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OPEN PEER REVIEW

The Effect of Lovastatin on the Electrophysiological Properties of CA1 Pyramidal Neurons in a Rat Model of Alzheimer Disease

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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 · 25 Feb 2021

Referee 1 Reviewer

MAJOR REVISION 25 Feb 2021

Abstract: Briefly explain the size of the study population and the groups, mention the major findings, and express the differences between indicators using statistical analysis.

Objective: This section should mention the aim of the study, not the methodology. It needs correction.

Results: Usually, differences in findings regarding the research variables are reported as significant differences (only Pv) in this section. Different tests, such as the T-test, and df should be mentioned in or under the tables (please pay attention to lines 151,159,165,173).
Discussion: In general, this section usually begins with the major findings related to the aim of the study and discusses other findings step by step.

Appropriate statistical tests have not been used: the groups have not been compared with each other, and it is not clear whether the methods or the same groups differ from each other.

In some diagrams, the shape was compared before and after, but no comparison was made between the groups. Therefore, it is recommended to use sign or McNemar tests.

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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.

Response to the questions of respected reviewer 1

The incomplete sentences in the text were corrected.

In the objective section, the aim of the research was stated.

The international names of the manufacturing companies were used.

To confirm the lesion site in the tissue samples prepared from the brain, images prepared from the atlas were also included.

Why did you use DMSO? DMSO was used as the solvent of lovastatin. The choice of solvent was based on articles. In the research conducted, after examining the effect of different doses of lovastatin on the activity of hippocampal CA1 neurons, the effect of the drug solvent (DMSO) on the activity of CA1 pyramidal neurons was also examined.

The conclusion should be based on the article's own data. In the research conducted, the results indicated that lovastatin at high doses (doses of 20 and 30 mg) increases the activity of pyramidal neurons of the Alzheimer's model rats, which has also been emphasised in the conclusion.

Reference 17 for the induction of the disease was corrected.

The method has many ambiguities: on what basis were the concentrations used selected? These concentrations are very high for intracerebral injections. In this study, the effect of different doses of the drug lovastatin on the activity of hippocampal pyramidal neurons of Alzheimer's model rats was examined. For this purpose, we first created the disease model (by inducing electrical current to the NBM nucleus). After 7 days, electrical recording was performed from these rats. For recording, the recording electrode was placed in the desired region, and after finding a neuron that had a stable signal, a 15-minute baseline recording was first taken from it, and then the drug lovastatin at doses of 10, 20, 30 mg/kg was injected intraperitoneally in separate groups, and recording continued for another 105 minutes and its effect on neuronal activity was examined. The selection of the different doses of lovastatin was based on a behavioural study that was carried out and whose result was published. In the behavioural study, doses (20, 10, 5, 1 mg/kg) of lovastatin were used, and we observed the best responses at doses of 10 and 20; we used these doses, together with the 30 mg/kg dose, in the electrical recording. Published article:

Effect of lovastatin on cognitive impairments induced by bilateral electrical lesion of the nucleus basalis magnocellularis in a model of Alzheimer's disease in adult male rats. Feyz Scientific-Research Bimonthly, Volume 21, Issue 5, Azar and Dey 1396, pages 421-431.

Response to the questions of respected reviewer 2

How was the sample size selected, since the number of rats in the groups is very large? The choice of the number of samples was based on articles. In fact, the difficulty of electrophysiology work and recording of neuronal activity is that, in several samples in which the disease model has been induced, when we start recording neuronal activity, after hours of searching in the desired brain region we may not be able to find any neuron that has stable activity to record from, and this leads to the number of samples in each group being high. Of course, this is an issue that exists in all electrophysiology work, whether extracellular or intracellular recording.

Why was one-way analysis of variance not used, and the results examined only within groups with the paired t-test: In the present research, the aim of the study was to examine neuronal activity before and after injection of the drug or solvent; after finding a stable neuron in the desired region, a 15-minute baseline recording (baseline) was first taken, then the drug was injected, and recording of neuronal activity continued for another 105 minutes. At the end of the electrical recording, the recording after drug injection was compared with the baseline in the same group. However, in accordance with the respected reviewer's comment, the findings of one-way analysis of variance were also added to the results.

Some graphs are not designed attractively; for example, graph four is not a clear graph at all. The bar graphs show the activity of a typical neuron in the group concerned. In these graphs, each column (bar) represents the activity of that neuron during one minute (as stated below the graph), [showing] what change occurs in these columns (which represent neuronal activity) after minute 15, when the injection was made. Of course, if

the respected reviewer's opinion is that these bar graphs are redundant, I will remove them from the text of the article.

Note: Graph 4, which related to the solvent group, was removed from the text of the article in accordance with the respected reviewer's comment on removing the graphs of non-significant groups.

The places that are not significant at all could be left unreported as graphs, and it could just be stated in the text in which groups the within-group comparison was not significant. In accordance with the respected reviewer's comment, in the groups that were not significant at all, the related graphs were removed and only their results are stated in the text.

Usually in groups one response is evaluated after the study; combine the graphs into one graph and show the different groups with different colours. It is not possible to combine the graphs into one graph, because in each group the electrical recording must be compared with the baseline of the same group. Each group has a different baseline from the other groups.

Response to the questions of respected reviewer 3

The abstract was corrected according to the respected reviewer's comment, and the points mentioned were included in the abstract.

The objective section of the article was corrected, and the aim of the research conducted was stated.

In the results section, according to the respected reviewer's comment, only the P-values are reported, and the T-test and df were removed.

Appropriate statistical tests have not been used; among other things, the groups have not been compared with each other, and it is not clear whether the methods,

i.e., the groups, differ from each other or not. It is necessary to mention that the aim of the present study was to examine neuronal activity in the desired region (hippocampus) before and after drug injection; for this purpose, the T-test was used. However, according to the respected reviewer's comment, the test for comparing the groups with each other has also been added to the results.

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2 Revision 1

0 comments

No public comments in this round.

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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.

Response to the questions of the respected reviewer

1. In the text, instead of ($p<0.05$), their exact values were inserted.
2. In the statistical analysis section, the names of all tests used were added.
3. The horizontal axis of graph eight was corrected.

3 Revision 2

0 comments

No public comments in this round.