Reviewer’s report


Version: 1 Date: 27 Jul 2019

Reviewer: Karl Neff

Reviewer's report:

Thank you for this interesting study comparing the results of CST and ITT between a group of athletes (ATL) and a sedentary control group (NPAC) matched for BMI and age (but not for fat mass or lean muscle mass).

The results show that there are differential responses within multiple pituitary axes. These data are clear and well-presented. However, they are not novel. The effect of exercise on pituitary/hypothalamic function is well documented, and while the authors data contribute to consolidation of this evidence base, they do not really offer any new insights.

I appreciate that the use of paired CST and IST allows for some distinction between adrenal and pituitary function in the ATL group, and this is something that could be developed to enhance our understanding of the HPA axis in the ATL cohort. However, we have known for many years that HPA responsiveness is enhanced by exercise. The element that you can really contribute to the evidence base is that the basis for this effect seems to be pituitary or hypothalamic rather than adrenal. This is not a novel concept, but your data do aid our understanding of this effect.

The biggest problem for your paper is that you claim to demonstrate evidence for a hormonal conditioning process. You do not. The data you present show that responses to ITT differ between ATL and NPAC participants at one moment in time. This could be due to differences in any number of confounding variables such as muscle mass (fat mass is clearly different between groups despite comparable weights and BMIs, inferring significant differences in muscle mass), diet or sleep. The ATL group may eat or sleep very differently to the NPAC group. How can we say it is the exercise or training of the ATL group that produce the proposed pituitary effect, and not simply changes in diet or sleep hygiene?
So while we can say there is a difference between groups, we cannot say for sure why this difference occurs. Even if we assume there is a difference that is due to training or exercise, to prove that there is pituitary adaptation, a persistent effect would need to be demonstrated. To do this, you would need to recruit a sedentary group, put them on an exercise programme for a period of at least a few weeks, and then allow them to become sedentary again, while testing them with ITT and CST at each phase. This is a large undertaking, and now not possible in your study. By design, the ATL group exercise frequently. How can we be sure that the ITT differences seen are not due to recent exercise (rather than a chronic adaptation)? There are no longitudinal data in your paper. We cannot say based on the data presented that there is a persistent pituitary response to exercise. Therefore the proposal that there is evidence for a pituitary 'adaptation' is fundamentally flawed.

I think you have some good data, but the conclusions drawn are not supported by the data presented. Therefore, I cannot recommend publication of this paper in its current form. I would recommend redrafting your paper to focus on the evidence that the hormonal changes seen are due to a pituitary or hypothalamic effect, rather than a primary adrenal effect. Again, this is expected, but your paper does offer some confirmatory data that may be suitable for publication.

I hope the above is useful. Thank you again for your paper.

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.

No

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

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal