Author's response to reviews

Title: Postoperative cognitive dysfunction after inhalational anesthesia in elderly patients undergoing major surgery: the influence of anesthetic technique, cerebral injury and systemic inflammation.

Authors:

Yong Qiao (feishi_xin@126.com)
Hao Feng (feishi_xin@126.com)
Xin Zhao (zhaoxin2015@yeah.net)
Heng Yan (feishi_xin@126.com)
He Zhang (feishi_xin@126.com)
Tao Zhao (feishi_xin@126.com)

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Reviewer(s)' Comments to Author:

The authors thank the reviewer's for sparing their valuable in reviewing our manuscript.

Answers to Reviewer Terrie Vasilopoulos:

1. My major concern is with the statistical approach. The current approach involves multiple t-tests (or ANOVAs) on related outcomes. However, there is no mention of correcting for multiple comparisons. Performing multiple related tests increases the probability for false positives. Thus, keeping the p-value threshold at p < 0.05 is not appropriate. These analyses need to address this concern some way. One way would be to do a more omnibus, repeated measures analysis that includes the multiple end points. I would recommend a mixed modeling approach because it can control for within-person correlations. Also, you could then directly control for covariates.

a. At the very least, the present analyses need to have p-values corrected for multiple comparisons and the authors need to consult a statistician as to which type of correction is most appropriate. Though, using an omnibus approach as mentioned above would probably have more power. Also, I would prefer that raw p-values are reported, so that readers can assess the impact of the multiple comparisons adjustments themselves. Again, I think this paper would benefit from having a statistician review it.

Response: We agreed with the reviewer's view, and we had invited a statistician to review it. We used ANOVAs to compare three groups, and LSD post hoc test to compare two groups. We have added the additional tables to support our views. (Table 2-7)

2. Additionally, I think using a mixed modeling approach would better suit the analyses for the inflammatory factors. This way, interactions between group and
inflammatory markers could be directly tested. 

Response: We agreed with your view, and used a mixed modeling approach to analyze the inflammatory factors on figure 3.

3. I think the discussion needs more commentary as to why methylprednisolone would be a good pre-treatment for POCD. Could it be due to its anti-inflammatory effects? Are there other studies that have found similar results?

Response: We have added more commentary to explain a good pre-treatment of methylprednisolone for POCD (page 18, line 283-289).

Answers to Reviewer John Bebawy:

1. A Table is needed, including p values, showing all comparisons done by the authors

Response: We have added the additional tables to support our views. (Table 2-7)

2. Line 136-9: this is unclear, remifentanil is not used to maintain BIS, usually sevoflurane or propofol is. Please clarify this sentence.

Response: We have changed the expression of this part (page 9, line 136-139).

3. Line 148-50: it is unclear which opioid was used for PCA, please include.

Response: We have added the opioid of PCA (page 10, line 148).

4. Line 205-10: please move this sentence to Discussion, not a result

Response: We agreed with your view. Because this sentence was similar with part of discussion, we deleted it.

5. Line 215-19: please move this sentence to Discussion, not a result

Response: We agreed with your view. Because this sentence was similar with part of discussion, we deleted it.

6. Line 117: change "internal jugular venous pressure" to "internal jugular central venous pressure"

Response: We have changed "internal jugular venous pressure" to "internal jugular central venous pressure" (page 8, line 117-118).

7. Line 188: please include location of manufacturer (for example, Chicago, Illinois, USA)

Response: We have added the location of manufacturer of SPSS (page 12, line 189).

All of the indicated errors and omissions have been corrected in line with the referee’s comments.