Author’s response to reviews

Title: Right median nerve electrical stimulation for acute traumatic coma (the Asia Coma Electrical Stimulation trial): Study protocol for a randomized controlled trial.

Authors:

Xiang Wu (drwuxiang@163.com)
Chao Zhang (1607376163@qq.com)
Junfeng Feng (fengjfmail@163.com)
Qing Mao (neurojack@163.com)
Guoyi Gao (guoyigao@gmail.com)
Jiyao Jiang (ACESACES@126.com)

Version: 1 Date: 06 Jun 2017

Author’s response to reviews:

Dear Pro. Cobo,

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate you very much for your positive and constructive comments and suggestions on our manuscript entitled “Right median nerve electrical stimulation for acute traumatic coma (the Asia Coma Electrical Stimulation trial): Study protocol for a randomized controlled trial” by Xiang Wu; Chao Zhang; Junfeng Feng; Qing Mao; Guoyi Gao; Jiyao Jiang. (ID: TRLS-D-16-00894)

We have studied your comments carefully and have made revision which marked in red in the paper. We have tried our best to revise our manuscript according to the comments. Attached please find the revised version, which we would like to submit for your kind consideration.

We would like to express our great appreciation to you for comments on our paper.

Looking forward to hearing from you. Thank you and best regards.

Your sincerely,

Guoyi Gao

Corresponding author:
1. Follow the recommendations on SPIRIT item 17a in order to fully specify who is masked and the way to guarantee it

Response: we have specified the blind method in “Data collection and follow-up” of the revised version.

2. Fully specify the main outcome and analysis

Response: we have added the concrete analysis of the main result in “Statistical analysis” of the revised version.

3. Consider useful advice to prevent data loss

Response: we have carefully studied the article recommended. We believe that this trial is carefully designed and will be strictly conducted so as to prevent data missing as much as possible. Patients’ data will be collected according to the case report form(CRF). We hope that there won’t be any loss to follow-up patient, but we still allow for some when calculating sample size. Were there any data missing, we would apply proper adjustment approaches mentioned in the article recommended.

4. Specify that the final report will follow the CONSORT statement as well as its extension to non-pharmacological interventions

Response: we made a statement that the final report will follow the CONSORT statement as well as its extension to non-pharmacological interventions in “overview” of the revised version.

5. Discuss the rationale and the risks for not having criteria for modifying allocated interventions (SPIRIT item 11b)

Response: usually, the assigned study intervention may need to be modified or discontinued because of harms, lack of efficacy or withdrawal of participant consent. Right median nerve electrical stimulation has been adopted as a safe, inexpensive, non-invasive therapy. It will not increase the incidence of complications which is demonstrated in the previous study. Besides, we specified on the consent form that this treatment might not show satisfactory efficacy on all of the patients and we will make sure that all representatives will fully understand before signing the consent form. So there will be little chance for withdrawal of participant consent because of harm or lack of efficacy. Therefore, there will be low risk for not having criteria for modifying allocated interventions.

6. Discuss the rationale and the risks for not having criteria for strategies to improve adherence (item 11c)
Response: Adherence to intervention protocols refers to the degree to which the behavior of trial participants corresponds to the intervention assigned to them. The 2 weeks RMNS treatment will be conducted by the clinician under the consent of the representative of comatose patient. So the whole intervention will be supervised by clinicians. There won’t be any risk of non-adherence.

7. Discuss the rationale and the risks for not having criteria for methods for any additional analyses (20b)

Response: the concrete analysis of the main result is mentioned in “Statistical analysis”. No additional analysis would be needed according to protocol.

8. Discuss the rationale and the risks for not having criteria for plans for communicating important protocol modifications (25)

Response: we don’t have plans for communicating important protocol modifications because our previous pilot study didn’t show any defect in current protocol especially in eligibility criteria, outcomes or analyses. We believe that there is very low risk for not having criteria for plans for communicating important protocol modifications.

9. Discuss the rationale and the risks for not having criteria for provisions for ancillary and post-trial care (30)

Response: we totally agree that ancillary and post-trial care should be provided in the trials whose treatment may cause obvious adverse events or harm. As is mentioned previously, however, right median nerve electrical stimulation is a safe, inexpensive, non-invasive therapy and it will do no harm to the trial participants which is demonstrated in the previous study. Besides, we have stated that this trial will be performed in accordance with the Declaration of Helsinki. So there is no risk of not having criteria for provisions for ancillary and post-trial care.

10. Provide the SPIRIT figure

Response: we have provided the SPIRIT figure (Figure.2) and legend in the revised version.