Author's response to reviews

Title: Effects of whole grain rye crisp bread for breakfast on appetite and energy intake in a subsequent meal: two randomized controlled trails with different amounts of test foods and breakfast energy content

Authors:

Tina Forsberg (tifo0001@stud.slu.se)
Per Åman (per.aman@slu.se)
Rikard Landberg (rikard.landberg@slu.se)

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Author's response to reviews: see over
Dear Editor,

Please find attached the revised version of our paper entitled “Effects of whole grain rye crisp bread for breakfast on appetite and energy intake in a subsequent meal: two randomized controlled trials with different amounts of test foods and breakfast energy content” and the comments /changes suggested by the reviewers.

Let us know if further changes are needed.

Best regards,
Rikard Landberg

Reviewer's report
Title: Effects of whole grain rye crisp bread for breakfast on appetite and energy intake in a subsequent meal: two randomized controlled trials with different amounts of test foods and breakfast energy content
Version: 2 Date: 17 December 2013
Reviewer: Mette Kristensen

Reviewer's report:

Reviewer comments:
This paper covers the findings from two small appetite studies on the effect of rye crisp bread.

A major concern is that it is unclear why two separate studies were conducted? Was there an a priori hypothesis on the effect of meal size? It seems that a rationale for the composition of the test meals where both proportion of crisp bread and caloric content is changed at the same time making it difficult to conclude on the effects of either of them, is missing. Also, why was a comparator not a white wheat crisp bread not also included?

To choose a suitable amount of crisp bread to study was not easy, since no previous studies had been conducted on crisp bread regarding satiety. The basis for the selected amount in the first study was to obtain a similar rye fiber intake as used in the studies Isaksson et al. (with porridge and soft bread).

To be able to evaluate the magnitude of the effect of crisp bread in relation to other rye products found in previous studies, we selected to use the same control as in these studies, soft wheat bread. But we are aware of the difficulties in comparing across studies.

Testing rye crisp bread against a refined wheat crisp bread control would be useful when evaluating the effect of rye or process effects per se. However, the aim with the present study was rather to evaluate if rye crisp bread showed beneficial effects comparable to other rye products. The best would have been to include refined wheat crisp bread as well, but we did not have the possibility to include three periods at the time of the studies.
The results from the first study led us to the conclusion that the subject were provided too much energy and volume to make differences easy to detect (after 4 h subjects were still full from the refined products). We therefore reduced the total energy intake and also the amount of non-cereal calories. In this case, we got a clearer and consistent response in the second study. In the second study both proportion of crisp bread and caloric contents were changed simultaneously and we agree that both factors probably play a role. However, this was not a factorial experiment and the aim was rather to obtain conditions where we have stable and clear responses. These conditions can be used in future studies to dissect the underlying mechanisms for the observed effects. Such studies have now been conducted in our group and results are currently under evaluation.

We have made the following clarifications in the manuscript in response to the raised criticism above.

Line 92-97, page 5:
“The aim of the present study was to investigate short term effects on satiety, hunger and desire to eat as well as energy intake in a subsequent meal after a normal breakfast with iso-caloric rye crisp bread (RB) or refined wheat bread (WB). Because there is no common practice regarding amounts used in pre-load studies [4], we evaluated the effects in two separate randomized controlled meal studies where two different amounts of test products and breakfast energy contents were tested.

Line 275-279, page 13:
“The amount of breakfast product and the total energy intake was reduced in study two, in order to investigate whether more consistent effects on appetite and subsequent meal energy intake could be obtained at a somewhat lower intake of product and lower total energy intake. The difference between treatments in study two was similar in magnitude (20-28%) as in study one, but more consistent as a statistically significant difference in self-rated satiety was also found.”

Introduction:
The introduction is too long. It should be focused on the area of rye (whole grain) foods and appetite rather than longer term effects. Ex lines 76-83 covers longer-term studies and should be removed as well as lines 66-68 on hunger and weight regulation. Also, lines 85-91 could be shortened.

We fully agree that the introduction got too long. It has now been shortened. For example, we removed the following section:

“In epidemiological studies, a high intake of whole grain foods have been consistently associated with lower BMI, lower abdominal adiposity and a reduced risk for obesity compared to low or no whole grain intake [13, 14]. Partly, these beneficial effects may also explain the consistent reduction in risk of developing chronic disease such as type 2 diabetes, coronary heart disease and colorectal cancer among people who consume high amounts of whole grain [15-19]. However, results from the limited number of randomized controlled trails reported up to date,
have not shown any clear effects of whole grain foods on weight, but 2 out of 3 studies showed small, but statistically significant effects on body fat [13].”

L86: Abbreviate VAS the first time
Thank you, now corrected.

The aim of the study should be described in the end of the introduction, and not both here and in the first paragraph of the method section – please combine.

We agree and now combined the description in the method section with the aim (line 92-97):

“The aim of the present study was to investigate short term effects on satiety, hunger and desire to eat as well as energy intake in a subsequent meal after a normal breakfast with iso-caloric rye crisp bread (RB) or refined wheat bread (WB). Because there is no common practice regarding amounts used in pre-load studies [4], we evaluated the effects in two separate randomized controlled meal studies where two different amounts of test products and breakfast energy contents were tested.”

The following section was removed from the materials and methods:

“Two randomized controlled meal studies were conducted to evaluate the effects of isocaloric whole grain rye crisp bred (RB) versus refined wheat bread (WB) as part of a normal breakfast on appetite and energy intake in a subsequent meal.”

Methods:
Please describe the overall design before detailed info on VAS (L138-144). This should be described later under a separate point including the information on the validation.

Thank you for the suggestion. We agree and therefore we made a new subsection called “appetite ratings and energy intake after ad libitum lunch” after the “Study design and subject” section. (see material and method section)

L111: please specify who were blinded? participants, investigators, statisticians, others?
We have now clarified:

Thank you for this remark. Actually, strictly speaking the study was not blinded at all, since the investigator who served breakfasts also was involved in the statistical analysis and therefore may have remembered the treatment coding (A or B treatment). We have therefore removed “Single-blinded”.

L121: seems strange that a wish to become pregnant is relevant in a study of 1-2 weeks?
We agree, but this is according to our standard protocol for human intervention studies in “normal healthy populations” and we do not want to include anyone who would like to become
pregnant during the study. In this case it could have been omitted due to the short duration of the study, but it was not and therefore it should be reported.

L122: Delete sentence on age and just add the range of age allowed under inclusion criteria. Was there a BMI range as a inclusion criteria? Was menopausal status and cycle taken into account?
We kept the age sentence, since we find it important and because it was one of the inclusion criteria. Yes, BMI was included. No menopausal status and cycle was not taken into account. We only measure the criteria that were set up.

We added to Line 109, page 6: “BMI < 18 or >30”

L124: Was water allowed during fasting? Was it limited / fixed?
Thank you for making this remark. We have now added to line 125-126, page 7: “During fasting subjects were asked to refrain from water intake at least 2 hours before the study.”

L136: Seems like weight, height and birthdate is recorded twice, both before and after a meal?
Thank you for the remark. Now changed by deleting this at the second place and by changing the sentence at line 126-131, page 7 to:
“Upon arrival, participants were weighted (with 0.01 kg precision), height was measured (0.5 cm precision) and they were asked about their date of birth, last meal and drink. Furthermore, participants were provided with a hand-held computer, model z22 (Palm Inc, Sunnyvale, USA) and instructed on how to use the electronic VAS to score their feelings of hunger, fullness and desire to eat. Participants were seated together at round tables in two separate rooms according to treatment.

L157: unclear what complete blinding refers to?
Method for height and weight should be described in more detail and apparatus noted.
We have now written the precision for weight and height measurements. We will not provide information regarding manufacturer of the scale and tape used for length measurement, since we assume that these devices are basic equipment for this kind of studies with low likelihood of giving variable results. We normally do not state the brand of test tubes in laboratory research experiments.

L165; what is table spread?
Sorry, a Swedish word… We now changed this to “margarine”.

L179-180: Unclear whether the pickle and beetroot is served in fixed amounts?
Unclear what measures were taken to standardize the amount of frying oil? What is the energy density and composition of the dish? Was the amount of water fixed?
Thank you for this remark. We have now clarified by adding the following information:
“….that had been commercially manufactured and then fried in 5 g of rape seed oil per 1000 g before serving. All participants were served a plate with 600 g of ‘Pyttipanna’ (709 kJ/100g) and a glass with 90 g of pickled beetroot (200 kJ/100g), a glass of water (200 mL) and an empty plate.”

Information about the pickled beetroot was already stated (90g).

L192: How was AUC calculated? All above zero or not? With the trapezoidal method?

Yes trapezoid rule was used. Now added to line 185-186, page 9:
“AUCs were calculated using the trapezoidal rule.”

Unclear what the reviewer mean with “all above zero”? The VAS scale does not contain numbers below zero and hence there could be no values below 0 for AUC. We also did not encounter any 0 values in our dataset so it was not a problem to deal with.

L194: why was sex not included in the model? Was baseline included as a covariate? Sex was not included since the number of men was too few to make such adjustment appropriate. We made analysis with base-line values included as a covariate (not shown), but the results were similar, therefore we preferred to present a more simple model.

Moreover, we find it a bit risky to include the base-line value, since measurement at this time point is probably subjected to larger measurement errors than the other measurement time points due to the fact that this value will be placed at the end of the scale under a situation when the subject is considerably more hungry/less full than comparing to the other data points. The impact of such a differential measurement error may cause over all bias in any direction.

Results:
Generally, there is no need to apply the term significant / significantly as the p-value indicate level of significance and only differences which are in fact significant should be referred to as differences.

This is a matter of taste, but we changed according suggestion in order to save some words.

The term “overall” is used a few times, however it is clear what it refers to. Is it a reference to the repeated measures analysis?
We have now removed the term “overall” since it is not needed and may only confuse the reader.

L259: A reference to fig 2H is missing.
Thank you. This has now been added at line 251, page 12. (Figure 2H).

Discussion:
L 280-282: What is the importance of this statement?
We have deleted this statement, since the practical implication was small and we were asked to shorten the discussion (comment by reviewer 2).

L289: Here it is specified that the participants were not blinded highlighting the importance of specifying blinding under the methods.
We agree, but we have now removed the sentence in M&M saying that they were blinded.

L294-300: The macronutrient composition of the meals differ between study 1 and 2, which may also affect appetite.
That is a good comment. We have therefor now included this possibility by adding the following sentence (line 288-289, page 14):
“However, the macronutrient composition differed slightly between our two studies and that could also have affected the results.”

L342-346: The viscosity of the luminal content may be as high for RB as for porridge, as the author also states. However, the authors contradict themselves when stating that microstructure does not matter, as it does seem to affect immediate satiety (t=30 min) and thus can also be speculated to affect satiation. However, this may be related to differences in meal volume (incl. fluids) which is not discussed.

We agree that this was a bit confusing and perhaps even contradicting. We therefore changed the sentences in order to clarify that we believe the effect is due to features related to the fiber and bioactive compounds rather than differences in food product volume (line 326-331, page 15-16):
“We did not assess the mechanisms underlying the beneficial effects of replacing WB for RB in the present study. However, it is interesting that RB, which has a smaller volume and different microstructure than soft bread or porridge resulted in similar effects on self-reported appetite ratings and reduction in energy intake [15-18, 20, 31]. This suggests that features of dietary fibre and or bioactive compounds of rye may be more important for the short-term effect (≤ 4 h) on self-rated appetite and energy intake than for example test product volume.”

L353-357. These references to phenolics seem highly speculative, please revise.
The two references provided have found effects on appetite and weight attributed to benzoxazinoids and correlations between phenolic acids and responses on postprandial glucose and insulin secretion, respectively. It is therefore not speculative in that sense, but we do not believe that the effect of these compounds would have the largest impact and we therefore rephrased the sentence slightly (line 338-340, page 16):
“The impact of bioactive compounds such as benzoxazinoids and phenolic acids on glycemic response appetite has been investigated recently, but needs to be studied further to reach a conclusion [18, 34].”
L362-363: Please refrain from concluding on long term effects based on these data. This is not appropriate.
We agree and have therefore omitted the last sentences from the conclusion (also from the abstract).

Table 2: I suggest the table is rearranged to ease the comparisons of treatments within study by having all study 1 product characteristics on the left and study 2 on the right, and RB up and WB below as it is already.
We think this is a matter of taste and our opinion is that it is easier to compare between studies when presenting the data as now. The current presentation is also more space efficient since no duplication of column titles is needed. If the editor does not insist, we rather keep the tables as they are.

Table 3: I suggest the same structure as for table 2.
See arguments above.

Figures: All figures are lacking error bars, also P values are lacking for some percentage changes (fig 2G+H)

Since all comparisons are made within individuals, it would be highly misleading to report error bars representing SD or SEM, since this will to a great extent reflect the (large!) variation between subjects. The error-bars will also graphically make it more difficult to easily get hold of the differences between the treatments. We therefore rather would like to keep it as it is now, which is similar to how this kind of data has been presented before in many publications.

Reviewer's report
Title: Effects of whole grain rye crisp bread for breakfast on appetite and energy intake in a subsequent meal: two randomized controlled trails with different amounts of test foods and breakfast energy content
Version: 2 Date: 9 January 2014
Reviewer: Arkadiusz Kozubek

Reviewer's report:
This is a first approach to determine the effect of whole grain rye crisp bread on appetite and energy content preformed on humans. The methods used are appropriate and well described that the replication of the work is possible. Data presented in this manuscript are convincing and well controlled. In general manuscript fullfill required standards of very good scientific articles. Both title and abstract reflect accurately the content of the article. The writing is good and acceptable.
Major Compulsory Revisions
- The chapter List of abbreviations is empty
Thank you for this remark. We have now added a list of abbreviations made.
- The description of methods used and mentioned in Table 1 as "Uppsala method" is missing. For replication of the work this is an important point. Thank you for this remark. We have now added the references for the different method.

Minor Essential Revisions
Discussion and Conclusions could be shortened by at least 25%
We have removed some parts from the discussion and also tried to reformulate some sentences to make them shorter. The discussion is now reduced to little less than four full pages, which we think is acceptable.

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