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Archives of Neuroscience
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Peer Review Report for "Polycystic Ovary Syndrome Can Lead to Neurocognitive Changes in Female Rats Treated with Letrozole"

Author(s): Movahedeh Mohammadi, Iman Fatemi, Zahra Taghipour, Mahdieh Azin, Ayat Kaeidi, Elham Hakimizadeh , Raziyeh Taghizadeh, Mahsa Hassanipour

Review Timeline:

Submit Date: 12 Dec 2020
Revised Date: 11 May 2021
Accepted Date: 17 May 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) — 29 Dec 2020

Dear AE,
I agree with the publication of the manuscript.
Thanks.

Nastaran Rahimi: Reviewer | **Revision** (0) — 3 Apr 2021

Dear AE,
Comments for the authors:
Abstract
1- The animal kind did not mention in the abstract part.
2- When ovaries were removed?
3- The result part needs a more detailed response to the related test.
4- The discussion should be more specific and related to this manuscript.
Introduction
1- As is mentioned in the manuscript, the effect of PCOS on anxiety, depression, and memory has been reported in previous studies; the authors did not reach their aim in this manuscript.

Method

1- The Y-maze test needs to be clarified. How did the authors find the memory impairment?

Result

1- In the figures, the PCOS should be written completely, the units of measurements should be mentioned.

2- In the Y-maze test, what does it mean “mean percent alternation”?

Thanks.

REFEREE: Associate Editor | **Revision** (0) 5 Apr 2021

Dear EIC,

The manuscript needs major revision. Please revise the manuscript based on reviewers' comments.

Thanks.

REFEREE: EIC | **Revision** (0) 10 Apr 2021

Dear Author,

The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.

Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dr. Mahsa Hassanipour
E-mail: mhasanipoor@gmail.com

April 2021

To:
Dr. Zahid Hussain Khan;
Editor-in-Chief, *Archives of Neuroscience*

Dear Dr. Zahid Hussain Khan,

Thank you very much for sending us the results of the review on our manuscript entitled " Polycystic ovary syndrome can lead to neuro-cognitive changes in female rats treated with letrozole " (ID: 112023) which has been considered as “major revision”.

We would like to appreciate the reviewers for the time and effort that they spent on our manuscript. Definitely, their comments and suggestions will improve the manuscript quality. Attached, please find the revised version of the manuscript. Below we have explained the way that we have dealt with the reviewer’s comments and suggestions. We hope that you find this revised version acceptable for publication in *Archives of Neuroscience*.

Reviewer comments are written in red and our responses in black.

Sincerely,

Mahsa Hassanipour,
Pharm D., PhD.
Assistant Professor of Pharmacology,
Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

Reviewers' Comments:

Reviewer 1:

Abstract

1- The animal kind did not mention in abstract part.

Answer: "Twenty female Wistar rats (eight-week-old; 160±10 g) were used throughout the study". The animal kind was added to this section.

2- When ovaries were removed?

Answer: Ovaries were removed after termination of study by a surgical procedure. This part was added to the manuscript. "Ovaries were removed after behavioral tests and assessed histologically to confirm induction of PCOS"

3- The result part needs more detailed response of related test.

Answer: This part was edited and highlighted as follow: "PCOS animals developed depressive-like behaviors compared with control in forced swimming test ($p<0.001$). Anxiety-like behaviors were detected in letrozole-induced PCOS group ($p<0.05$). Moreover, animals with PCOS exhibited memory impairment in comparison with normal animals in Y maze memory assessment ($P<0.05$)."

4- The discussion should be more specific and related to this manuscript.

Answer: This part was edited and highlighted as follow: "PCOS rats showed neuro-cognitive decline in the model of letrozole administration. Future studies should be conducted in order to clarify the exact mechanisms of these changes and possible approaches to restore them"

Introduction

1- As it is mentioned in the manuscript, the effect of PCOS on anxiety, depression, and memory has reported in previous studies; the authors did not reach to their aim in this manuscript.

Answer: In this study we aimed to investigate the behavioral alterations in rats which were under treatment of letrozole for induction of PCOS. Meaning that we aimed to show if behavioral decline will appear with this model of PCOS induction (because this model is easy to perform) and in the case of observing the neuro-behavioral changes such as depression, anxiety or memory impairment in the future studies we will design a preventive or therapy approach to encounter the related behavioral changes in PCOS.

Method

1- The Y-maze test needs to be clarified. How the authors find the memory impairment?

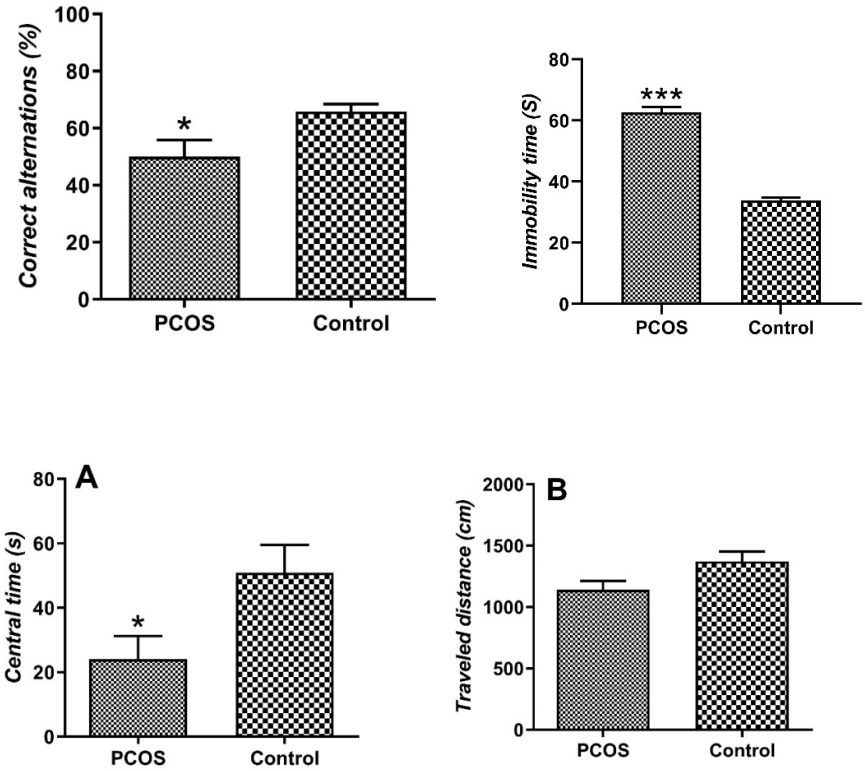
Answer: The Y-maze can be used to assess short term memory in mice. Spontaneous alternation, a measure of spatial working memory, can be assessed by allowing mice to explore all three arms of the maze and is driven by an innate curiosity of rodents to explore previously unvisited areas. So, a decrease in the percent of correct alternation exhibits the impairment of the working memory. In this study PCOS group showed decrease percent in this memory task.

- Kraeuter AK, Guest PC, Sarnyai Z. The Y-maze for assessment of spatial working and reference memory in mice. InPre-Clinical Models 2019 (pp. 105-111). Humana Press, New York, NY.

Result

1- In the figures, the PCOS should be write completely, the units of measurements should be mentioned.

Answer: The related changes were performed and here are the figures:



2- In Y-maze test, what does it mean “mean percent alternation”?

Answer: The Y-maze test evaluates the working memory. Animals are placed in the center of the maze and freely explore the maze for 8 min. The sequence of arm entries is visually counted by an investigator. A correct alternation is defined as consecutive full entries into each of the three arms. The percent of correct alternation is calculated as the number of

correct alternations vs the total number of arm visits. Mean percent of alternations was changed to “correct alternations (%)”

We used the following references for this pharmacologic experiment:

- Hakimizadeh E, Fatemi I, Allahtavakoli M. The effect of hydroalcoholic extract of pistachio on anxiety and working memory in ovariectomized female rats. Pistachio and Health Journal. 2020; 3 (3): 72-83.

- Hakimizadeh E, Kaeidi A, Taghipour Z, Mehrzadi S, Allahtavakoli M, Shamsizadeh A, Bazmandegan G, Hassanshahi J, Aflatoonian MR, Fatemi I. Ceftriaxone improves senile neurocognition damages induced by D-galactose in mice. Iranian Journal of Basic Medical Sciences. 2020 Mar;23(3):368.

Reviewer 2:

I agree with the publication of the manuscript.

Answer: Thanks for your kind attention.

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Nastaran Rahimi: Reviewer | **Revision** (1) 15 May 2021

Dear AE,
The authors respond to all of my concerns. The manuscript is suitable for publication, now.
Thanks.

REFEREE: Associate Editor | **Revision** (1) 17 May 2021

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (1) 17 May 2021

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.