**Reviewer’s report**

**Title:** The interplay of BDNF-TrkB with NMDA receptor in the process of propofol-induced cognition dysfunction in Hippocampus of neonatal rats

**Version:** 0  **Date:** 27 Apr 2017

**Reviewer:** Rany Makaryus

**Reviewer's report:**

This is an interesting study looking at the effects of BDNF-TrkB on NMDA receptor in the setting of neonatal anesthesia exposure in the rat model. There are a couple major concerns on this manuscript as currently presented: 1) There are no statements about how the animals did during the anesthesia. What was the mortality rate among the animals treated with propofol, what was the specific propofol dosage given, how did the animals do under anesthesia, for example, what was the respiratory rate, were they monitored for oxygen saturation, were they given supplemental oxygen, did they have their heart rate checked throughout the anesthesia? These are all very important questions, as there may be concerns that the results are secondary to effects of hypoxia, hypercarbia, hypotension, bradycardia, and/or other physiological disturbances during the experiments. We would not be able to understand this, unless there was some additional data reported about the anesthesia model used. If this data is not available for the currently reported animals, we would need to see data from additional experiments with animals undergoing anesthesia using propofol. 2) This study is looking at the effects of propofol in the developing brain. The mechanism of anesthesia neurotoxicity in the developing brain is unique to the time period of neuronal development and synaptogenesis. The authors, however, link these findings to post-op cognitive dysfunction (POCD). POCD may be related; however, that is a very different disease process compared to that of anesthesia induced neurotoxicity in the developing brain. If the animal model was that of an older rat with multiple co-morbidities undergoing anesthesia exposures, then this connection would be ok. The model used, however, is that of neonatal animals that are still going through the neurodevelopment process. It is not appropriate, therefore, to correlate the findings in the neonatal brain with those of POCD. From the introduction, it seems that the authors are making a connection that the effects of anesthesia in the developing brain will be the same as that in the older brain that leads to POCD, and this needs to be adjusted. Other Concerns: The six groups receiving propofol (P, PN, PD, PND, PNK, and PMD groups) were listed but differences between these groups were not defined in the methods section.

Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Unable to assess

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons
CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal