

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Effects of whole-body vibration training on lower-limb motor function and neural plasticity in stroke patients: protocol for a randomized controlled clinical trial
<b>AUTHORS</b>	Zhang, Mingkai; jianing, wei; Wu, Xueping

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Bernardo-Filho, Mario Universidade do Estado do Rio de Janeiro
<b>REVIEW RETURNED</b>	09-Mar-2022

<b>GENERAL COMMENTS</b>	Please, see my comments in the attached file. – contact publisher to view.
-------------------------	--

<b>REVIEWER</b>	Amorim, Paula University of Beira Interior, Health Sciences Faculty
<b>REVIEW RETURNED</b>	28-Apr-2022

<b>GENERAL COMMENTS</b>	<p>The authors present a study protocol on the effect of whole-body vibration training (WBVT) on lower-limb motor function and neural plasticity in stroke patients. The timing of intervention is not very clear: is the aim of the study to be applied in a subacute phase (<math>\geq 3</math> months and <math>&lt; 6</math> months)? Will the study patients in the chronic phase (<math>&gt; 6</math> months after stroke?) – this should be clarified in the title. Although it is an interesting issue to be studied, the authors should involve rehabilitation experts to be more precise on the terms used. The language lacks technical medical terms and consequent doubts on what the authors mean to transmit. For instance, «lower-limb disfunction» (page 1, line 27) is too vague – what do the authors mean to convey to the reader? Sensibility disfunction, motor disfunction, balance disfunction, coordination disfunction?... Another example: «because the participants will be ill and weak» (page 9 line 8, page 10, line 7) – this expression is not suitable for a scientific paper because it lacks objectivity.</p> <p>The Introduction repeats the same idea several times and should be revised to be shorter and less repetitive. For instance, on page 6 the authors repeated several times the effect of WBVT on reduction of spasm/muscle tension («spasticity» is the medical term they should use) and improvement of motor control/function.</p> <p>Another aspect to be revised is the idea that all the neural plasticity is always good. Maladaptive neural plasticity exists, which regards to the hindered functional recovery of the development of an unwanted symptom, such as compensatory movement pattern, delayed-onset involuntary abnormal movements.</p> <p>The physiopathology explained in the introduction part is incomplete because it only refers to the reduction or inhibition of the excitability</p>
-------------------------	--

	<p>of the motor cortex on the affected brain hemisphere, but doesn't mention the hyperexcitability that occurs in the contralateral region after a stroke.</p> <p>With regards to the methodology and the aim of the study, despite the title, the abstract and the introduction refers to the WBVT as being the intervention which the authors want to study, the fact is that there are 3 subgroups of participants: one is the control group which the authors don't specify if the participants do any active rehabilitation program («the CG will maintain their routine daily lives» - page 7 line 40). Another (the RRT group) is a routine rehabilitation training in which the participants will receive exercise interventions in the Sports Laboratory of Shanghai University of Sport» - the authors don't mention what this intervention includes. The WBVT group will receive the same exercise interventions as the RRT group plus WBVT. First, it isn't ethically correct if the control group doesn't receive any rehabilitation program at a subacute phase after stroke because the therapeutic window for recovery isn't not closed yet (this should be clarified by the authors) and secondly, with this methodology, the authors will compare doing nothing in terms of Rehabilitation (control group) with the RRT and RRT+WBVT, which will be an intervention bias. Is the RRT the conventional treatment for a patient with stroke in a subacute phase in that region? If not, will RRT be an intervention that the authors also want to study?</p> <p>Finally, in stroke rehabilitation, the determinants of motor recovery after stroke are early intervention, task-oriented training and repetition intensity. The authors only mention the importance of a repeated sensory input.</p> <p>With these comments, my suggestion is that the authors should revise the language and the methodology with the help of rehabilitation experts and after that submit a paper proposal again.</p>
--	---

### VERSION 1 – AUTHOR RESPONSE

Responds to the reviewer 1, Dr. Mario Bernardo-Filho's comments:

1. Responds to the comments: "To rewrite...Recent studies have shown....Studies have shown".

Response: We have made correction according to your comments.(page23 line23, marked copy)

2. Responds to the comments: "to rewrite the aim considering that is a protocol study...".

Response: We have made correction according to your comments.(page23 line25, marked copy)

3. Responds to the comments: Improving "Strengths and limitations of this study".

Response: 'strengths and limitations of this study' has been revised as required.(page23 line 51, marked copy)

4. Responds to the comments: "use (a) or (i) to avoid confusing with the references".

Response: We have rewrite this part according to your suggestion.(page 26 line 38, marked copy)

5. Responds to the comments: suggest to include references to justify "passive training method".

Response: Considering your suggestion, we have searched the relevant literature. In order to avoid ambiguity, we delete this part.

6. Responds to the comments: Suggest adding three references.

Response: Thank you very much for sharing the three references, which are very valuable for our research. We have added the three references.(reference 25,26,27)

7. Responds to the comments: suggest using "vibrating platform".

Response: We are very sorry for our incomplete writing, we have used "vibrating platform" according to your suggestion.(page 25 line 37, marked copy)

8. Responds to the comments: Suggest adding a reference.

Response: We have added the reference.(reference 33)

9. Responds to the comments:suggest avoiding the personal format in the manuscript, here, and

through the text.

Response: We have rewritten according to your suggestion.

10. Responds to the comments: Suggest using (a) or (i). (page 26 line 35, marked copy)

Response: We have rewrite this part according to your suggestion.

11. Responds to the comments: To add information about the guidelines SPIRIT in this section.

Response: We have added information about the guidelines SPIRIT in this section according to your suggestion.

12. Responds to the comments: To clarify daily training scheme in this part.

Response: We have added daily training scheme in this part. (page 26 line 55, marked copy)

13. Responds to the comments: to define the abbreviations used in the Figure.

Response: We have added the abbreviations used in Figure 1.

14. Responds to the comments: Suggest using "body mass" through manuscript.

Response: We are very sorry for our incorrect writing, and we have used "body mass" according to your suggestion. (page 27 line 28, marked copy)

15. Responds to the comments: to add in the legend the definitions of all abbreviations used in the Table.

Response: We are very sorry for our negligence of this part. And we have added definitions of all abbreviations used in table 1 to the legend.

16. Responds to the comments: "whole-body".

Response: We are very sorry for our incorrect writing, and we have revised here.

17. Responds to the comments: Suggest using (a) or (i).

Response: We have rewrite this part according to your suggestion. (page 27 line 49, marked copy)

18. Responds to the comments: To clarify unclear parts of exclusion and inclusion criteria.

Response: We have clarified the yellow part.

19. Responds to the comments: To clarify random method.

Response: We have re-described this part. (page 28 line 25, marked copy)

20. Responds to the comments: To clarify the criteria of "ill and weak".

Response: Since this is the first time I have written an English manuscript, there are many unclear parts. Thank you very much for helping me point out these parts. In order to make the expression clearer, we decided to delete this sentence.

21. Responds to the comments: To add ..vibrating platform...and the type of the vibrating platform.

Response: We have added "vibrating platform" and the type of the vibrating. (page 28 line 45, marked copy)

22. Responds to the comments: to add information of present amplitudes.

Response: Here is the ambiguity in the writing process, which has been deleted.

23. Responds to the comments: amplitude or peak-to-peak displacement? Please, confirm

Response: Thank you for sharing the references. Combined with the references and the whole body vibration platform to be used in this experiment, we have revised "amplitude" to "peak-to-peak displacement". (page 29 line 7, marked copy)

24. Responds to the comments: Change "Vibration training" to "whole-body vibration training".

Response: We have changed "Vibration training" to "whole-body vibration training" according to your comments. (page 29 line 14, marked copy)

25. Responds to the comments: to clarify about the location of the muscle and the place of the electrodes.

Response: We have described the electrode position in detail according to your suggestion. (page 32 line 11, marked copy)

26. Responds to the comments: to add reference about the methodology(SICI)

Response: We have added two references. (reference 42,43)

27. Responds to the comments: to add refrence and details about the technique...(isokinetic testing system)

Response: After further checking with the laboratory, we improved the information of the technique and added references. (reference 46)

28. Responds to the comments: To define “sf-36” and “MOCA”. (page 34 line 33, marked copy)

Response: We have defined these two indicators according to your suggestion.

29. Responds to the comments: To define the abbreviations at the end of Table 6.

Response: We have defined the abbreviations at the end of Table 6.

30. Responds to the comments: The references section must be improved.

Response: Thank you for sharing the references with us. We have improved the references.

Special thanks to you for your good comments!

Responds to the reviewer 2, Dr. Paula Amorim’s comments:

1. Responds to the comments: The timing of intervention is not very clear: is the aim of the study to be applied in a subacute phase ( $\geq 3$  months and  $< 6$  months)? Will the study patients in the chronic phase ( $> 6$  months after stroke?) – this should be clarified in the title.

Response: As written in the "exclusion and inclusion criteria", patients who have been ill for 3 months or more and meet other inclusion conditions can be recruited. Because these patients will return to the community for rehabilitation at this stage of rehabilitation, and our recruitment will also be in the community of Shanghai. In addition, we hope that the results of this study can eventually be applied to community rehabilitation of stroke. Therefore, we set the recruitment criteria as “duration of illness  $\geq 3$  months”.

2. Responds to the comments: the authors should involve rehabilitation experts to be more precise on the terms used. The language lacks technical medical terms and consequent doubts on what the authors mean to transmit. For instance, «lower-limb disfunction» (page 1, line 27) is too vague – what do the authors mean to convey to the reader? Sensibility disfunction, motor disfunction, balance disfunction, coordination disfunction?... Another example: «because the participants will be ill and weak» (page 9 line 8, page 10, line 7).

Response: We are very sorry for our incorrect writing, thank you very much for pointing out these mistakes, which is very helpful for our improvement. We have revised the professional terms in the full text. “Lower-limb motor dysfunction” applies to the full text; “spasm” change to “spasticity”; “Combined reaction” change to “associated reactions”; “Joint movement” change to “synergy movement”. “ill and weak” was deleted.

3. Responds to the comments: The Introduction repeats the same idea several times and should be revised to be shorter and less repetitive.

Response: We have made correction according to your comments. The repeated parts are integrated.

4. Responds to the comments: Another aspect to be revised is the idea that all the neural plasticity is always good. Maladaptive neural plasticity exists, which regards to the hindered functional recovery of the development of an unwanted symptom, such as compensatory movement pattern, delayed-onset involuntary abnormal movements.

Response: We are sorry for our negligence of maladaptive neural plasticity, we have added according your comments. (page 24 line 45, marked copy)

5. Responds to the comments: The physiopathology explained in the introduction part is incomplete because it only refers to the reduction or inhibition of the excitability of the motor cortex on the affected brain hemisphere, but doesn’t mention the hyperexcitability that occurs in the contralateral region after a stroke.

Response: We are sorry for our negligence, we have added the hyperexcitability that occurs in the contralateral region after a stroke. (page 24 line 45, marked copy)

6. Responds to the comments: The control group had no rehabilitation program.

Response: We are sorry for the incomplete description of the control group. In fact, These participants in the control group will be requested to maintain their original habits of lifestyle, while they also will receive usual care including usual stroke services available to the participants, including but not limited to, medical consultations offered by hospital, rehabilitation services by community-based organisations. And participants in the control group will receive telephone follow-up and health

lectures but will not receive any specific exercise training from the study scheme. The assessment results of the control group will also be compared with the other two groups. We have incorporated these supplements into the manuscript.(page 29 line 44, marked copy)

7.Responds to the comments: The RRT group is a routine rehabilitation training in which the participants will receive exercise interventions in the Sports Laboratory of Shanghai University of Sport» - the authors don't mention what this intervention includes.

Response: The RRT group will receive routine rehabilitation training in the Sport Laboratory of Shanghai University of Sport. And the training schedule of the RRT is shown in Table 3.

8.Responds to the comments: Is the RRT the conventional treatment for a patient with stroke in a subacute phase in that region? If not, will RRT be an intervention that the authors also want to study?

Response: RRT is a routine training method. And this kind of rehabilitation training is common in local communities or rehabilitation hospitals, but the effect is not good. Therefore, we hope to compare WBVT with RRT to explore whether WBVT is better than RRT.

9.Responds to the comments: in stroke rehabilitation, the determinants of motor recovery after stroke are early intervention, task-oriented training and repetition intensity. The authors only mention the importance of a repeated sensory input.

Response: We have added "early intervention", "task oriented training" and "repetition intensity" according to your comments.(page 25 line 20, marked copy)

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Bernardo-Filho, Mario Universidade do Estado do Rio de Janeiro
<b>REVIEW RETURNED</b>	04-Jun-2022

<b>GENERAL COMMENTS</b>	Congratulations. I am suggesting the acceptance of the manuscript, but it is necessary to correct some details in the manuscript that I am indicating in the attached file. – contact publisher to view.
-------------------------	--

<b>REVIEWER</b>	Amorim, Paula University of Beira Interior, Health Sciences Faculty
<b>REVIEW RETURNED</b>	02-Jun-2022

<b>GENERAL COMMENTS</b>	My previous suggestions were already clarified in this version.
-------------------------	---

#### VERSION 2 – AUTHOR RESPONSE

Responds to the reviewer 1, Dr. Mario Bernardo-Filho's comments:

1. Responds to the comments: Remove sentences and words labeled yellow.

Response: We have removed sentences and words labeled yellow according to your comments.(page 23 line 21, marked copy)

2. Responds to the comments: to correct the English language.

Response: We are very sorry for our incomplete writing, we have corrected it now. "present" to "presents". (page 23 line 46, marked copy)

3. Responds to the comments: I suggest improving the scientific language. Please, rewrite.  
Response: We have rewritten according to your comment. (page 25 line 48, marked copy)
4. Responds to the comments: To correct the English language.  
Response: We have corrected according to your comments. "aim" to "aims". (page 26 line 15, marked copy)
5. Responds to the comments: "timed".  
Response: We have corrected according to your comments. "time" to "timed". (page 27 line 32, marked copy)
6. Responds to the comments: The authors must put all the references in the same format following the guidelines of this journal.  
Response: We have revised according to your comments.