**OPEN PEER REVIEW**

## Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

## What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

## Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://brief.land/kowsar/knowledgebase/category/tree.html#opr.html

Jentashapir Journal of Cellular and Molecular Biology
Article DOI: 10.5812/jjcmb.121808
Published in: Jentashapir Journal of Cellular and Molecular Biology: 12(4); e121808

# Peer Review Report for "Region Specificity in Endogenous Opioid Peptides and Mu-opioid Receptor Gene Expression in Rat Brain Areas Involved in Addiction After Frequent Morphine Treatment"

**Author(s):** Shamseddin Ahmadi, Kayvan Masoudi, Shiva Mohammadi Talvar, Mohammad Zobeiri, Amir Khanizad, Shima Fotouhi, Mohammad Majidi

**Review Timeline:**

| | |
|---|---|
| Submit Date: | 11 Dec 2021 |
| Revised Date: | 28 Dec 2021 |
| Accepted Date: | 1 Jan 2022 |

**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) — 17 Dec 2021

Dear AE,
1. Why did the authors not measure the behaviors related to the targeted regions?
2. The authors should describe how these results can utilize in the clinic? If you use a drug systemic (like in addiction), it affects all regions, but not one region?
3. How long after the last drug administration decapitation was done because it is an essential variable in your experiments? was it the same in all animals in both experimental groups?
Thanks

**REFEREE**: Reviewer | **Revision** (0) — 18 Dec 2021

Dear AE,

1. The introduction section is too long. It is better to be short.
2. There are many editing and grammar mistakes. Be corrected.
3. What is the approval of your study model? It should be added to the discussion section.
4. Is it possible to make a correct assessment in this study only by examining the gene expression?

Thanks

**REFEREE**: Associate Editor | **Revision** (0) 18 Dec 2021

Dear EIC,

According to the comments made by reviewers, this manuscript needs a minor revision.

Thanks

**Seyyed Ali Mard**: EIC | **Revision** (0) 18 Dec 2021

Dear Author,

Thank you for considering JJCMB for the publication of your manuscript. It needs a minor revision. Please do it within ten days. Your main text has a high percent of similarity and has to paraphrase before submitting the revised paper. You will receive the file of similarity report as attached file.

Best Regards

EIC, Dr. Mard

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.

**Response to Reviewers' Comments:**

The author would like to thank the Editor in Chief and respected reviewers for their valuable and precise consideration and comments on the first version of our manuscript. You had encouraged us to revise the manuscript, and we have done that as much as possible for us in the revision time. We have taken all of the reviewer suggestions into account, and we hope that the explanations and revisions of our work to be satisfactory.

Reviewer 1:
1. why the authors did not measure the behaviors related to the targeted regions?

- ✓ Response: The main aim of the present study was to explore alterations of the endogenous opioid peptide system in brain reward areas after a frequent regimen of morphine treatment. The examined areas are involved in different behaviors such as learning, memory, pain modulation, anxiety, and etc. We have reported changes in some of these behaviors in our previous reports and we have also added some of our previous reports and some references by other investigators in the discussion section (Page 9 of the revised manuscript) in the revised version of the manuscript.

2. The authors should describe how these results can utilize in the clinic? if you use a drug systemic (like in addiction) it affects all regions, but not one region?

- ✓ Response: Thank you for your valuable comment. Different brain areas are affected by opioids such as morphine and our results also support this issue. We have shown in the present study that there is a region specificity in the influence of morphine on the endogenous opioid system in the brain areas involved in addiction. In addition, the present results indicate that the opioidergic systems in some brain areas such as the midbrain, striatum, and prefrontal cortex are more sensitive to repeated morphine treatments. Based on the reviewer’s comment, we have revised the conclusion section (Page 12 of the revised manuscript) according to the obtained results.

3. how long after the last drug administration decapitation was done because it is a very important variable in your experiments? was it the same in all animals in both experimental groups?

- ✓ Response: Two hours after the injection at the morning session on day 8, each rat from both experimental groups was decapitated and the intended brain areas were dissected. We have added this clarification to the “Brain Dissection” section in the revised version of the manuscript (Page 5 of the revised manuscript).

Reviewer 2:

1. The introduction section is too long. It is better to be short.

- ✓ Response: Thanks a lot for your valuable comment. We have revised the introduction in the revised version of the manuscript and reduced it as much as possible.

2. There are many editing and grammar mistakes. Be corrected.

- ✓ Response: We have corrected the whole manuscript for typos and grammatical mistakes in the revised version of the manuscript.

3. What is the approval of your study model? It should be added to the discussion section.

- ✓ Response: We used a regimen of repeated morphine treatment in rats for 8 successive days. We have previously reported the induction of morphine tolerance and dependence using this regimen. In our previous reports, we have used the hotplate test of analgesia and naloxone-precipitated withdrawal test to approve induction of tolerance and dependence on morphine, respectively after 8 days of repeated injections. We have added the citation to our previous reports to the discussion section (Page 8 of the revised manuscript).

4. Is it possible to make a correct assessment in this study just by examining the gene expression?

- ✓ Response: With respect to the reviewer's valuable comment, this study has some limitations such as needing to examine protein levels of the examined genes. However, alterations at mRNA levels are the first step of other changes such as protein translation and also affecting signaling pathways. We have added the limitation of this study to the discussion section (Page 12 of the revised manuscript).

**OPEN PEER REVIEW**

**Revision (1)**

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

**Seyyed Ali Mard**: EIC | **Revision** (1) 1 Jan 2022

Dear Author,
The revised manuscript followed the reviewers' comments. Therefore, it is my pleasure to inform you that your manuscript entitled "Region Specificity in Endogenous Opioid Peptides and Mu-Opioid Receptor Gene Expression in Rat Brain Areas Involved in Addiction after Frequent Morphine Treatment" is now accepted for publication in JJCMB. You will receive the uncorrected proof of your paper within ten days. Please check the whole parts to avoid any errors in each piece of your paper.
Best regards
EIC, Dr. Mard