Author's response to reviews

Title: Does continuous endurance exercise in water elicit a higher release of ANP and a higher plasma concentration of FFAs in pre-obese and obese men than high intensity intermittent endurance exercise? - Study protocol for a randomized controlled trial

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Author's response to reviews:

Dear Editor

Does continuous endurance exercise in water elicit a higher release of ANP and a higher plasma concentration of FFAs in pre-obese and obese men than high intensity intermittent endurance exercise? – Study protocol for a randomized controlled trial

We thank you for your e-mail from July 29, 2013.

Find below the answers to the questions raised by the handling editor, the editorial office and the reviewer.

All changes are marked in red in the revised study protocol.

We hope the revised protocol will be suitable for publication in ‘TRIALS’. 
Handling editor's comments:

"First, the protocol is missing a clear, step-by-step description of how randomization will be implemented in such a fashion as to ensure allocation concealment. It is also missing a statistical analysis plan.

Answer: We agree with the handling editor and adapted the randomization section. A statistical analysis plan is also inserted.

The two major concerns are the language and the sample size calculation.

Answer: We agree with the handling editor. We had the manuscript edited by a native speaker and added a sample size calculation using power analysis.

The paper needs to be edited by a native English language speaker. With respect to the sample size calculation, to calculate sample size for a crossover trial, one needs either the within patient standard deviation or the standard deviation for the difference between the two measures. It is unclear which the authors are using and where these data are obtained from. Certainly "An n of fourteen results from the calculated effect sizes and pooled scatters" is not at all clear."

Answer: We agree with the handling editor and made the necessary adaptations. For the power analysis, we inserted 'Our assumptions for the power calculation were mainly based on the results of Fenzel et al. [18] who recently reported an increase of ANP from 29.8±3.4 pmol/l to 82.5±8.3 pmol/l. Assuming an increase from 35 to 55 with a SD of 10 we would need 8 patients in each group for achieving a power of 90% on the 1% significance level (two sided test). With an assumed drop out of 2 in each group, we need 20 persons in total'.

Editorial requests:

1) Please ensure the title conforms to journal style for study protocol articles. The title should follow the format? ___________: study protocol for a randomized controlled trial.

Answer: We agree with the handling editor and adapted the title accordingly

2) Please remove the results section; this is not needed for a protocol article.

Answer: We agree with the handling editor and removed the results section.
Reviewer's report

Title: Does continuous endurance exercise in water elicit a higher release of ANP and a higher plasma concentration of FFAs in pre-obese and obese men than high intensity intermittent endurance exercise? - A pilot study

Version: 1 Date: 18 July 2013

Reviewer: Max LAFONTAN

Reviewer's report:

The design: The proposed study seems convenient to adequately test the hypothesis raised by the applicants.

The proposed rationale sounds. The comparison between endurance exercise and high intensity intermittent endurance exercise in water is original. It could be tolerated more easily by the obese persons. Plasma levels of ANP are known to be increased during water immersion (at rest but also during exercise).

The protocol possesses an important clinical interest. The results could be useful to select the most adapted protocol of physical exercise optimizing lipid mobilization/utilization in pre-obese and even obese patients.

Major Compulsory Revisions

The background is well covered.

1) Probably, after submission of the proposal two recent studies have also revealed an impact of ANP on brown/beige fat and human skeletal muscle and a review was published (1-3). Particularly, the impact on the oxidative capacity of human skeletal muscle is of interest for the authors. A comment will be useful in the background chapter.

Answer: We agree with the expert reviewer and included the suggested comments in the background chapter.

2) It has been proposed that the increase in fat mass could lead to an enhanced expression of NPR-C in fat cells that would diminish the local actions of ANP on fat cells and also lead to decreased plasma ANP levels. Any comment? Obese and overweight subjects have been described to exhibit low plasma NP levels. Any comment?
Answer: We agree with the expert reviewer and included the suggested comments in the background chapter.

3) Some important details are missing concerning the characteristics of the work load and the practical organization of the exercise sessions. Are they chosen according to the anaerobic threshold of each patient? What is the separation between the exercise sessions?
Answer: We agree with the expert reviewer and made the suggested corrections.

4) p.8: Some details are missing concerning the moment of the day selected to perform the exercise period. It is an important point to clarify. What is the rationale for a selection of a 6-h fast? An overnight fasting period will be a little bit longer and could be followed by exercise in the morning. A standardized diet two days before will be better.
Answer: We agree with the expert reviewer and made the suggested corrections.

5) p.7: The BMI range >25.0 and <34.9 will provide a mix of obese an overweight will bring heterogeneity. Why not a narrower range with obese only >30.0 and <34.9? Any comment on this point?
Answer: We agree with the expert reviewer and changed the BMI range accordingly

Minor Essential Revisions
5) p.7: The BMI range >25.0 and <34.9 will provide a mix of obese an overweight will bring heterogeneity. Why not a narrower range with obese only >30.0 and <34.9? Any comment on this point?
Answer: We agree with the expert reviewer. This relevant question shall be addressed in a separate paper.

2) p.6-7: OK for inclusion and exclusion criteria (see comments on BMI)
Answer: We agree with the expert reviewer and adapted the inclusion and exclusion criteria.

3) p.8: outcomes: for primary outcomes: BNP is known to possess lipolytic effects. It could be useful to determine both ANP and BNP. Secondary outcomes: Glycerol is a better index for lipolysis than free fatty acids (which are partly used during exercise).
Answer: We agree with the expert reviewer and changed the manuscript accordingly
Fourteen participants seem sufficient. The applicants mention ten to fourteen in the Abstract. Why? Detailed information's are provided concerning safety, duties of the investigator, evaluation of risks-benefit ratio, quality control and quality assurance.

Answer: We agree with the expert reviewer and changed the manuscript accordingly

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
'I declare that I have no competing interests'