Author’s response to reviews

Title: Dual effect of the Valsalva maneuver on autonomic nervous system activity, intraocular pressure, Schlemm’s canal, and iridocorneal angle morphology

Authors:
Li Sun (dr.lilysun1996@gmail.com)
Wei Chen (450741814@qq.com)
Zhiqi Chen (66czq@163.com)
Yan Xiang (xyz2000832@163.com)
Jingmin Guo (GJM696@163.com)
Tian Hu (hutian.rush@foxmail.com)
Qiongfang Xu (492517989@qq.com)
Hong Zhang (dr_zhanghong@vip.163.com)
Junming Wang (eyedrwjm@163.com)

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Author’s response to reviews:

1) The anthropometric measurements such as the body mass index(BMI) of the participants should be measured and included in the data analysis. The BMI has an impact on the heart rate.

   BMI and other various anthropometric measurements were measured before every subject in our study, and have been added into the revised manuscript.

2) We recommend you to do multivariate analysis.

   Thank you. We have re-analyzed our data as suggested.

3) Please use high quality OCT images and clearly outline the ARA750, TIA500, and TISA500 parameters.

   We have added an OCT image where the ARA750, TIA500, and TISA500 parameters are clearly represented.
4) Did you check for the presence of anisocoria at dim and bright conditions? Did you check for the presence of afferent pupillary defect? You should mention this in the exclusion criteria.

All OCT tests were performed under a standardized darkroom photopic condition (ca. 3.5 lux). All subjects underwent an ophthalmic examination, and afferent pupillary defects were one of our exclusion criteria. We have revised our exclusion criteria and added the test condition into the revised manuscript.

5) We recommend you to repeat the measured parameter bilateral and to check if there is any differences.

The measurements of SCAR and PD were performed by 2 observers. The intraclass correlation coefficients (ICC) test was used to analyze the re-test reliability. We have added this information into the revised manuscript, including in the ‘Statistical analysis’ section.

Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.

The following issues should be corrected:

1- Please clarify the problem with recent citations, and solving of research in introduction section.

We have revised the introduction section to fix these problems, and have cited further recent articles.

2- Please clarify setting of study in details.

We have revised the setting of our study in the revised manuscript.

3- Please clarify methods of assessment anterior chamber depth, angle, IOP.

We have revised the methods section, including clarification of the methods of assessment of the anterior chamber depth, angle, and IOP, and added a figure that outlines the anterior chamber depth and angle.

4- Please clarify exclusion criteria in details.

We have revised our exclusion criteria in the revised manuscript.
5-Please added the reference of standard valsalva maneuver.
We have added references for the research method for the VM (Ref 2, 3, 4).

6-Please added a table including demographic and clinical characteristics of patients.
Thank you for your advice. We have made a table that outlines the demographics and clinical characteristics of our patients.

7- Please added a table including correlations between the variables.
Thank you for your comment. We have added a table and a figure to show the correlations between our measured variables. (Table 3 and Figure 11)

8- Discussion should be condensed.
We have condensed the discussion, and provided a more specific focus on our topic.

9- Some typographical errors should be corrected.
Typographical errors have been corrected, and the language has been edited by a native English speaker at a professional editing company.

The study investigated the dual effect of Valsalva maneuver on autonomic nervous system activity, intraocular pressure, Schlemm's canal, and iridocorneal angle morphology, and presented plausible results regarding body adaption to Valsalva maneuver. However, there are certainly some points need to be fully addressed before we can consider it for publication.

1. The clinicians usually take more than 15s to do OCT, IOP measurement during VM. How they obtain ECG and measure BP, IOP, and take OCT in such a short time needs to be explained in the text.

All measurements were taken by the same experienced examiner, whose technical operation was very skilled. Every subject struck the correct pose on the measuring instrument before blowing, and held positions during the VM, after which measurements were taken. The IOPs were measured using a non-contact tonometer, and it took no more than 5 s to finish 3 IOP measurements. The time required by the OCT for 1 scan was approximately 3s. ECGs were monitored in real-time during the entire process, and our time periods of interest were collected from these recordings. A blood pressure cuff was placed on the hand before the subjects performed the VM, and we started measuring as soon as they entered the strain phase. The ECGs and BP were measured simultaneously. In the 3 OCT scans, IOP measurements, and BP and ECG measurements, every subject was asked to perform a separate VM. Therefore, 15 s was
sufficient to finish 1 image or data acquisition process. We have corrected our errors and clarified this procedure in the revised manuscript.

2. In figure 1, please use a frame to indicate which area is enlarged and show the enlarged image in the other place. Don't stack on top of the original area. For all bar images, please plot with dots and bars simultaneously; this is easier for the readers to see the differences among groups.

We have revised figure 1, and made all figures as bar graphs, in the revised manuscript.

3. There are some typo or gramma errors in the main text. For instance, line 145, line 283-284. Full name PACG in line 271.

Typo and gramma errors have been corrected, and the language has been edited by a native English speaker at a professional editing company.

4. Is there any literatures support that Mean ocular perfusion pressure (MOPP) is calculated as: MOPP = 2/3MAP - IOP?

We have cited literature that supports this calculation of mean ocular perfusion pressure in the revised manuscript. (Ref 17)

5. "its influence on IOP could be counteracted even reversed by the changes of blood flow and ocular anatomy" -- I don't think the last sentence of your conclusion is one of your findings. You are speculating something might explain IOP elevation in phase 2, but this is not your key findings in the study. Also, a lot of other key results were not well summarized in the conclusion.

Thank you for your comment. According to results, we have revised our discussion as suggested, and re-summarized our conclusions. Possible explanations for IOP fluctuation during the VM were summarized in the conclusions.