Reviewer's report

Title: Exploring mechanisms of fatigue during repeated exercise and the dose dependent effects of carbohydrate and protein ingestion: a repeated measures controlled trial

Version: 1  Date: 28 November 2013

Reviewer: Lewis James

Reviewer's report:

Major Compulsory Revisions

Generally the manuscript was interesting and describes two studies that should be of interest to readers with an interest in sport and exercise science/nutrition. There is already a substantial amount of literature published on this specific topic (i.e. many studies documenting the effects of different carbohydrate/protein amounts, type and timing on muscle glycogen resynthesis or performance) and I think it would be worth further clarifying what makes the described studies novel.

There are numerous spelling, punctuation and grammar errors throughout the manuscript and these should be corrected and the manuscript thoroughly proof read prior to subsequent submission. I have not listed all of these as they are too numerous, but one consistent error throughout the manuscript is the authors’ continual switch between future and past tense, at times even within the same sentence.

Do the authors really feel they can assess the dose response effects of carbohydrate ingestion on exercise capacity adequately with their study design? I feel the study design is adequate to examine mechanisms of fatigue, but the order effect and assumptions/expectations that are introduced by the study design means that capacity cannot truly be measured. I.e. by using this design you are telling the subjects they will exercise longer on the high carbohydrate treatment. That said, the data you have presented for phase 1 suggests this is not the case. Did all subjects exercise longer in the second trial than the first? It would appear from the mean (SD) data that this might not be the case.

It might be useful to the reader for you to state what the practical relevance of this study is. I.e. in what situation might someone exercise to fatigue (maximally) twice within 4 hours? Also, is it not likely that in practice athletes or occupational exercisers would have a substantial meal between exercise sessions? I understand the point of the experiments is to examine mechanisms of fatigue, but there are not many situations under which this exercise scenario might occur, which questions whether it is worth looking at mechanisms of fatigue in the current study design.

Does the study design truly explore whether a dose-response relationship exists? You only have two levels of carbohydrate intake (0.3 g/kg/h and 1.2 g/kg/h). It
would have made more sense, to me at least, if phase 1 had involved at least three levels of carbohydrate intake to establish the dose-response relationship (e.g. 0.4 g/kg/h, 0.8 g/kg/h and 1.2 g/kg/h) and this would then also be consistent with phase 2.

I liked the section related to the use of exercise capacity and completely agree with the authors. I would add, in many settings lots of athletes actually undertake exercise that is very similar to exercise capacity testing. For example pace is often set by the faster runners/ cyclists etc. with the majority of athletes attempting to hold onto the pace set for as long as possible before slowing their pace and dropping off the back of a group/ athlete.

Line 91. Please clarify why you chose this protein fraction.

Line 98. Why sucrose and not glucose?

Line 159-162. Please include more information here. What was analysed and by whom?

Line 229. It is not clear here whether all subjects do all trials or whether 8 do phase 1 and 8 do phase 2. Please clarify.

Line 254. Why is there an SD for how long subjects will abstain from caffeine?

Line 294. Venous blood sample?

Line 292-294. This section needs additional information. How many times will they be permitted to do this? Does the 2 minutes count in their capacity score?

Line 327. How will expired gas be collected at the point of fatigue. More information needed here. If they’ve had 2 min walking, this gas sample may not capture steady state conditions.

Line 414. You stated earlier that the first morning urine sample will be collected, but here you say 30 min pre-exercise. Will both be collected or are these the same sample?

Line 491. It would be good to know what metabolites were going to be measured.

Line 588-591. Why do the scales have inconsistent anchors? The top of the scale is termed “extremely” for GI comfort and “very very” for fullness and thirst. For me, “extreme” is more than “very very” and thus the scales have different end points.

Table 1. Are the energy density values correct here? I make the energy density of the sucrose-protein solution 514 kcal/ L given the additional lactose and fat contained in the protein supplement. Why not adjust the amount of sucrose/ protein added to the drinks to match energy density.

Discretional revisions

Line 233. Possibly a little pedantic, but are you sure you will measure a true max
and not just peak? It is unlikely all subjects will plateau.

Line 272. Possibly a little pedantic again, but this section is titled “environmental control”, but you didn’t situate subjects in a controlled environment. You just measured the conditions of the environment they were in. Please amend.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**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'