Author's response to reviews

Title: The higher exercise intensity and the presence of allele I of ACE gene elicit a higher post-exercise blood pressure reduction and nitric oxide release in elderly women

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Author's response to reviews: see over
To Editor-in-Chief

Fu-Tien Chiang, PhD
BioMed Central

Ref. Revised version of manuscript no.: MS: 5050781585518262 Titled: “The higher exercise intensity and the presence of allele I of ACE gene elicit a higher post-exercise blood pressure reduction and nitric oxide release in elderly women: an experimental study”.

Dear Editor,

The authors would like to thank the Editor for the opportunity of undertaking this review process. Below you can find responses to the comments raised by the reviewers. Along with the changes made in the manuscript to address the reviewers’ suggestions and make it clearer for the readers, the overall quality of the writing was improved. All changes in the manuscript are highlighted in yellow.

Sincerely,

The authors

RESPONSES TO THE REVIEWER

Reviewer: Ai-Hsien Li

1. The authors should explain the reasons of some contradictory data including:

   a. Why the Bp increased in controlled group (Tab. 2)?

   Reply: The authors truly acknowledge the importance of the reviewer’s concern. The authors believe that anxiety yielded from the waiting time (60 minutes) until the end of data
collection procedures may have produced some degree of distress that may have contributed to the augmentation observed. Acutely, stress episodes have been shown to increase blood pressure by increasing cardiac output and heart rate but without affecting peripheral resistance (Zimmerman & Frohlich, 1990). In addition, even moderate stress has been found to increase levels of catecholamines, cortisol, vasopressin, endorphins and aldosterone, which may in part explain the increase in blood pressure. This may not have occurred in the experimental session (90% AT) due to the protective effect of exercise in situations of acute stress, as observed by MacDonald et al. (2001). Given that our work did not include assessments on stress mediators in its original design, the authors felt (and still fell) compelled not to draw attention to this phenomena in the text, therefore avoiding drifting attention from the major results of the paper, as is the effect of ACE genotypes on post-exercise NO release and BP response. This information was included in the chapter discussion (P.16).

b. Why the NO2 increase in control group (DD group) in Tab. 3, yet also presents with a BP increase (Tab. 2)?

Reply: Thank you for the opportunity to comment on that. Due to the fact that this variable (blood pressure) is regulated by several mechanisms (humoral, endothelial and neural), we can infer that the increase in blood pressure among DD genotype may be due to overlap of complementary input signals, with a probable prevalence of humoral and neural mechanisms in blood pressure control. Moreover, one should remember that the variation on salivary nitric oxide levels remained non-significant (p>0.05, table 3 and Figure 1). Studies (Busjhan et al., 2008; Jalil et al., 2002; Todd et al., 1995) have reported that individuals carrying the DD genotype have higher levels and activity of the angiotensin converting enzyme (ACE), which therefore could result in a greater increase in blood pressure by increasing the conversion of angiotensin I to II, causing vasoconstriction and also to increase water and sodium reabsorption by the kidneys, increasing blood volume and blood pressure. This information was included in the chapter discussion (P.16).
2. In this study only enrolling female gender, it will make use doubt the role of gender regarding the post-exercise hypotension. The authors have discuss the differences between this study and other previous ones, but more comprehensive hypothesis could be provided.

**Reply:** As an experimental control, only women aged 60 years or older were enrolled in this analysis so to avoid biases related to gender. For instance, Charkoudian et al. (2001) indicate that women with lower estrogen levels show higher values of diastolic and mean arterial pressure. In addition, estrogen-based replacement therapy improves endothelial function and decreases the activity of angiotensin converting enzyme (Higashi et al., 2001). In this sense, the authors understand that the present work poses a contribution by investigating specific age stratum and gender, and therefore controlling for possible hormone-related confounding variables in this scenario. This information was added to Methods.

3. The conclusion should emphasize the implication could only be applied to elderly female groups (for the same reason as 2.)

**Reply:** The authors comply with the reviewer’s observation. As requested, the conclusion of the study now emphasizes that these results can be applied to the elderly segment only. Plase, see below.

“*Therefore, the ACE genotype seems to have a role in the NO release and BP responses during post-exercise recovery in elderly women. Any extrapolation of these results to other gender or age strata requires caution.*” . (Conclusion, paragraph 3, page 17, lines 1 and 2).

4. The authors use the term “cardio-protective”, which might be a non-specific one and should be defined much more clearly. Otherwise, they should use “post-exertional hypotensive”..?

**Reply:** The authors once again comply with the reviewer’s observation. This expression (cardio protective) was replaced by the following sentence:
“However, both groups had a protective effect of aerobic exercise on preventing the increase of DBP and MAP during post-exercise period.” (Conclusion, paragraph 1, page 17, lines 2, 3 and 4).

5. Spelling error: “Matherial and method” should be “material and method”

Reply: This misspelling has been corrected as requested by the reviewer.

Reviewer: Paul Chan

However, there are many typographical errors that required careful revision. And I suggest that the paper should be review extensively before it is submitted again. For example:

P3 Abstract L4 nitric oxide should be small letters

P5 L3 bradikinin should be bradykinin

P10 L8, instrument should provide city and country.

P13 L3

P15 L1

P20 references 9, letters

P25 ref 41

p26 ref 43 no footstops is necessary

P28 table 1 glycaemia should be glycemia if this is an American style journal
footnotes L2 should be diastolic

P29 table 2 also letters

P30 table 3 L2 separated, missed a t

Also, for an original paper, the total number of references of 50 are too many.

Reply: Thanks a lot for helping us improve our manuscript. All requests were accepted and corrected.

Reviewer: Jyh-Ming Jimmy Juang

1. Why does this study choose women only?

Reply: Thanks for asking. Please, refer to the answer to query #2 provided for reviewer 1.

2. Please clarify or show all kinds of the anti-hypertension agents in all groups because many medicine may affect the NO levels.

Reply: Thank you for the opportunity to clarify this. The subjects of this sample reported the use of only two drugs, both diuretics (hydrochlorothiazide and indapamide), and none of these seem to have a direct effect on the release of nitric oxide. This information was added to Methods.

References


