PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Cardiovascular disease risk marker responses to breaking up prolonged sedentary time in individuals with paraplegia: the Spinal Cord Injury Move More (SCIMM) randomised crossover laboratory trial protocol
AUTHORS	Withers, Thomas; Croft, Louise; Goosey-Tolfrey, Victoria L; Dunstan, David; Leicht, Christof; Bailey, Daniel

VERSION 1 – REVIEW

REVIEWER	Kathleen A. Martin Ginis University of British Columbia, Canada
REVIEW RETURNED	26-Feb-2018

GENERAL COMMENTS	This is a very interesting study that will address a very important question that has not yet been examined in people living with SCI. The results have tremendous practical implications and will potentially lay the foundation for intervention research. Given my expertise is in the psychological and behavioural areas of physical activity, my review focuses on these elements and some design aspects of the study. --will participants be stratified based on gender, lesion level and completeness? -why recruit only paras? --recruitment sources seem biased toward recruiting physically active individuals. Is this deliberate? -why exclude those doing >300 min/week? --the rationale for the physical activity protocol is presented in the sample size section. It needs to be presented earlier so readers know why this particular protocol is being used. --Feasibility measures are being collected during the experiment. However, it would be valuable to engage with people with SCI as the protocol is being designed, to ensure it is indeed practical and tolerable. It would be a shame to lose participants once the study begins, because of protocol elements that weren't discussed a priori with people with SCI in order to troubleshoot. --I don't understand why 'determinants' of sedentary behaviour (they are actually correlates not determinants until proven to be so) are being measured. Why would participants' social cognitions regarding sedentary behaviour be expected to differ between conditions? Or, are the authors hypothesizing that in the experimental condition, participants social cognitions regarding their ability to OVERCOME being sedentary might change? This needs to be clarified. Also, given the volume of criticism levelled at the TPB in recent years, I'd suggest sticking to the COM-B framework for this study.

	--It's stated the psych measures will be measured at baseline and the end of each protocol. I presume what the authors mean is immediately before and after each protocol (as opposed to at study baseline and then after the protocol). Please clarify; change in measures of affect in response to the two protocols could produce very interesting results and it will be important to do an immediate pre-protocol assessment. Also, refer to literature on when to measure mood/affect post-exercise so as not to miss the window for detecting changes. --I'm not clear on how Schwarzer's scale can be adapted to measure self-efficacy for sedentary behaviour. Again, do the authors mean self-efficacy to avoid, or break up sedentary behaviour? --with inclusion of psych measures, it will be important to control for social contact with the experimenters in the two conditions, and to ensure that the participant does the same activities at the two experimental sessions --can data collection staff be blinded? A personal request: I know my name often comes up in data bases as 'Ginis KAM' but my legal last name--the one that I put on journal articles (and it then gets changed by the data base people) is 'Martin Ginis'. Could you please cite me this way in the reference list. Thank you

REVIEWER	Ashraf S. Gorgey Hunter Holmes McGuire VA Medical Center, United States
REVIEW RETURNED	27-Feb-2018

GENERAL COMMENTS	Dear Authors, I read with interest your study entitled “Protocol for evaluating cardiovascular…..SCIMM Study”. In the current protocol, the authors testing an interesting hypothesis that interrupted sedimentary time by introducing 2 minutes of moderate intensity exercise will have favorable outcomes on cardio-metabolic health in persons with paraplegia. There are number of concerns that I have to list 1. It is really frustrating to read a manuscript where the authors do not cite important contribution in the field of spinal cord injury research. This is clear by lack of references that support the wealth of knowledge in the area of SCI and cardiovascular disease. The authors do not even list one study that addressed this important topic in the field of SCI. If you type in PubMed “spinal cord injury and cardiovascular comorbidities”, you will get 62 studies you did not cite any of these studies not even acknowledging other contribution. Best Match □ Cragg JJ et al. Cardiovascular disease and spinal cord injury: results from a national population health survey. Neurology. (2013) □ Gorgey AS et al. Effects of spinal cord injury on body composition and metabolic profile - part I. J Spinal Cord Med. (2014) 2. The feasibility of this approach is questionable for number of reasons, the study is only tested those with injury level below T7, no clear justification of why including those with T1-T7 and moreover, no alternative intervention prescribed for those with tetraplegia C1-C7 who currently represents 55% of the SCI population according to US statistics. 3. This is an independent field and it is called spinal cord injury medicine and not a field that you mixed with other population of physical disabilities, you must cite the work that has been done.

	There is no acknowledgment of previous work in body composition, metabolism, dietary habits. I don't understand what research message are we trying to share if we do not acknowledge previous work and use one reference (9-11) for everything in spinal cord medicine. 4. In the introduction paragraph, please refer to the work of Bauman and Spungen, 1994 and 2008; Nash et al. Gater et al and Gorgey et al. Speaking of glucose intolerance and insulin resistance (Duckworth et al. 1980; 1983; Bauman and Spungen, 1994 and 2008), dyslipidemia and lipemia stress test (Nash et al.), Obesity and body composition (Gater and Gorgey; Gorgey et al. 20014), for poor dietary habits (Groah et al; Gorgey et al.) 5. The introduction is very shallow and has no depth in it, you need to carefully introduce the problem to your audience and highlight that this problem is multi-factorial including decreased leisure time and physical activity and energy expenditure. Please see also "Buchholz AC et al. Greater daily leisure time physical activity is associated with lower chronic disease risk in adults with spinal cord injury. Appl Physiol Nutr Metab. 2009 Aug;34(4):640-7. 6. In line 60, you refereed to CVR risk marker but you did not refer to what markers you have selected or what is the rationale of selecting these markers, you have decided to measure systolic and diastolic blood pressure acutely but you did not tell us how is this likely to be translated to cardiovascular health parameters that can be of value to the SCI population. 7. why did you exclude paraplegia above T6, have you included complete/incomplete SCI, where is AIS classification? Mixing complete and incomplete is a serious flaw and you need to control for this, which is likely to increase your sample size and a factor that you have to consider when you do your power calculation. At least you have to stratify individuals based on their levels of physical activity, I would highly suggest using METs to ensure that your individuals were stratified in the correct group. 8. The study needs to have a physical activity questionnaire or you can better measure their VO2 peak, someone with a VO2 peak of 22 ml/kg/min will be completely different in his outcomes than someone with 12 ml/kg/min. I have realized that using a cross-over design may account for this problem, especially, if you are planning to use a within repeated measure analysis of variance similar to two-way ANOVA; however, I highly suggest introducing either a physical activity questionnaire or measuring VO2 peak or even both. The authors need to set clear criteria on how they are planning to handle this issue in their analysis. 9. Using a questionnaire to determine their level of injury and their AIS classification is another major problem. You need to have a physician or a physical therapist in the team who accurately determine their level of injury and their AIS classification 10. For body composition assessment using DXA, please refer to Spungen et al. 2004; Gorgey et al. 2012; Gorgey et al. 2015. 11. There are concerns about subjects' level of physical activity and completeness of your injury especially in regard to the acute nature of the study and your primary outcomes.

	12. Your primary and secondary outcomes need to be clearly defined and you have to provide clear rationale how these parameters are linked to cardio-metabolic heath in persons with SCI. 13. The use of RPE as a sole index for determine the intensity of exercise is questionable especially in persons with SCI. Replication of this study for persons with tetraplegia or those with T1-T6 may be difficult. 14. You need to provide a clear protocol about your intervention, by saying in line 125 gradually increasing, it is unclear by how much you need to be more specific. What is the cycling pattern 50 rpm, 60 rpm or what? 15. Line 133 “What is this”, look like communication between authors that were left 16. Why not performing oral glucose tolerance test or lipemia stress test since your entire study is dealing with acute injury. 17. Please provide a figure highlighting your timeline, it is very difficult to follow the way you are listing for all your events. 18. Why there are no figures highlighting plans of recruitment, data analysis or some of the outcomes that are likely to be measured in the study.

VERSION 1 – AUTHOR RESPONSE

Reviewers' Comments to Author:

Reviewer: 1
Reviewer Name: Kathleen A. Martin Ginis
Institution and Country: University of British Columbia, Canada Competing Interests: None declared.

This is a very interesting study that will address a very important question that has not yet been examined in people living with SCI. The results have tremendous practical implications and will potentially lay the foundation for intervention research.

Given my expertise is in the psychological and behavioural areas of physical activity, my review focuses on these elements and some design aspects of the study.

Response: we thank the reviewer for the kind thoughts on the interest and potential value of the findings of our study. We value the comments made below, especially those in regard to the psychological and behavioural areas.

--will participants be stratified based on gender, lesion level and completeness?

Response: The study is not powered to stratify based on gender, lesion level and completeness - this would require a much larger sample size and would pose a risk of not being able to complete the study due to challenges with respect to recruitment and access to the population. In addition, postprandial glucose responses do not appear to differ between paraplegics with complete versus incomplete lesions (Lines 56-58) and it may thus not be appropriate on this basis to stratify based on this factor. However, data for these variables will be collected and all statistical models will adjust for these covariates that may explain residual outcome variance (line 297). With regards to gender, if we recruit sufficient numbers of each gender then we may stratify on this basis and conduct exploratory analysis; however, this may be unlikely due to the higher prevalence of SCI in males. Individual responses for CVD risk marker outcomes will also be compared between the conditions to determine the number of participants who respond to the experimental protocols and this may give insight regarding responses based on individual differences (line 300). We have also aimed to make the sample more homogenous by only including individuals with lesions at T6 and below.

-why recruit only paras?

Response: We appreciate the difficulty in targeting a homogenous sample in terms of lesion level and completeness. However, we aimed to reduce the heterogeneity of the sample by assessing only paraplegics – this would ensure sympathetic innervation to major organs at the T5 level so that heart rate and catecholamine responses would be unaffected by injury and thus reduce the impact of innervation variations on the study outcomes (see lines 112-115). We plan to use the findings of this study, that examine the effects of breaking up sedentary time for this time in spinal cord injured individuals, to inform a future study in tetraplegic individuals.

--recruitment sources seem biased toward recruiting physically active individuals. Is this deliberate?

Response: the recruitment strategy is not biased toward physically active individuals and the recruitment methods has been revised to clarify this (lines 132-135).

-why exclude those doing >300 min/week?

Response: this threshold was selected as high levels of physical activity (60 min of MVPA per day) may offset the detrimental association of sedentary time with health outcomes as now explained on line 123. Individuals who could be considered as being highly active may thus be unlikely to respond to the intervention.

--the rationale for the physical activity protocol is presented in the sample size section. It needs to be presented earlier so readers know why this particular protocol is being used.

Response: the rationale for the physical activity protocol is now specified earlier in the methods on lines 195-198.

--Feasibility measures are being collected during the experiment. However, it would be valuable to engage with people with SCI as the protocol is being designed, to ensure it is indeed practical and tolerable. It would be a shame to lose participants once the study begins, because of protocol elements that weren't discussed a priori with people with SCI in order to troubleshoot.

Response: The study protocol was designed in collaboration with experts in the SCI field to maximise the feasibility of the study. People with SCI will be involved at the dissemination stage to ensure that the findings and reports are valuable to the target population. This is a valuable suggestion and based on this we will engage with people with SCI in the development of the next stage intervention study. Furthermore, we have had excellent compliance from the participants that have enrolled to the study so far.

--I don't understand why 'determinants' of sedentary behaviour (they are actually correlates not determinants until proven to be so) are being measured. Why would participants' social cognitions regarding sedentary behaviour be expected to differ between conditions? Or, are the authors hypothesizing that in the experimental condition, participants social cognitions regarding their ability to OVERCOME being sedentary might change? This needs to be clarified. Also, given the volume of criticism levelled at the TPB in recent years, I'd suggest sticking to the COM-B framework for this study.

Response: the term ‘determinant’ has now been corrected to ‘correlates’ as suggested on line 268. The reviewer’s interpretation in that we are “hypothesizing that in the experimental condition, participants’ social cognitions regarding their ability to OVERCOME being sedentary might change” (in addition to mood and wellbeing) is correct and this has now been clarified on lines 268-271.

--It's stated the psych measures will be measured at baseline and the end of each protocol. I presume what the authors mean is immediately before and after each protocol (as opposed to at study baseline

and then after the protocol). Please clarify; change in measures of affect in response to the two protocols could produce very interesting results and it will be important to do an immediate pre-protocol assessment. Also, refer to literature on when to measure mood/affect post-exercise so as not to miss the window for detecting changes.

Response: It has now been clarified on line 269 that these measures will be taken immediately before and after each experimental condition. We agree that affective responses to these conditions could produce interesting results and thank the reviewer for acknowledging this. We have now documented the time frame observed in previous studies in terms of mood and affect responses to exercise that demonstrate the appropriateness of the measurement timings in the current study (lines 279-281).

--I'm not clear on how Schwarzer's scale can be adapted to measure self-efficacy for sedentary behaviour. Again, do the authors mean self-efficacy to avoid, or break up sedentary behaviour?

Response: we have now clarified on line 276 that this scale has been adapted to measure self-efficacy to avoid long periods of sedentary time.

--with inclusion of psych measures, it will be important to control for social contact with the experimenters in the two conditions, and to ensure that the participant does the same activities at the two experimental sessions --can data collection staff be blinded?

Response: Although the staff present will be standardised between conditions, given a restriction with resources it is not possible to blind staff who are collecting the data as these same staff are required to ensure compliance with the experimental protocols. We acknowledge this is a potential limitation and will look to address this in future studies. Participants will be permitted to work on a laptop computer, read, talk, or watch DVDs during each condition and they will be asked to engage in the same activities during both conditions (line 206).

A personal request: I know my name often comes up in data bases as 'Ginis KAM' but my legal last name--the one that I put on journal articles (and it then gets changed by the data base people) is 'Martin Ginis'. Could you please cite me this way in the reference list. Thank you

Response: we have now amended our reference list so you are cited as Martin Ginis.

Reviewer: 2
Reviewer Name: Ashraf S. Gorgey
Institution and Country: Hunter Holmes McGuire VA Medical Center, United States Competing Interests: No COI to declare.

Dear Authors,
I read with interest your study entitled “Protocol for evaluating cardiovascular…..SCIMM Study”. In the current protocol, the authors testing an interesting hypothesis that interrupted sedimentary time by introducing 2 minutes of moderate intensity exercise will have favorable outcomes on cardio-metabolic health in persons with paraplegia. There are number of concerns that I have to list

Response: we thank the reviewer for highlighting our hypothesis as being interesting and appreciate the comprehensive review below that will help in strengthening our study and manuscript.

1. It is really frustrating to read a manuscript where the authors do not cite important contribution in the field of spinal cord injury research. This is clear by lack of references that support the wealth of knowledge in the area of SCI and cardiovascular disease. The authors do not even list one study that addressed this important topic in the field of SCI. If you type in PubMed “spinal cord injury and cardiovascular comorbidities”, you will get 62 studies you did not cite any of these studies not even acknowledging other contribution.

Best Match
- Cragg JJ et al. Cardiovascular disease and spinal cord injury: results from a national population health survey. Neurology. (2013)
- Gorgey AS et al. Effects of spinal cord injury on body composition and metabolic profile - part I. J Spinal Cord Med. (2014)

Response: We thank the reviewer for highlighting this issue and have now included discussion of research relating to SCI and cardiovascular disease in the introduction on lines 36-47 that makes reference to the following articles:

- Cragg, J.J., et al., Cardiovascular disease and spinal cord injury: results from a national population health survey. Neurology, 2013. 81(8): p. 723-8.
- Gorgey, A.S., et al., Effects of spinal cord injury on body composition and metabolic profile - part I. J Spinal Cord Med, 2014. 37(6): p. 693-702.
- Bauman, W.A. and A.M. Spungen, Disorders of carbohydrate and lipid metabolism in veterans with paraplegia or quadriplegia: A model of premature aging. Metabolism, 1994. 43(6): p. 749-756.

2. The feasibility of this approach is questionable for number of reasons, the study is only tested those with injury level below T7, no clear justification of why including those with T1-T7 and moreover, no alternative intervention prescribed for those with tetraplegia C1-C7 who currently represents 55% of the SCI population according to US statistics.

Response: we aimed to reduce the heterogeneity of the sample by assessing only paraplegics with injuries below T5 (we have now corrected from “below T6” to “below T5” in the methods on line 110 – this would ensure sympathetic innervation to major organs at the T5 level so that heart rate and catecholamine responses would be unaffected by injury and thus reduce the impact of innervation variations on the study outcomes (see lines 112-115). We plan to use the findings of this study, that examine the effects of breaking up sedentary time for this time in spinal cord injured individuals, to inform a future study in tetraplegic individuals.

3. This is an independent field and it is called spinal cord injury medicine and not a field that you mixed with other population of physical disabilities, you must cite the work that has been done. There is no acknowledgment of previous work in body composition, metabolism, dietary habits. I don’t understand what research message are we trying to share if we do not acknowledge previous work and use one reference (9-11) for everything in spinal cord medicine.

Response: We thank the reviewer for highlighting this issue and have now included discussion of research relating to body composition, metabolism, dietary habits in SCI in the introduction on lines 42-47, 53-64.

4. In the introduction paragraph, please refer to the work of Bauman and Spungen, 1994 and 2008; Nash et al. Gater et al and Gorgey et al. Speaking of glucose intolerance and insulin resistance (Duckworth et al. 1980; 1983; Bauman and Spungen, 1994 and 2008), dyslipidemia and lipemia stress test (Nash et al.), Obesity and body composition (Gater and Gorgey; Gorgey et al. 20014), for poor dietary habits (Groah et al; Gorgey et al.)

Response: we have now discussed the important work in relation to glucose tolerance (postprandial glucose), lipid profile, and body composition in SCI in the introduction in lines 42-47 and 53-64.

5. The introduction is very shallow and has no depth in it, you need to carefully introduce the problem to your audience and highlight that this problem is multi-factorial including decreased leisure time and physical activity and energy expenditure. Please see also “Buchholz AC et al. Greater daily leisure time physical activity is associated with lower chronic disease risk in adults with spinal cord injury. Appl Physiol Nutr Metab. 2009 Aug;34(4):640-7.

Response: This is a valuable comment from the reviewer and the introduction has been modified and discusses this multi-factorial problem. The Buchholz et al study has been discussed on line 73.

6. In line 60, you refereed to CVR risk marker but you did not refer to what markers you have selected or what is the rationale of selecting these markers, you have decided to measure systolic and diastolic blood pressure acutely but you did not tell us how is this likely to be translated to cardiovascular health parameters that can be of value to the SCI population.

Response: The CVD risk markers to be studied are now specified on lines 86-89 and the introduction rationalises the importance of these risk markers in terms of CVD risk and the adverse levels seen in SCI on lines 45-47 and 53-64. In addition to highlighting the adverse effects of these risk markers on CVD outcomes, we have also highlighted the potential importance of the study findings in this context on line 91.

7. why did you exclude paraplegia above T6, have you included complete/incomplete SCI, where is AIS classification? Mixing complete and incomplete is a serious flaw and you need to control for this, which is likely to increase your sample size and a factor that you have to consider when you do your power calculation. At least you have to stratify individuals based on their levels of physical activity, I would highly suggest using METs to ensure that your individuals were stratified in the correct group.

Response: We selected to exclude individuals with injuries at T5 and above as this would ensure sympathetic innervation to major organs at the T5 level so that heart rate and catecholamine responses would be unaffected by injury and thus reduce the impact of innervation variations on the study outcomes (see lines 112-115). Participants will be asked to provide medical records for injury level and AIS classification (line 120). Unfortunately, we do not have resources to access a physician or therapist to accurately determine these factors.

Both complete and incomplete SCI is being included based on evidence that this does not affect postprandial glucose or fasting lipids in paraplegic individuals (lines 56-60). It may thus not be appropriate to assume that there would be variable postprandial responses in this study based on completeness. However, the sample size calculations presented are conservative based on the nature of the protocol. Furthermore, the analysis will adjust for completeness as a potential covariate (line 297). Individuals responses for CVD risk marker outcomes will also be compared between the conditions to determine the number of participants who respond to the experimental protocols and this may give insight regarding responses based on individual differences (line 300-302).

The study is not powered to stratify based on physical activity levels - this would require a much larger sample size and would pose a risk of not being able to complete the study due to challenges with respect to recruitment and access to the population. Furthermore, self-report physical activity questionnaires are subject to large measurement error and criterion validity for physical activity questionnaires versus objective measures (accelerometry) is low (r=0.3), such as the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD); see van der Ploeg (2007) The Physical Activity Scale for Individuals with Physical Disabilities: Test-Retest Reliability and Comparison With an Accelerometer; J Phys Act Health. It may thus not be appropriate to stratify individuals based on self-report physical activity. However, we will consider this for future studies and will seek to include an objective measure of physical activity in future studies.

8. The study needs to have a physical activity questionnaire or you can better measure their VO2 peak, someone with a VO2 peak of 22 ml/kg/min will be completely different in his outcomes than someone with 12 ml/kg/min. I have realized that using a cross-over design may account for this problem, especially, if you are planning to use a within repeated measure analysis of variance similar to two-way ANOVA; however, I highly suggest introducing either a physical activity questionnaire or measuring VO2 peak or even both. The authors need to set clear criteria on how they are planning to handle this issue in their analysis.

Response: As the reviewer suggests, a strength of this study is the crossover design that will account for differences in physical activity and fitness level. We chose to determine exercise intensity using RPE based on RPE being acceptably valid in individuals with SCI to determine physical activity intensity (line 168). The RPE 6-20 is the only accepted reliable scale in persons with SCI and with good instructional information it is likely to be the best measure to date for exercise intensity. This use of RPE is also in line with related sedentary behaviour research (line 160). RPE is also suggested as a practical approach for health care professionals and scientists (lines 169-171).

Please also see response above regarding oxygen consumption and physical activity questionnaires. Lastly, we can confirm that our analysis approach will be similar to a within repeated measures ANOVA.

9. Using a questionnaire to determine their level of injury and their AIS classification is another major problem. You need to have a physician or a physical therapist in the team who accurately determine their level of injury and their AIS classification

Response: We appreciate that using self-report to determine level of injury and AIS classification is a limitation to the study design. Unfortunately, we do not have resources to access a physician or therapist to accurately determine these factors and will thus ask participants to provide medical records for injury level and AIS classification (line 120).

10. For body composition assessment using DXA, please refer to Spungen et al. 2004; Gorgey et al. 2012; Gorgey et al. 2015.

Response: We have now referred to the work of these researchers in relation to DXA assessment on lines 146-148.

11. There are concerns about subjects' level of physical activity and completeness of your injury especially in regard to the acute nature of the study and your primary outcomes.

Response: As described above, we appreciate that using self-report to determine level of injury and AIS classification is a limitation to the study design. Unfortunately, we do not have resources to access a physician or therapist to accurately determine these factors and will thus ask participants to provide medical records for injury level and AIS classification (line 120). Please also see explanation above regarding concerns regarding self-report physical activity measurement error.

12. Your primary and secondary outcomes need to be clearly defined and you have to provide clear rationale how these parameters are linked to cardio-metabolic heath in persons with SCI.

Response: The primary and secondary outcomes are stated on lines 86-89 and lines 253-258. The introduction rationalises the importance of these risk markers in terms of CVD risk and the adverse levels seen in SCI on lines 45-47 and 53-64.

13. The use of RPE as a sole index for determine the intensity of exercise is questionable especially in persons with SCI. Replication of this study for persons with tetraplegia or those with T1-T6 may be difficult.

Response: We chose to determine exercise intensity using RPE based on RPE being acceptably valid in individuals with SCI to determine physical activity intensity (line XX). This is also in line with related sedentary behaviour research (line 168). RPE is also suggested as a practical approach for health care professionals and scientists (lines 169-171). We will use the experiences and findings from this study to inform development of a future study with individuals who have higher injuries and we appreciate the methodology may need to be adapted to suit this population. However, this will be the first study to provide preliminary evidence regarding the effects of breaking up sedentary time in SCI, which we believe is an important first step in this field.

14. You need to provide a clear protocol about your intervention, by saying in line 125 gradually increasing, it is unclear by how much you need to be more specific. What is the cycling pattern 50 rpm, 60 rpm or what?

Response: Further detail regarding the preliminary exercise test has now been provided on lines 162-164. The cycling will be at approximately 70 rpm as indicated on line 161 and 189.

15. Line 133 “What is this”, look like communication between authors that were left

Response: This should have read “Figure 1 shows the experimental protocol” and it appears as though there was an error during the submission process which changed this text. It should now be displaying correctly on line 174.

16. Why not performing oral glucose tolerance test or lipemia stress test since your entire study is dealing with acute injury.

Response: A limitation of some previous research examining postprandial responses to breaking up sedentary time is the use of liquid meals. These are not reflective of mixed macronutrient meals that are consumed as part of normal dietary intake. Furthermore, the macronutrient composition of meals in this study was chosen as it is generally representative of UK guidelines for a balanced diet (Lines 221-223). We did not include an oral glucose tolerance test or lipaemia stress as part of preliminary measures for descriptive purposes as this would increase the burden to the participants and may result in lower recruitment rates and higher withdrawals.

17. Please provide a figure highlighting your timeline, it is very difficult to follow the way you are listing for all your events.

Response: The timeline for the study can be seen in Figure 1.

18. Why there are no figures highlighting plans of recruitment, data analysis or some of the outcomes that are likely to be measured in the study.

Response: Figure 2 shows the protocol for the experimental conditions including when outcomes are measured. Figure 1 shows the timeline for the study which has now replaced Table 1.

VERSION 2 – REVIEW

REVIEWER	Ashraf S. Gorgey Hunter Holmes McGuire VA Medical Center, USA
REVIEW RETURNED	16-Apr-2018

GENERAL COMMENTS	I would like to congratulate the authors for their hard work. The authors have carefully addressed all my concerns.

REVIEWER	KATHLEEN MARTIN GINIS UBC, CANADA
REVIEW RETURNED	28-Apr-2018

GENERAL COMMENTS	Again, I have reviewed this paper with a focus on the psychosocial elements. The authors have done a good job of addressing the issues I raised in the original submission. My only lingering concern

	is with regard to the timing of the measures which is currently indicated as "within 45 min of the last bout of activity". The timing of the measures of mood need to be standardized across participants, as there is an affective rebound effect that occurs after exercise. If the measurement is not standardized across participants, you may be measuring affect at different points in the rebound trajectory (i.e., some participants at lower points and some at higher points). It's not clear, as stated, if all participants will complete the mood measures at the same time point or simply at some time point within the 40 minute window. Again, this needs to be standardized. My advice would be to standardize administration of the mood measures at 20 minutes post-exercise and to then administer the remaining measures in a systematically rotated method such as a Williams Square design.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: KATHLEEN MARTIN GINIS

Institution and Country: UBC, CANADA

Competing Interests: NONE

Again, I have reviewed this paper with a focus on the psychosocial elements. The authors have done a good job of addressing the issues I raised in the original submission. My only lingering concern is with regard to the timing of the measures which is currently indicated as "within 45 min of the last bout of activity". The timing of the measures of mood need to be standardized across participants, as there is an affective rebound effect that occurs after exercise. If the measurement is not standardized across participants, you may be measuring affect at different points in the rebound trajectory (i.e., some participants at lower points and some at higher points). It's not clear, as stated, if all participants will complete the mood measures at the same time point or simply at some time point within the 40 minute window. Again, this needs to be standardized. My advice would be to standardize administration of the mood measures at 20 minutes post-exercise and to then administer the remaining measures in a systematically rotated method such as a Williams Square design.

Response: We would like to thank the reviewer for taking the time to review our manuscript and for this additional valuable suggestion. We have now revised lines 270-284 to clearly specify the exact timing that the completion of these questionnaires commences and the order in which they are completed. Although the mood questionnaire is not being completed first and the order of the questionnaires is fixed (we cannot change this as data collection has already begun), we anticipate that there will be minimal variation within participants with regards to the time taken to complete each questionnaire. We thus feel that this will enable valid between-condition comparisons. However, we will acknowledge this as a potential limitation when we report the findings of the study. We will follow the reviewer’s advice when planning future studies in this area.

Reviewer: 2

Reviewer Name: Ashraf S. Gorgey

Institution and Country: Hunter Holmes McGuire VA Medical Center, USA Competing Interests: None

I would like to congratulate the authors for their hard work. The authors have carefully addressed all my concerns.

Response: We would like to thank the reviewer for taking the time to review our manuscript and are pleased that all of the concerns have been addressed.