic stimulation. The present review included controlled studies with at least 10 subjects enrolled to ensure the quality of the studies. Moreover, we excluded observational studies, and only papers in English were included. To minimize possible bias, the study selection-process was carried out independently by two authors (EO, MI)*”.

Answers to Reviewer 00484563

We thank the Reviewer for his/her comments on the paper and provide answers to the raised issues below. Changes to the paper requested by the Reviewer are indicated as highlighted in the manuscript.

This is a well-written and thorough review of the results of the recent literature on the clinical trials of the procedure of transcranial magnetic stimulation (TMS) in the treatment of chronic pain. The manuscript provides a good coverage of the performed trials aiming to treat neuropathic and non-neuropathic pain with a clear description of the various practical, technical and physiological aspects related to this modern clinical practice. It provides also a good attempt to analyze the possible cellular and molecular mechanisms underlying the analgesic effects of this procedure.

1. Despite my deep belief that the authors have made an excellent update, a concise and simplified comparison between TMS and electrical stimulation of the same cortical areas would be of great benefit for clinicians and scientists.

We thank Reviewer for his/her suggestion. In recent years these two techniques have become available to safely stimulate the human brain. We have added a brief comment on page 8 relative to the different mechanisms of action of the two stimulations. tDCS does not induce action potentials in axons as rTMS does, but it cause polarization of neurons changing their average level of discharge. Several studies examined the tDCS applied to the motor cortex as a possible treatment of chronic pain, but a recent Cochrane review (O'Connell NE et al. *Cochrane Database Syst Rev.* 2014) does not suggest a significant analgesic effect of this technique.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Anesthesiology*.

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