

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Critical Care Medicine

ESPS manuscript NO: 28421

Title: Female gonadal hormone effects on microglial activation and functional outcomes in a mouse model of moderate traumatic brain injury

Reviewer's code: 02446061

Reviewer's country: Mexico

Science editor: Fang-Fang Ji

Date sent for review: 2016-07-01 19:24

Date reviewed: 2016-07-19 09:48

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Dear authors: The manuscript is interesting. However, I suggest addition of some data before to consider it to be published in WJA. a) Several recent articles describe the role of hormones on the traumatic brain in mice models. Please add some of these.

We thank the reviewer for their thoughtful comments and suggestions. While work is limited in the field of mild TBI and gonadal hormones, we do discuss some similarities between MTBI and severe TBI in terms of gonadal hormone effects. Specifically, we have added the following references:

J Neurotrauma. 2015 Jun 1;32(11):765-79.

J Neurotrauma. 2013 Sep 1;30(17):1531-41.

b) You should be specific on the number of animals used in your experiments. Why only 5 OVX was used for behavior evaluation?

For clarification all animal numbers used for each cohort are detailed under *Experimental Groups* in the **Material and Methods** section. Animal numbers were based on our ability to detect specific outcome effects for each cohort. Since prior work was limited in this field and, thus, accurate formal power analyses were impossible, we based our animal numbers on prior experience with the severe TBI model.

c) You should add the strategy to design your experiments in order to minimize suffering and numbers of animals.

A statement to this effect is included under **Materials and Methods**. Specifically, anesthesia was used for all pain-inducing procedures; this is detail under each procedure. Animal numbers were minimized to detect an effect for each experimental cohort.

d) The results are poorly discussed regarding the comparison with similar (murine) models of trauma (and results from these studies). The discussion is centered in the traslational medicine.

We recognize that a great deal of work involving sex and gonadal hormone influence has been done with trauma and pre-clinical trauma models. An in depth review and discussion of this prior work is far beyond the scope of this manuscript. However, we have now added statements regarding prior work with models of mild TBI and sex/gonadal hormones.

e) Conclusions are partially supported for results and discussion. A improved presentation of results (comparison among groups) and a deeper discussion could let us to consider the manuscript for publishing. Regards, Reviewer

We thank the reviewer for their thoughtful comments and suggestions. All group comparisons are presented in the **Results** and responses to peer-review have improved and deepened the **Discussion**.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Critical Care Medicine

ESPS manuscript NO: 28421

Title: Female gonadal hormone effects on microglial activation and functional outcomes in a mouse model of moderate traumatic brain injury

Reviewer's code: 00220901

Reviewer's country: Turkey

Science editor: Fang-Fang Ji

Date sent for review: 2016-07-01 19:24

Date reviewed: 2016-07-24 21:51

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The manuscript entitled "Female gonadal hormone effects on microglial activation and functional outcomes in a mouse model of moderate traumatic brain injury" is well-written and the study is well designed. The subject is original, important and clinically relevant. I have only minor comment as follows: 1. In discussion section, it would be better adding a paragraph regarding the effects of TBI induced pituitary dysfunction, which could be a potential confounding factor for the results. Clinical and experimental studies clearly demonstrated that 10 to 50 % of patients develop hypopituitarism during acute and chronic TBI including all severities (Tanriverdi F et. al. Endocrine Reviews, June 2015, 36(3):305-342). Gonadotropin deficiency (FSH/LH deficiency finally results in decreased estrogen and progesterone) is one of the most common pituitary hormone deficiencies especially during acute phase of TBI. This factor may also explain the heterogeneity in the outcome after TBI in young female rats.

We thank the reviewer for their insightful comments. We have added a section in the Discussion section that now includes this point and contains the suggested reference.