Reviewer’s report

Title: Exogenous hydrogen sulfide alleviates surgery-induced neuroinflammatory cognitive impairment in adult mice by inhibiting NO signaling

Version: 0 Date: 13 Oct 2019

Reviewer: Kong Eric You-Ten

Reviewer's report:

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Thank you for the opportunity to review this manuscript.

Reviewer A:

1. Abstract: Methods is a repeat of the Results??

2. P2 L21: To Investigate the effects and mechanisms…

3. P2 L23-29: This paragraph is a repeat of the results??

4. Methods: P5 L100-103: Group description is confusing and unclear:

Did the "YY4137 group (intraperitoneal injection 50 mg/kg GYY4137 in phosphate buffered saline (PBS) 1 h before surgery was performed)" had the surgery with exposed carotid or the sham surgery.

Did the " L-NAME group (water intake with 15 mg/kg in drinking water on Day 1 before surgery lasting to Day 3 post-surgery)" had the surgery with exposed carotid or the sham surgery.
Why was the GYY4137 given only on preop day 1, whereas, the L-NAME given for 4 days (preop Day to Postop Day 3).

5. Results: Figure 2 D: Can you please provide an explanation to why the level of iNOS with S+G+L appears to be as high as S (surgery group) and not decreased.

6. The results showed that L-NAME and GYY both reduced IL1, TNF and NO. This implies that these drugs are anti-inflammatory in general and are not that specific. It is unclear to conclude that NO is the cause of improving spatial learning and memory capacity, or if it was simply the reduction of inflammation from decreased of all inflammatory cytokines (IL1, TNF and NO).

7. It would have been more conclusive on the role of NO in surgery-induced POCD if NO or iNOS knock-out mouse was used.

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

No

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.

No

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:

Needs some language corrections before being published

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- Abstract: Methods is a repeat of the Results??- Methods: P5 L100-103: Group description is confusing and unclear: Did the “YY4137 group (intraperitoneal injection 50 mg/kg GYY4137 in phosphate buffered saline (PBS) 1 h before surgery was performed)” had the surgery with exposed carotid or the sham surgery. Did the “L-NAME group (water intake with 15 mg/kg in drinking water on Day 1 before surgery lasting to Day 3 post-surgery)” had the surgery with exposed carotid or the sham surgery. Why was the GYY4137 given only on preop day 1, whereas, the LNAME given for 4 days (preop Day to Postop Day 3). - The results showed that L-NAME and GYY both reduced IL1, TNF and NO. This implies that these drugs are anti-inflammatory in general and are not that specific. It is unclear to conclude that NO is the cause of improving spatial learning and memory capacity, or if it was simply the reduction of inflammation from decreased of all inflammatory cytokines (IL1, TNF and NO). It would have been more conclusive on the role of NO in surgery-induced POCD if NO or iNOS knock-out mouse was used. Can you please comment on whether these knockout have been used to demonstrate effects on POCD?
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