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OPEN PEER REVIEW

Effects of Magnesium Oxide and Zinc Oxide Nanoparticles on Motor Activity, Electrocardiographic Parameters, and Oxidative Stress in an Acute Restraint Stress Model of Rats

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

1 comment · 16 Jan 2022

Editor-in-Chief

MAJOR REVISION 16 Jan 2022

Dear Dr. Mozhgan Torabi
Thank you for considering JJCMB for the publication of your manuscript entitled "Effects of MgO and ZnO nanoparticles on motor activity, oxidant/ antioxidant balance of the brain and ECG parameters in the animal model". In accordance with the comments made by reviewers, this manuscript needs a major revision. Revise it meticulously and painstakingly and then resubmit it. Mentioning the ethical approval, author contribution, and grant-funding resources is mandatory in this journal.
Best regard
EIC, Dr. S.A. Mard

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewers' Comments:

Thank you very much for your useful and constructive comments on my manuscript (ID=122462). I have now revised the manuscript accordingly.

I would like to draw your attention to the following answers to the comments,

Reviewer 1:

1. It is suggested that authors revise the background part and re-write it: for example it is better start with the stress, the mechanism of action and its outcome, the kinds of stress, the regions which it affect and finally explain about nanoparticles and its effects according previous studies.

- Thank you very much for your nice suggestion, we have corrected the background according to your suggestion, but due to limitation of words number in the manuscript according to the journal guideline, we could not explain more about the mechanism of action of stress and its outcome in the background. Also, the aim of the current study was not investigation of the effect of stress alone on evaluated parameters.

2. Please revise the title: mention the animal model of stress in the title.

- It was corrected.

3. In discussion please respectively discuss around the effect of the stress on different measured parameters, then discuss about the effect of nanoparticles in stress animal model.

- Thank you very much for your good suggestion, we have corrected the discussion according to your suggestion, but this study has focused on nanoparticles effects not stress mechanisms. Also, please pay attention that the aim of this study was investigation the influence of stress on nanoparticle effects.

4. Why the nanoparticles injection was done immediately after the stress protocol?

- The aim of the current study was to evaluate the effect of nanoparticles in an acute stress model and as you know by passing time acute stress effect can be eliminated. Also, according to our previous studies, nanoparticles of MgO and ZnO can influence behavioral parameters 30 min after injection so that nanoparticles were injected immediately after stress induction to reduce the interval time between stress induction and injections.

Reviewer 2:

1. The abbreviation of the words should be written in full for the first time in the abstract and full text of the article.

- It was corrected.

2. Please write changes in the ECG in the abstract of the article.

- It was added

3. The results of the brain hemispheres should be written in the abstract of the article.

- It was added

4. Please write about the effect of antioxidant imbalance on the brain and heart in the introduction.

- It was added, but due to limitation of words number in the manuscript based on journal guideline we could not explain more about them.

5. The English version of the article needs to be edited.

-Article edited.

6. The number of rats used as the study population should be mentioned in the method.

- Number of rats was mentioned in table 1 and added in the method. Number of animal in behavioral test was 6-10 and in biochemical and ECG parameters were 6.

7. Please write the CAS number of nanoparticles in the method.

- CAS number of Nano- MgO is 1309-48-4, CAS number of Nano-ZnO is 1314-13-2

8. No. 3-1 In the procedure section of the article should be written coherently or in this section, grouping mentioned and sampling, antioxidant measurement, and ECG test stated in other sections of the method.

- This section rechecked according to your suggestion

- 9. How were the animals sacrificed?

- Animals were sacrificed according to the guidelines using chloroform.

10. Please explain the method of MDA and CAT measuring in the method of the manuscript.

-It was added.

11. Why is stress done in three-time intervals of 90, 180, and 360 minutes, but the ECG is only examined in 90-minute stress conditions?

- Because according to the result of motor activity, just stress of 90 minutes could affect motor activity, also in our previous study it has been shown that 90-minutes stress can affect other behavioral and molecular factors so that we have selected this time to make sure that acute stress was induced.

12. Why in the ECG measurement only the dose of 5 mg/kg has been examined while in the method three doses of the drug have been written?

- All doses were used in behavioral testes and as you can in results, in non-stressed animal's dose of 10 *mg/kg* showed negative effect on locomotor activity, so that we have used dose of 5 *mg/kg* as a highest non-effective dose in the ECG parameters measurements.

13. In the method, the researcher has talked about different doses of nanoparticles and different times of stress induction, while in the results section, we see scattering in some doses of drugs and stressful times. Please explain the reason in the article.

- In the ECG measurement, according to the result of motor activity, we have used stress of 90 minutes and dose of 5 *mg/kg* of nanoparticles. This reason was added in the results section.

14. In order to evaluate antioxidants, it was better to measure TAC instead of catalase.

- Thank you very much for your suggestion and we will pay attention to it in our future study.

15. In the introduction, the beneficial effect of administered nanoparticles on the heart and brain was explained, while the results show the opposite. The reason for this difference should be clearly explained in the discussion section of the article.

- Thank you very much for your attention, and it was added to discussion, but it is notable that the introduction was explained the beneficial effects of zinc and magnesium on the heart and brain not nanoparticles effects, also, there are few studies about nanoparticles effects on the heart and specifically on the ECG parameters so that, in a part of this study we have tried to evaluate and compare the effect of both nanoparticles on ECG parameters in normal and stress situation in male rat.

Reviewer 3:

Thank you for inviting me to review that manuscript.

The manuscript which is entitled by "Effects of MgO and ZnO ….." is well designed. But, there are some comments to improve it for publication in this journal.

1. The title should be changed to “ Effects of MgO and ZnO nanoparticles on the brain, electrocardiogram parameters, and oxidative stress in rat stress model”

- It was changed according to your suggestion.

2. The manuscript is full of a large number of grammatical errors, and punctuation in the text and abstract.

- It was edited.

3. The brain injury and cardiac injury should be explained by pathology in the introduction (in summary, such as oxidative stress). Therefore, an introduction to the pathophysiological process of brain and cardiac injury should be added to the manuscript.

- It was added, but due to limitation of words number in the manuscript based on the journal guideline, we could not explain more about them.

4. In the method section, the study groups should be explained.

- It was added.

5. The results in the text is different from figures regarding p-value. Also, the numbering of figures in the text is not similar to in the caption of figures. Figure 3 is divided as follows: 3a, 3b,….

- The results rechecked for p-value and figures number corrected.

6. The caption of figures must be improved. The caption of figures and table should be completed and explained about the figures and amount of doses of MgO and ZnO in below of the figures.

- They were corrected.

7. Please added references in the discussion section. For each result, similar and opposite studies should be added discussion to improve your manuscript. There are not a correlation among sentences and paragraph in the discussion.

- Discussion was edited, but it is notable that there are not many studies about nano-MgO and nano-ZnO effects on cardiovascular function and we could not find more similar or negative studies.

EIC Decision:

Dear Dr. Mozhgan Torabi

Thank you for considering JJCMB for publishing your manuscript entitled "Effects of MgO and ZnO nanoparticles on motor activity, oxidant/ antioxidant balance of the brain and ECG parameters in the animal model". In accordance with the comments made by reviewers this manuscript needs a major revision. Revise it meticulously and painstakingly and then resubmitted it within seven days. Mentioning the ethical approval, author contribution and grant- funding resources are mandatory in this journal.

Best regard

EIC, Dr. S.A. Mard

2 Revision 1

1 comment · 8 Mar 2022

Editor-in-Chief

MINOR REVISION 8 Mar 2022

Dear Dr. Torabi
Thanks for submitting the revised manuscript. Here you can find the issues that should be revised in the manuscript:
1. There are some grammatical errors that should be checked and revised by a native speaker. Of note, there are many sentences in the manuscript that need to be expressed in the passive voice to make the text fluent.
2. Keywords should be rewritten based on the MeSH format.
3. All the figures and tables should be cited in the manuscript. For example, Figures 1 and 2 are not referenced in the text of the article.
4. Would you please clarify whether Figure 1 shows a result obtained by the authors or just information about the purchased particle? If it was obtained during the project, please add the necessary information to the methods and results sections. If the latter is true, it is not necessary to include it in the manuscript.
5. Would you please clarify whether Figure 2 shows results obtained by the authors or is just a typical template for an ECG graph? If the latter is true, it is not necessary to include it in the manuscript.
6. Use P-value instead of P throughout the manuscript, tables, and figures.
7. Figure legends are key elements of scientific writing, allowing readers to fully understand the content of your figure without having to refer to the main text.
8. The groups that were compared in the statistical analysis should also be clearly identified in the table and figure legends.
9. The statistical asterisks (*, **, *** or ****) should be described in the data analysis section and legends.
10. The X/Y-axes should be defined in all bar charts.
11. The full name (not the abbreviated name) of the organization or institution that has registered the ethics code for this research should be mentioned in the relevant section.
12. The funding/support organization should be clarified, even if the research was funded at the authors' own expense.

Best Regard

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Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Associate Editor,

Thank you very much for your useful comments on the manuscript (ID=122462). The manuscript has been revised based on your comments. I would like to draw your attention to the following answers to the comments,

1- There are some grammatical errors which should be checked and revised by native speaker. Of note, there are many sentences in the manuscript that need to be expressed in passive voice to make the text fluent.

- Grammatical errors edited and sentences were re-write in passive voice.

2- Keywords should be re-write based on the MeSH format.

-Keywords edited.

3- All the figures and tables should be cited in the manuscript, respectively. For example, Figures 1 and 2 are not referenced in the text of the article.

- Figures 1 and 2 were deleted.

4. Would you please clarify that Figure 1 is related to the obtained result by the authors or it is just an information about the purchased particle? If it obtained during the project, please add the necessary information to the methods and results sections. If the later one is true, it is not necessary to put it in the manuscript.

- Figure 1 was deleted.

5. Would you please clarify that Figure 2 is related to the obtained results by the authors or it is just a typical template for ECG graph? If the later one is true, it is not necessary to put it in the manuscript.

- Figure 2 was deleted

6- Use the P-value instead of P, through the manuscript, tables or figures.

- P-value used through the manuscript, tables or figures.

7- Figure legends are key elements of scientific writing, so that the readers can fully understand the content of your figure without having to refer to the main text.

- Figures legends edited.

8- The groups which were compared in the statistical analysis should also be clearly identified in the table and figure legends.

- The groups which were compared in the statistical analysis identified in all tables and figures and figure legends.

9- The statistical asterisks (*, **, *** or ****) should be described in the data analysis section and legends.

- The statistical symbols described in the data analysis section and legends.

10- The bar X/Y-axis should be defined in all charts.

- X/Y –axis defined in all charts.

11- The Full name (not abbreviated one) of the organization or institution that has registered the ethics code of this research should be mentioned in the relevant section.

- This study was approved by the research ethics committee of Shahid Chamran University of Ahvaz, Ahvaz, Iran: EE/96.24.3.88369/scu.ac.ir. (It was placed at the end of the manuscript).

12- Funding/Support organization should be clarified even if it is at the authors' own expense.

- This study was financially supported by the research council of Shahid Chamran University of Ahvaz, Ahvaz, Iran (Grant number: 98/3/05/14909) (It was placed at the end of the manuscript).

3 Revision 2

1 comment · 9 May 2022

Editor-in-Chief

MINOR REVISION 9 May 2022

Dear Dr.Torabi
Please revise the manuscript based on the reviewer comments:

1- There are some grammatical errors which should be checked and corrected by a native speaker.
2- Delete *, & and + in all text except legends and figures.

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Revision 3

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Associate Editor,

Thank you very much for your useful comments on my manuscript (ID=122462). I have now revised the manuscript accordingly. I would like to draw your attention to the following answers to the comments,

1. There are some grammatical errors which should be checked and revised by native speaker.

- Grammatical errors edited.

2. Delete *, & and + in all text except legends and figures.

- All *, & and + deleted in text but Asterisks in tables 2 and 3 should not be deleted.

3. In response to the comment why 6 groups were used for ECG recording?

- "Since, motor activity was affected by the stress of 90 minutes and both nanoparticles at the dose of 5 *mg/kg* could not change it in the non-stressed rats; accordingly they were selected evaluating the ECG parameters".

It is described within manuscript.

4 Revision 3

0 comments

No public comments in this round.