Reviewer’s report

Title: Maternal Sciatic Nerve Administered Bupivacaine Induces Hippocampal Cell Apoptosis in Offspring

Version: 1 Date: 30 Jun 2020

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?
Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?
Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?
Yes - experiments and analyses were performed appropriately

STATISTICS - Is the use of statistics in the manuscript appropriate?
Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
Yes - the author's interpretation is reasonable

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound?
If not, can revisions be made to make the work technically sound?
Yes - current version is technically sound

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: The major finding of this manuscript is that use of bupivacaine in pregnancy may result in substantial placental transfer, to induce neurotoxicity in the offspring. The authors have used an animal model of Wistar rats to assess this adverse effect of bupivacaine on the hippocampus of the offspring. They also propose a mechanism for the same, based on inhibition of Akt activation. This manuscript could contribute to further understanding of the side effects of local anesthetics, in this case, bupivacaine, on the neonatal brain. Future research in this area could focus on the adverse effect of maternal bupivacaine on the fetus. But to replicate the same in humans would probably require substantially long periods of follow-up. The methodology seems consistent with a well-conducted animal trial. The authors seem to have followed almost all the protocols in designing this study. The only thing that authors could
possibly have done is, maybe design a model where the exposure to bupivacaine would have occurred during labor/delivery. This might have allowed them to measure fetal blood pH just before delivery from the umbilical cord. As we know, numerous investigators, using different animal models, have studied the effects of fetal acidemia on local anesthetic distribution across the placenta, demonstrating fetal accumulation as the fetal pH decreases. This could have allowed them to factor the influence of fetal pH on eventual neurotoxicity from bupivacaine.

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No

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.

Yes

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

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