# Repetitive head impacts affect mediolateral postural sway entropy in the absence of vision following a competitive athletic season: preliminary findings

Brian Szekely, Sushma Alphonsa, Katelyn Grimes, Barry Munkasy, Thomas Buckley, Nicholas Murray

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1st editorial decision

27-Jul-2019

Ref.: Ms. No. JCTRes-D-19-00015
Repetitive head impacts affect mediolateral postural sway entropy following a competitive athletic season: preliminary findings
Journal of Clinical and Translational Research

Dear Dr Murray,

The editor in chief has now commented on your paper. You will see that he is advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript.Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the

reviewers to rapidly verify all changes made.

Your revision is due by Aug 26, 2019.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: GENERAL / MAJOR

* In the Relevance for Patients section of the abstract you propose that clinicians should undertake certain tests to assess the ramifications of RHI. The tests you conduct seem to have higher assessment resolution than what is commonly used. The key question is: does a standard clinician (or physician or physical therapist at a university) understand how you conducted your tests based on the text you provided? It would really help to explain the mechanics of the tests if the answer is "no." Along the same lines, it would be wise to provide the definition of sample entropy and its practical meaning (to enable readers to understand your results).
* Would it be possible to include more personalized details, such as showing individual results (per athlete) in both groups as well as providing a more elaborate demographics table (e.g., amount of minutes played). It would be interesting to see whether there is a possible correlation between minutes played (i.e., more probability of RHI) and ordinal variables (SampEn ML).
* In the Discussion it is posited that the results are consistent with what had been hypothesized. However, postural control changes in the ML direction were observed in both groups, meaning that these changes had nothing to do with RHI. Please explain how this is in line with what had been hypothesized. Accordingly, the title (i.e., the conclusion of the study) does not seem to be supported by the findings per se.
* Please limit the number of abbreviations. The paper is nice and short already; no real need to use excessive abbreviations, especially those used only incidentally throughout the paper.
* In your resubmission, please remove all information that could identify you or the affiliated institute to ensure complete blinding.

SPECIFIC / MINOR

* Abstract: Eyes closed should be abbreviated as (EC) at first mention. SRC is not written out in full at first mention.
* Introduction, 1st paragraph, last sentence: please reformulate the essence regarding which clinical assessments are used to reflect their improper application in the context of the physical changes induced by RHI. It is unclear what is meant by "…to aid the effects of RHI exposure."

\* Methods, section 2.1, Table 1: please perform statistical analysis on the demographics to show that there were no significant differences between the study cohorts. Do not forget to add the methodological description to section 2.4.
\* Section 2.3, second paragraph: please denote the abbreviation Ai consistently.

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Author's response

Response to Reviewers

Thank you for your time and effort in reviewing this article. Each comment is addressed below:

Reviewer #1: GENERAL / MAJOR
\* In the Relevance for Patients section of the abstract you propose that clinicians should undertake certain tests to assess the ramifications of RHI. The tests you conduct seem to have higher assessment resolution than what is commonly used. The key question is: does a standard clinician (or physician or physical therapist at a university) understand how you conducted your tests based on the text you provided? It would really help to explain the mechanics of the tests if the answer is "no." Along the same lines, it would be wise to provide the definition of sample entropy and its practical meaning (to enable readers to understand your results).

Thank you for your comment. The authors have amended the text to better explain the mechanics of the tests use, specifically sample entropy. Within the text I provided a mathematical definition for Sample entropy, "SampEn was calculated as the negative natural logarithm of Ai, divided by Bi, where AI was the number of similar vector lengths (m + 1) that were within the tolerance range (r) of all possible (m + 1) vectors and Bi was the total number of similar vector lengths at m that were within r at every possible vector length of m. I also have included a plausible clinical definition, as Sample entropy is still in the process of being established for clinical use. However, clinical articles on static postural control entropy have noted that the greater entropy value, the better the overall health is of the postural system (Donker et al., 2008; Pelykh, Klein, Bötzel, Kosutzka, & Ilmberger, 2015; Rigoldi et al., 2013).

\* Would it be possible to include more personalized details, such as showing individual results (per athlete) in both groups as well as providing a more elaborate demographics table (e.g., amount of minutes played). It would be interesting to see whether there is a possible correlation between minutes played (i.e., more probability of RHI) and ordinal variables (SampEn ML).

Thank you for your comment. We have included a figure (figure 1) that includes individual results per task at each pre- and post- season. However, we do not have access to the minutes played for these athletes at this time.

\* In the Discussion it is posited that the results are consistent with what had been hypothesized. However, postural control changes in the ML direction were observed in both groups, meaning that these changes had nothing to do with RHI. Please explain how this is in

line with what had been hypothesized. Accordingly, the title (i.e., the conclusion of the study) does not seem to be supported by the findings per se.

Thank you for noting this. The authors understand that there are no group differences within this paper. We would like to clarify that, the current study results are consistent for SampEn AP. However, in the ML direction we saw a three-way interaction- Group x Task x Time and also Group x Time for the best fit model. This was specifically driven by the group and task (see main effects in table 2). We reported this novel finding of the effect driven by RHI in the postseason (see figure 2) however only for EC which indicated the influence of RHI in the absence of vision. We have clarified this in our discussion and believe these are interesting results to acknowledge. We agree that the results of SampEn ML do not support our Rebuttal letter hypotheses. The opening paragraph in the discussion has been mended to address this, as well as the discussion to make clear that there were no differences between groups. Furthermore, we have changed the title to be more transparent and to highlight the effect of no vision in RHI.

* Please limit the number of abbreviations. The paper is nice and short already; no real need to use excessive abbreviations, especially those used only incidentally throughout the paper. Thank you for your comment. We have removed abbreviations as SRC (sport related concussion), DV (dependent variable), and COP (center of pressure), cumulative impact burden (CIB), MLA (mean linear acceleration) * In your resubmission, please remove all information that could identify you or the affiliated institute to ensure complete blinding.

Thank you for your comment. We have removed all the identifying information. Specifically in the Acknowledgments section.

SPECIFIC / MINOR

* Abstract: Eyes closed should be abbreviated as (EC) at first mention. SRC is not written out in full at first mention.

Thank you for this edit. We have amended the text to say 'sport related concussion.'

* Introduction, 1st paragraph, last sentence: please reformulate the essence regarding which clinical assessments are used to reflect their improper application in the context of the physical changes induced by RHI. It is unclear what is meant by "…to aid the effects of RHI exposure."

Thank you for your suggestion. The authors have amended the text to state which clinical assessments have been used to measure RHI previously.

* Methods, section 2.1, Table 1: please perform statistical analysis on the demographics to show that there were no significant differences between the study cohorts. Do not forget to add the methodological description to section 2.4.

Thank you for your comment. We have added that statistically analyzed the demographics data and have presented them in the table and section 2.4.

\* Section 2.3, second paragraph: please denote the abbreviation Ai consistently.

Thank you for your comment. The text has been mended to "Ai"

References for the response to reviewers
Donker, S. F., Ledebt, A., Roerdink, M., Savelsbergh, G. J. P., & Beek, P. J. (2008). Children with cerebral palsy exhibit greater and more regular postural sway than typically developing children. Experimental Brain Research. Experimentelle Hirnforschung. Experimentation Cerebrale, 184(3), 363–370.
Pelykh, O., Klein, A.-M., Bötzel, K., Kosutzka, Z., & Ilmberger, J. (2015). Dynamics of postural control in Parkinson's patients with and without symptoms of freezing of gait. Gait & Posture, 42(3), 246–250.
Rigoldi, C., Cimolin, V., Camerota, F., Celletti, C., Albertini, G., Mainardi, L., & Galli, M. (2013). Measuring regularity of human postural sway using approximate entropy and sample entropy in patients with Ehlers–Danlos syndrome hypermobility type. Research in Developmental Disabilities, 34(2), 840–846.
References added to the manuscript

Physionet.org. (2016). Index of physiotools sampen matlab 1.1-1. Retrieved August 5. 2019, from (https://www.physionet.org/physiotools/sampen/matlab/1.1-1/sampen.m).
R Core Team (2018) R: A Language and Environment for Statistical Computing. R Foundation
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2<sup>nd</sup> editorial decision

04-Sept-2019

Ref.: Ms. No. JCTRes-D-19-00015R1
Repetitive head impacts affect mediolateral postural sway entropy in the absence of vision following a competitive athletic season: preliminary findings
Journal of Clinical and Translational Research

Dear Dr Murray,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

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Your revision is due by Oct 04, 2019.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #2: The submitted manuscript presents potentially interesting preliminary data however, the authors need to be very careful about over interpreting the results. Please see comments below:

1. Hypothesis: Is this your correct hypothesis. That you expected to find no differences in postural sample entropy between the RHI and control group? This seems to be more of a null hypothesis.

2. There is mention of the EC ML SampEn increasing for both groups, however this is not the case. The control groups EC SampEn remained fairly consistent as observed in fig 2. I agree the RHI group does have some differences and this is where the interesting preliminary data is but be careful in your interpretation not to speak to points that your data do not support. the discussion requires revision of points directed at the interpretation of results based on this error in reporting,

3. In the first part of the discussion you have the sentence "Specifically, we compared athletes who had no prior diagnosis of sport related concussion to a group of non-RHI athletes (CON) with no diagnosed sport-related concussion". Should that first group have had RHI over the season but no history of concussion diagnosis?

4. What are the details on the RHIs? How many did each person have in the season? Were there sig differences within that group? Did they have any in previous seasons?

5. Could the lack of significance be due to under powering? You based your power analysis on previous research however, perhaps those data used need to be reassessed based on the results you obtained in this study.

Author's response

Response to Reviewers

Thank you for your time and effort in reviewing this article. Each comment is addressed below:

REVIEWER #2:

1. Hypothesis: Is this your correct hypothesis. That you expected to find no differences in postural sample entropy between the RHI and control group? This seems to be more of a null hypothesis.

This hypothesis was expected due to prior research reporting no differences in repetitive head impacts (RHI) postural control. Murray et al., 2017, Buckley et al., 2019, and Dierijck et al., 2018 all observed that there were no differences in static and dynamic postural control. However, in the studies that used entropy only compared either anteroposterior (AP) and eyes open (EO) conditions. Prior research has noted that the loading/unloading response controls mediolateral (ML) postural control, while changes in AP postural control are entirely controlled by the left and right limb center of pressure changes (Winter et al., 1993; Winter et al., 1996). Furthermore, When the eyes are closed (EC), there is an increased reliance on peripheral proprioception, as well as vestibular inputs (Paillard and Noe, 2015; Winter et al., 1993) Thus, it is imperative to understand each of these conditions affect postural control in order to better understand how RHI is affecting each postural control mechanism.

Our hypothesis was to verify if postural control regularity, as measured by sample entropy, in the ML direction and EC condition was also non-significant within those that have RHI. There is no relevant data that has been currently published that would support a significant change across season in the postural regularity context. However, as aforementioned, all facets of postural control regularity have not been clearly researched.

2. There is mention of the EC ML SampEn increasing for both groups, however this is not the case. The control groups EC SampEn remained fairly consistent as observed in fig 2. I agree the RHI group does have some differences and this is where the interesting preliminary data is but be careful in your interpretation not to speak to points that your data do not support. the discussion requires revision of points directed at the interpretation of results based on this error in reporting,

Thank you for your comment. We have mentioned this in the opening paragraph of the discussion with the following sentences, "However, the effect of Time and Task across the two seasons for SampEn in the ML direction was driven by the EC task in the RHI group. Additionally, the EC task was significantly affected during post-season for RHI, while no changes were noted for the CON group. The novelty of the current results is driven by the SampEn in ML directions and highlight the effect of the EC task has not been reported in the literature." We have changed the last statement at the end of the third paragraph of the discussion to, "Therefore, the novelty of the current study highlighted that across one athletic

season there was an increase in SampEn in the ML direction for EC that was
driven by the RHI group." Furthermore, we stated in the opening paragraph of the conclusion,
"The current study findings indicate center of pressure changes from pre- to post-season that
shift the sensory reliance towards more proprioceptive and vestibular input, and less towards
contributions from the visual system; which was driven by the RHI than the CON group."

3. In the first part of the discussion you have the sentence "Specifically, we compared athletes
who had no prior diagnosis of sport related concussion to a group of non-RHI athletes (CON)
with no diagnosed sport-related concussion". Should that first group have had RHI over the
season but no history of concussion diagnosis?

Thank you for your comment. Any participant that had a prior history of a concussion
was excluded from the study. We mentioned in the participants section of our methods that,
"Participants were excluded if they self-reported a medically-diagnosed sport-related
concussion or had a history of neurological, cognitive, or behavioral disorders." To clarify this
point the authors have edited the previous sentence to, "Participants from any group were
excluded if they self-reported a medically-diagnosed sport-related concussion or had a history
of neurological, cognitive, or behavioral disorders." In the first part of the discussion, we have
changed the text to, "Specifically, we compared RHI athletes who received repetitive head
impacts across the season but had no previously diagnosed sport related concussion to a group
of non-RHI athletes (CON) with no diagnosed sport-related concussion.

4. What are the details on the RHIs? How many did each person have in sport-related the
season? Were there sig differences within that group? Did they have any in previous seasons?

Thank you for your comment. The authors were not able to get the head individual
impact frequencies across the season or from multiple seasons. We did report the group average
as that was provided to us from the company rather than the individual frequency data. In the
future, we have a project that will address head impact frequency and its relationship to postural
control regularity. The authors have updated the limitations of the study, "The current study has
a few limitations. Firstly, we were not able to track the individual head impact frequencies
across the season or from prior seasons in the RHI group. Therefore, we could not separate the
RHI athletes into high-or low-impact groups. Thirdly, we were able to only account for the
male differences due to the choice of sport." In addition to this statement, the authors have
added the following to the end of the procedures section of the methods, Individual head impact
data were not collected in the RHI group across the season or from prior seasons. However, the
RHI group means ± standard deviations for mean linear acceleration and number of head
impacts were given from The Head Impact Telemetry System (HITS;1000Hz, Riddell,
Chicago, IL. USA) sensors that were placed in the helmet. The RHI group experienced a mean
linear acceleration of 30.7±6.8g over the course of 52 practice and 19 game/scrimmage

sessions. The number of impacts recorded across all RHI participants was 2,207 with 204 (9.2%) over 90g.

5. Could the lack of significance be due to under powering? You based your power analysis on previous research however, perhaps those data used need to be reassessed based on the results you obtained in this study.

We acknowledge these shortcomings however the lack of significance was only observed for the AP direction. This study still contributes with new findings in the ML direction specifically seen in the POST season during eyes closed stance. We argue that the sample size should not be an issue as RHI did show increased SampEn in the ML direction during eyes closed that has not been reported thus far. Additionally, Murray et al 2016 did not show any significant changes as they only used eyes open task which was confirmed through our findings as well. Therefore, it wouldn't be necessary for Murray et al 2016 to reassess their results as it is consistent with our study findings for the eye open task. This is an opportunity for us and future studies to expand on our findings to include more participants with both genders, across multiple seasons and include high and low impact groups.

3rd editorial decision

06-Jan-2020

Ref.: Ms. No. JCTRes-D-19-00015R2
Repetitive head impacts affect mediolateral postural sway entropy in the absence of vision following a competitive athletic season: preliminary findings
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers:

Reviewer #2: The authors have revised the manuscript to address my concerns as well as improve clarity of the study and results.