

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Longitudinal changes in oculomotor function in young adults with mild traumatic brain injury in Sweden– an exploratory prospective observational study
AUTHORS	Matuseviciene, Giedre ; Johansson, Jan; Möller, Marika; Godbolt, Alison; Pansell, Tony; Deboussard, Catharina

VERSION 1 – REVIEW

REVIEWER	Nabin Joshi SUNY College of optometry, USA
REVIEW RETURNED	22-Aug-2017

GENERAL COMMENTS	<p>Title page The study can be best classified as a pilot study which needs to be clear in the title.</p> <p>Page 2, line 33 Rather than “a significant difference”, the direction of difference would be more helpful.</p> <p>Line 49 “persistence of accommodative insufficiency” sounds better than “remaining accommodative insufficiency”</p> <p>Page 3 Line 16 Are NPC and fusional range measurements considered “objective”? Please provide references.</p> <p>Line 19 “Small sample size” – doesn’t it warrant the study to be labelled as a pilot?</p> <p>Page 5 Line 49 Some recent papers from Thiagarajan et al and Scheimann et al have looked at new protocols. Discussion of those papers in the introduction would broaden the quality of the introduction section.</p> <p>Pages 6 to 8 Very well written. However, please elaborate with a short paragraph on how NPC and fusional measurements were measured with some references.</p> <p>Page 9 Line 6 Please comment on spatial and temporal resolution of the eye tracker used.</p>
-------------------------	---

	<p>Line 36 Why parametric statistics were performed for oculomotor measures? Page 10 Line 35- "non injured", j is missing Results and discussion section- Surprisingly high number of orthopedic controls with AI, what could be the reasons behind this finding? The reduction of NPC goes against most papers, and in most of the patients NPC was better than the controls in the follow-up? What could be the potential reasons for it? The number of patients with mTBI is confusing. It starts out at 15, then falls to 13, and then again falls to 12 for symptom score analysis? This questions the utility power analysis that was described above. For accommodative facility in mTBI, please provide numbers. "Marginal" is very non-specific. Most papers have also suggested reduced positive fusional vergence, and an increase in saccades due to erroneous initial saccades. But, here you present opposite results. Figure 3- Wasn't PFV normal? Then, why was it correlated with the symptom score? Accommodation, vergence and pupils are affected in mTBI or TBI. The reason being they share a common neural network which manifests physiologically as a "near triad". Hence, what could be the reason behind a decrease of accommodative amplitude in isolation, without being accompanied by other components of the triad is possible, or would be a case. Please speculate. AI without decrease in accommodative facility or CI seems a little unusual on the first read. Is there anything in the literature suggesting probably a different neural network for facility as you describe a "structural" damage to some pathway in early parts of the discussion? And finally, what could be the reasons behind the high symptom scores in patients with mTBI in the follow ups, since most of the vision-related biomarkers except AI returned to near-normalcy?</p>
--	---

REVIEWER	<p>Jun Maruta Assistant Clinical Professor Department of Rehabilitation Medicine Icahn School of Medicine at Mount Sinai USA</p>
REVIEW RETURNED	06-Sep-2017

GENERAL COMMENTS	<p>[General comments]: The authors found near vision problems in patients with mTBI within days post-injury, as identified with objective measures. The problems were reduced when the patients were reassessed a few month later. These findings are used to leverage a discussion regarding the contribution of mTBI to clinical symptoms that follow the injury. The methodology, findings, and their interpretation seem generally tenable, but the presentation needs to be improved. Whether an injury to the brain, as opposed to the traumatic experience, has a specific contribution to the ensuing symptomatology can be more clearly addressed, given that one of the control groups consisted of orthopedic patients without a head injury. When reporting statistical results, in addition to p-values, the values of applicable test statistics and degrees of freedom should be included. The manuscript seems to have some logical gaps.</p>
-------------------------	---

	<p>For example, the authors set out to test specific hypotheses; therefore, a statement such as "...marginally reduced by was statistically non-significant" is not consistent with the approach or informative. If any arithmetical difference was suggestive of a real or expected difference that was statistically under-powered, please provide specific values that can establish a larger-scale study design. Also, the accounting for subjects (recruitment vs. enrollment) is not clear. See specific comments below. Other problems include editorial ones. For example, "follow up" should be hyphenated when "follow" is not used as a verb. A comma should be used before "and" to separate the last item in a series. Commas seem underused overall. Either musculoskeletal or orthopaedic should be used consistently to refer to a group. "mTBI group" and "orthopaedic group" are often missing "the." Figure legends should be marked clearly or be placed together at the end of the manuscript.</p> <p>[Specific comments]: //Page 2, ABSTRACT: The acronym "mTBI" is not defined. The acronyms "RPQ" and "NPC" are defined but not used. Orthopaedic controls were initially introduced as musculoskeletal. Objective - Capitalize "To." Consider rewriting "whether objectively measurable disturbances are observed" as "whether visual disturbances can be demonstrated with objective measures." Consider changing "detectable" to "measured." Participants - Please use a comma before "and 15 non-injured." Remove "all." Results - Consider rewriting "Six out of 13 mTBI patients still had accommodative insufficiency at follow up" as "Six out of 13 mTBI patients who were followed up had accommodative insufficiency." Consider rewriting "between the groups" as "between the experimental and control groups" (or "among the groups" although analyses among the three groups do not seem to have been performed).</p> <p>//Page 3, ARTICLE SUMMARY: Line (approximately) 13: Remove "also." Lines 20-21: Consider rewriting the listed point as "The generalisability of this study is limited because the sample of patients with mTBI was small in size and restricted in age range."</p> <p>//Page 4. Lines 6-10: The sentence seems to state: 1) biosocial factors may hamper recovery; and 2) biosocial factors may affect symptom-based outcome assessment. Please clarify how these two points connect to the next sentence, "There is a need for objective methods..." Lines 19-20: Consider rewriting "the brain including cortical and subcortical areas" as "cortical and subcortical structures of the brain." Lines 24-25: The sentence is awkward because there are only several sensory modalities and all of them are important. Consider rewriting it as "The reliance of vision is such that..." Line 25: I think that "Specific visual symptoms" needs to be modified with something like "self-reported" in order for the rest of the paragraph to make sense. Line 53: Consider rewriting "maintains eye alignment" as "causes eye alignment" or "aligns the two eyes."</p>
--	---

	<p>//Page 5. Lines 28-30: I suggest changing "initiated without delay" to "executed in quick succession." Lines 38-40: Consider rewriting the sentence as "Parameters of saccades, such as latency and accuracy, have been..." Line 57: I suggest adding "(orthopaedic)" after "musculoskeletal." Add "to" before "a non-injured control group."</p> <p>//Page 6. The acronyms ACRM, LOC, and PTA are defined but not used subsequently. Line 58: The exclusion criteria include contraindications for MRI, but Pages 7 and 10 seem to indicate CT rather than MRI. If MRI, please explain if a patient could be recruited but not included in the analysis. Also, MRI is not defined until Page 8. CT is first used in Page 7 without a definition while in Page 10 "computer tomography" is used without the acronym.</p> <p>//Page 7. Line 38: Consider inserting "with" before "minor" and changing "musculoskeletal" to "orthopaedic." Line 56: I think that "adjacent days" should be "an adjacent day" unless the testing spanned for more than two days.</p> <p>//Page 8. Lines 4-9: I suggest deleting the sentence unless MRI contraindications were indeed part of the exclusion criteria (see comment re Page 6, Line 58). Line 19: Consider rewriting ", max 64" as " with a maximum score of 64." Lines 22-23: The abbreviation "ICD-10" is not used subsequently. Consider simply writing "International Classification of Diseases, 10th revision." Line 23: Use a hyphen - "work-related." Line 26: Use a comma before "e.g." or place the e.g. clause in parentheses as in Page 6. Please check the journal's convention. Lines 31-36: Consider breaking up the sentence in two, as in "...symptoms is 21. This value gave good sensitivity...in otherwise healthy young adults who presented to..." Line 50: Define AI here rather than in Page 10. Line 54: CI has been defined in Page 4.</p> <p>//Page 9. Line 11: Use a semi-colon after "(3) anti-saccades" to follow the convention used under (1) and (2). Please clarify if latency was of correct saccades or otherwise (currently written as "latency...of erroneous saccades"). Line 13: Consider rewriting ", diameter 5 mm" as "with a diameter of 5 mm." Line 31: The Kruskal-Wallis test does not seem to have been used. Please clarify. If this test was not used, remove "(two groups)" after "Mann-Whitney U." Lines 40-45: Power calculation is for research planning; therefore, the paragraph is misplaced. Regardless, the source of the 70% and 10% estimates is not clear. The 70% rate should be part of the second paragraph of INTRODUCTION. Also, it is not clear if the recruitment process was stopped for each group when the number reached 15 or the process continued for a set period of time to arrive at the numbers presented in RESULTS.</p>
--	---

	<p>Lines 54-56: Consider simply stating "15 orthopaedic controls." Line 58: Please explain from what this mTBI patient was excluded. It appears that this patient was recruited and tested.</p> <p>//Page 10. Lines 3-6: Please explain from what the two control subjects were excluded. Please also clarify whether the two mTBI patients were part of the 15. Line 10: "range (2-9 days)" should be "(range 2-9 days)." Line 21: Change "minor trauma" to "orthopaedic." Line 25: Consider rewriting "lack of time and inconvenience" as "related to time and convenience." Lines 33-39: Move "Mann-Whitney U test" to where the p-value associated with it first appears. Line 42: Consider adding "the two" before "control groups." Lines 42-45: I think it is inappropriate to suggest without a statistical evidence that the scores decreased. Consider changing the sentence to "The difference over time between summed symptom scores in the mTBI group did not reach statistical significance (Wilcoxon signed rank test, $z = ??$, $p = 0.092$)." Lines 48-53: Clarify which statistical test was used. Lines 56-58: Rewrite the sentence "Insufficient accommodation..." as "AI and CI were identified."</p> <p>//Page 11. Lines 3-5: Consider rewriting "CI/AI" as "CI and AI." Use commas: "...combined CI and AI, and..."; "At follow-up, one mTBI patient still had CI, and six others had AI"; and "...had AI at baseline, and six at..." Lines 11-14: "NPC" has been defined. Clarify which statistical tests were used. Line 30: Change "compare" to "compared." Line 33: Use the acronym "AI." Lines 37-39: Combine this one-sentence paragraph with the preceding paragraph. Consider rewriting the sentence as "Performance changes in accommodative facility in the mTBI group from baseline to follow-up did not reach statistical significance (include test statistics)." Lines 54-58: Clarify what was compared (prism diopters or proportions of individuals with < 20 prism?).</p> <p>//Page 12. Lines 4-6: Clarify what test was used. Add a comma after "pro-saccade task." Given the use of "or," I think that "...differences...were..." should be "...difference...was..." Remove "the" from "the groups." The second sentence in the paragraph does not seem to add any information to the first one. Lines 13-26: Rephrase so as to just state that any difference was statistically non-significant. Remove "equally," which cannot be substantiated. Lines 38-45: The cutoff score has been stated in METHODS. Fisher's exact test should be mentioned in METHODS. Consider rewriting the passage as "Objective vision diagnoses based on CI or AI were compared with CISS symptom scores (Table 2). No significant association was found based on Fisher's exact test."</p> <p>//Page 13. Table 2: The table title should include RPQ, e.g. "...versus CISS and RPQ scores." Line 31: I think "score" should be "scores."</p>
--	--

	<p>Line 45: Consider rewriting the sentence as "We objectively measured transient visual disturbances..."</p> <p>Lines 54-56: I would soften the statement by inserting "may be" after "therefore" since the recommendation is not universally accepted.</p> <p>//Page 14.</p> <p>Lines 5-6: Change "then" to "than." That patients with mTBI report more symptoms than those with other injuries have also been found by Hoge et al., 2008, NEJM, and Bryant et al., 2010, Am J Psychiatry, although these authors appear to indicate that an injury to the brain has no specific contribution to the increase. The role of mTBI in post-injury symptoms may be elaborated by the findings of the current paper.</p> <p>Lines 11-12: Change "potential" to "potentially." Use a hyphen - "vision-based."</p> <p>Lines 16-24: I believe "mean" rather than "median" is correct. Remove "at baseline" as testing was done only once. "Within 10 cm" can be 5 cm – rewrite it as "just within 10 cm." The second sentence is awkwardly placed. Consider rewriting this passage as "However, the mean NPC of these mTBI patients was just within 10 cm, which may or may not be considered clinically meaningful (9, 32), and therefore not pose a clinical sign for further examination of CI."</p> <p>Line 30: Replace "trough" with "through."</p> <p>Line 33: Consider changing "motor function (vergence eye movements)" to "low-level motor functions."</p> <p>Line 45: Consider changing "maximally" to "optimally."</p> <p>Line 46: "May" and "can" are redundant - delete "may."</p> <p>Lines 51-52: The information in this one-sentence paragraph is redundant with Page 15, Lines 8-10, "Capo-Ante et al. found significantly..."</p> <p>Line 58: Use the acronym "AI."</p> <p>//Page 15.</p> <p>Line 24: Replace "minor trauma" with "orthopaedic."</p> <p>Line 29: Delete "studies."</p> <p>Line 33: Provide references.</p> <p>Line 38: The word "minor" is not needed here.</p> <p>Lines 42-44: The sentence needs a word or phrase to clarify its relationship to the last sentence of the previous paragraph. Consider replacing "where" with "in which." Delete "was expressed as latency distribution." Specify "several" as "four."</p> <p>Lines 48-49: Remove "distribution" because "increased distribution" does not make sense. Also remove the two "mean"s.</p> <p>Lines 55-58: Consider adding "having" in the first sentence so it reads, "The strength of our study is having two control groups." "Confound" is a transitive verb and needs an object. The authors should discuss specific insights derived from implementing this design. Otherwise, consider stating the point in INTRODUCTION.</p> <p>//Page 16.</p> <p>Lines 9-10: The statement is design-related, and the authors have justified the sample size. If an expected findings was not made because of unanticipated problems, discuss these specific problems as limitations.</p> <p>Line 19: Please specify "several aspects."</p> <p>Line 24: Change "selected" to "selective."</p>
--	--

REVIEWER	Alexandre Reynaud McGill University, Canada
REVIEW RETURNED	07-Sep-2017

GENERAL COMMENTS	<p>In general, the study is clean and well designed. The hypothesis and methods are clear and sound. However two major issues are the lack of clarity in the presentation of the results and a lack of discussion of the implications of the findings, in particular on stereo vision. A lot of tests have been performed but only a part of the results are reported in only 3 figures and 2 unclear tables. The paper would benefit greatly of a more thorough analysis, looking at correlations between all the measures performed.</p> <p>Furthermore, I think the paper would greatly benefit of reporting clearly the acquired data in readable figures, and in particular in showing more individual data as we know that TBI data can be highly variable.</p> <p>For instance pages 10,11,12: lots of data are reported in the text without appearing in any table or figure, I think it would be easier to process if it was reported in a table or graph.</p> <p>In general it would be very useful to see individual data, and in particular for non-significant differences.</p> <p>Fig1: which criterion was used to determine outliers ? was the analysis performed excluding them in p11 ?</p> <p>Table 2 and its description are very confusing, why not making a figure ?</p> <p>Maybe a scatterplot baseline/follow up, with different colors/symbols for groups and diagnosis</p> <p>Given the numerous abbreviations used, I would suggest to add a glossary at the end of the article</p> <p>There is no report on stereo acuity data whereas the authors say it was measured on 8-42. In fact I think it would be interesting to discuss the implications of the observed symptoms on stereo vision ?</p> <p>The discussion on page 15 lacks a bit of substance and should flow a bit better</p> <p>The interesting correlation observed between the CISS score and positive fusional vergence should be discussed</p> <p>The CISS and RPQ scores improvement at follow up might just be due to habituation, this should be discussed</p> <p>Minor points:</p> <p>6-20 in to</p> <p>testing periods are inconsistent between 2-29 7-53 and 10-13</p> <p>8-9 and 9-50: "data will be reported separately" why not combining everything in one unified article ?</p> <p>9-13: 5mm, please report in degrees</p>
------------------	---

	<p>9-21: I think the antisaccade condition should come before the self-paced one for clarity</p> <p>10-35 non-injured</p> <p>11-22 11-48 and figures captions: "min and max excluding outliers" is unclear, it could be interpreted as min and max, excluding outliers. please rephrase</p> <p>11-44 "The higher the negative value"</p> <p>14-4 than 14-58 sentence not clear</p> <p>15-18 theirs</p> <p>16-25 selective?</p> <p>Reviewing ethics committee and adequacy with the declaration of Helsinki should be mentioned</p>
--	--

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Nabin Joshi

Institution and Country: SUNY College of optometry, USA

Please state any competing interests: None declared.

Please leave your comments for the authors below

There is a need for multi-disciplinary efforts in mTBI remediation. It was a good study.

Response: Thank you.

Reviewer: 2

Reviewer Name: Jun Maruta

Institution and Country: Assistant Clinical Professor, Department of Rehabilitation Medicine, Icahn School of Medicine at Mount Sinai, USA

Please state any competing interests: None declared

Please leave your comments for the authors below

[General comments]:

The authors found near vision problems in patients with mTBI within days post-injury, as identified with objective measures. The problems were reduced when the patients were reassessed a few month later. These findings are used to leverage a discussion regarding the contribution of mTBI to clinical symptoms that follow the injury. The methodology, findings, and their interpretation seem generally tenable, but the presentation needs to be improved. Whether an injury to the brain, as opposed to the traumatic experience, has a specific contribution to the ensuing symptomatology can be more clearly addressed, given that one of the control groups consisted of orthopedic patients without a head injury. When reporting statistical results, in addition to p-values, the values of applicable test statistics and degrees of freedom should be included. The manuscript seems to have some logical gaps.

For example, the authors set out to test specific hypotheses; therefore, a statement such as "...marginally reduced by was statistically non-significant" is not consistent with the approach or informative. If any arithmetical difference was suggestive of a real or expected difference that was statistically under-powered, please provide specific values that can establish a larger-scale study design. Also, the accounting for subjects (recruitment vs. enrollment) is not clear. See specific comments below. Other problems include editorial ones. For example, "follow up" should be hyphenated when "follow" is not used as a verb. A comma should be used before "and" to separate the last item in a series. Commas seem underused overall. Either musculoskeletal or orthopaedic should be used consistently to refer to a group. "mTBI group" and "orthopaedic group" are often missing "the." Figure legends should be marked clearly or be placed together at the end of the manuscript.

Response: Thank you for your most valuable general and specific comments. We have made changes in the introduction and the discussion in order to improve the presentation and interpretation and to fill in logical gaps according to the comments above and the specific comments below. We also added the requested specified statistical details. English language and presentation issues have been corrected.

[Specific comments]:

//Page 2, ABSTRACT:

The acronym "mTBI" is not defined. The acronyms "RPQ" and "NPC" are defined but not used.

Orthopaedic controls were initially introduced as musculoskeletal.

Objective - Capitalize "To." Consider rewriting "whether objectively measurable disturbances are observed" as "whether visual disturbances can be demonstrated with objective measures." Consider changing "detectable" to "measured."

Participants - Please use a comma before "and 15 non-injured." Remove "all."

Results - Consider rewriting "Six out of 13 mTBI patients still had accommodative insufficiency at follow up" as "Six out of 13 mTBI patients who were followed up had accommodative insufficiency."

Consider rewriting "between the groups" as "between the experimental and control groups" (or "among the groups" although analyses among the three groups do not seem to have been performed).

Response:

*The acronym mTBI is defined in the title, and now also defined in the abstract.

*RPQ and NPC are removed from the abstract.

*We have changed "musculoskeletal" to "orthopaedic controls throughout the manuscript.

*English language and presentation issues have been corrected as requested.

*"between the groups" has been changed to "between the mTBI and control groups"

//Page 3, ARTICLE SUMMARY:

Line (approximately) 13: Remove "also."

Lines 20-21: Consider rewriting the listed point as "The generalisability of this study is limited because the sample of patients with mTBI was small in size and restricted in age range."

Response: Suggested changes have been made.

//Page 4.

Lines 6-10: The sentence seems to state: 1) biosocial factors may hamper recovery; and 2) biosocial factors may affect symptom-based outcome assessment. Please clarify how these two points connect to the next sentence, "There is a need for objective methods..."

Lines 19-20: Consider rewriting "the brain including cortical and subcortical areas" as "cortical and subcortical structures of the brain."

Lines 24-25: The sentence is awkward because there are only several sensory modalities and all of them are important. Consider rewriting it as "The reliance of vision is such that..."

Line 25: I think that "Specific visual symptoms" needs to be modified with something like "self-reported" in order for the rest of the paragraph to make sense.

Line 53: Consider rewriting "maintains eye alignment" as "causes eye alignment" or "aligns the two eyes."

Response:

*Thank you for the comments on the introduction, lines 6-10, 19-20, 24-25. The introduction has been rewritten in the light of the comments and suggested changes.

* Suggested changes on line 53 have been made.

//Page 5.

Lines 28-30: I suggest changing "initiated without delay" to "executed in quick succession."

Lines 38-40: Consider rewriting the sentence as "Parameters of saccades, such as latency and accuracy, have been..."

Line 57: I suggest adding "(orthopaedic)" after "musculoskeletal." Add "to" before "a non-injured control group."

Response: Suggested changes have been made. In order to be consistent we have changed "Musculoskeletal" to orthopaedic throughout the manuscript, also in line 57 mentioned here.

//Page 6.

The acronyms ACRM, LOC, and PTA are defined but not used subsequently.

Line 58: The exclusion criteria include contraindications for MRI, but Pages 7 and 10 seem to indicate CT rather than MRI. If MRI, please explain if a patient could be recruited but not included in the analysis. Also, MRI is not defined until Page 8. CT is first used in Page 7 without a definition while in Page 10 "computer tomography" is used without the acronym.

Response:

*The acronyms ACRM, LOC and PTA have been removed.

*All patients underwent a computerized tomography scan on a clinical basis, whilst the MRI scanning was a part of the study protocol.

*MRI and CT are now defined when they first appear in the text, and acronyms after this.

//Page 7.

Line 38: Consider inserting "with" before "minor" and changing "musculoskeletal" to "orthopaedic."

Line 56: I think that "adjacent days" should be "an adjacent day" unless the testing spanned for more than two days.

Response: Suggested changes have been made.

//Page 8.

Lines 4-9: I suggest deleting the sentence unless MRI contraindications were indeed part of the exclusion criteria (see comment re Page 6, Line 58).

Line 19: Consider rewriting ", max 64" as " with a maximum score of 64."

Lines 22-23: The abbreviation "ICD-10" is not used subsequently. Consider simply writing "International Classification of Diseases, 10th revision."

Line 23: Use a hyphen - "work-related."

Line 26: Use a comma before "e.g." or place the e.g. clause in parentheses as in Page 6. Please check the journal's convention.

Lines 31-36: Consider breaking up the sentence in two, as in "...symptoms is 21. This value gave good sensitivity...in otherwise healthy young adults who presented to..."

Line 50: Define AI here rather than in Page 10.

Line 54: CI has been defined in Page 4.

Response:

*Line 4-9 The MRI scanning was a part of the study protocol and imaging results will be presented separately.

*Line 19, 22-23, 26, 31-36, has been changed according to your suggestion.

*Line 50, 54 Thank you for pointing out the inconsistency in the use of acronyms.

//Page 9.

Line 11: Use a semi-colon after "(3) anti-saccades" to follow the convention used under (1) and (2). Please clarify if latency was of correct saccades or otherwise (currently written as "latency...of erroneous saccades").

Line 13: Consider rewriting ", diameter 5 mm" as "with a diameter of 5 mm."

Line 31: The Kruskal-Wallis test does not seem to have been used. Please clarify. If this test was not used, remove "(two groups)" after "Mann-Whitney U."

Lines 40-45: Power calculation is for research planning; therefore, the paragraph is misplaced. Regardless, the source of the 70% and 10% estimates is not clear. The 70% rate should be part of the second paragraph of INTRODUCTION. Also, it is not clear if the recruitment process was stopped for each group when the number reached 15 or the process continued for a set period of time to arrive at the numbers presented in RESULTS.

Lines 54-56: Consider simply stating "15 orthopaedic controls."

Line 58: Please explain from what this mTBI patient was excluded. It appears that this patient was recruited and tested.

Response:

*Line 11 have been changed as follows: "latency of correct saccades and proportion of erroneous saccades.."

*Line 13 changes have been made as required.

*Line 31 the statistical method used has been clarified for each calculation.

*Lines 40-45 thank you for this valuable comment. We have moved the text regarding power calculation to appear earlier in the method section and included references as requested. Furthermore we have rewritten the introduction and the 70% rate is now included. Recruitment ended when number of participants reached 15 in each group and this has now been explained in the method section.

*Lines 54-56 have been changed according to your suggestion.

*Line 58 Due to a protocol violation at the first visual assessment it was noted that three recruited persons, one mTBI patient and two orthopaedic controls, were erroneously recruited since they fulfilled one exclusion criteria; severe visual disturbance and strabismus. Therefoer new participants were included. This has been removed from the manuscript in order to avoid confusion.

//Page 10.

Lines 3-6: Please explain from what the two control subjects were excluded. Please also clarify whether the two mTBI patients were part of the 15.

Line 10: "range (2-9 days)" should be "(range 2-9 days)."

Line 21: Change "minor trauma" to "orthopaedic."

Line 25: Consider rewriting "lack of time and inconvenience" as "related to time and convenience."

Lines 33-39: Move "Mann-Whitney U test" to where the p-value associated with it first appears.

Line 42: Consider adding "the two" before "control groups."

Lines 42-45: I think it is inappropriate to suggest without a statistical evidence that the scores decreased. Consider changing the sentence to "The difference over time between summed symptom scores in the mTBI group did not reach statistical significance (Wilcoxon signed rank test, $z = ??$, $p = 0.092$)."

Lines 48-53: Clarify which statistical test was used.

Lines 56-58: Rewrite the sentence "Insufficient accommodation..." as "AI and CI were identified."

Response:

*Line 3-6 this has also been explained above. At the first visual assessment it was noted that three recruited persons, one mTBI patient and two orthopaedic controls, were erroneously recruited since they fulfilled one exclusion criteria; severe visual disturbance and strabismus. Therefore new participants were included. The text about this violence of the protocol has been removed from the manuscript in order to avoid confusion.

*Line 10 and 21 has been changed as requested.

*Line 25 we did not change.

*Lines 33-39, 42, 45, 48-53 the requested specified statistical details have been added.

*Line 56-58 has been changed as requested.

//Page 11.

Lines 3-5: Consider rewriting "CI/AI" as "CI and AI." Use commas: "...combined CI and AI, and..."; "At follow-up, one mTBI patient still had CI, and six others had AI"; and "...had AI at baseline, and six at..."

Lines 11-14: "NPC" has been defined. Clarify which statistical tests were used.

Line 30: Change "compare" to "compared."

Line 33: Use the acronym "AI."

Lines 37-39: Combine this one-sentence paragraph with the preceding paragraph. Consider rewriting the sentence as "Performance changes in accommodative facility in the mTBI group from baseline to follow-up did not reach statistical significance (include test statistics)."

Lines 54-58: Clarify what was compared (prism diopters or proportions of individuals with < 20 prism?).

Response:

* Line 3-5, 33 has been changed as requested

*Lines 11-14 the requested specified statistical details have been added and definition of NPC removed.

*Lines 37-39 This has been changed. We suggest leaving statistics out because there is no statistical difference to report.

*Line 54-58 "prism diopters" was compared.

//Page 12.

Lines 4-6: Clarify what test was used. Add a comma after "pro-saccade task." Given the use of "or," I think that "...differences...were..." should be "...difference...was..." Remove "the" from "the groups." The second sentence in the paragraph does not seem to add any information to the first one.

Lines 13-26: Rephrase so as to just state that any difference was statistically non-significant. Remove "equally," which cannot be substantiated.

Lines 38-45: The cutoff score has been stated in METHODS. Fisher's exact test should be mentioned in METHODS. Consider rewriting the passage as "Objective vision diagnoses based on CI or AI were compared with CISS symptom scores (Table 2). No significant association was found based on Fisher's exact test."

Response:

*Lines 4-6 English language issues have been corrected. We agree the second sentence does not add any information and it has been removed.

*Lines 13-26 and 38-45 the requested changes have been done. Fishers exact test was applied for analyses of association of categorical data and small sample size. This is now mentioned in the methods.

//Page 13.

Table 2: The table title should include RPQ, e.g. "...versus CISS and RPQ scores."

Line 31: I think "score" should be "scores."

Line 45: Consider rewriting the sentence as "We objectively measured transient visual disturbances..."

Lines 54-56: I would soften the statement by inserting "may be" after "therefore" since the recommendation is not universally accepted.

Response:

*Table 2. The title of table 2 has been changed and RPQ added.

*Lines 31, 45, 54-55 have been rewritten.

//Page 14.

Lines 5-6: Change "then" to "than." That patients with mTBI report more symptoms than those with other injuries have also been found by Hoge et al., 2008, NEJM, and Bryant et al., 2010, Am J Psychiatry, although these authors appear to indicate that an injury to the brain has no specific contribution to the increase. The role of mTBI in post-injury symptoms may be elaborated by the findings of the current paper.

Lines 11-12: Change "potential" to "potentially." Use a hyphen - "vision-based."

Lines 16-24: I believe "mean" rather than "median" is correct. Remove "at baseline" as testing was done only once. "Within 10 cm" can be 5 cm – rewrite it as "just within 10 cm." The second sentence is awkwardly placed. Consider rewriting this passage as "However, the mean NPC of these mTBI patients was just within 10 cm, which may or may not be considered clinically meaningful (9, 32), and therefore not pose a clinical sign for further examination of CI."

Line 30: Replace "trough" with "through."

Line 33: Consider changing "motor function (vergence eye movements)" to "low-level motor functions."

Line 45: Consider changing "maximally" to "optimally."

Line 46: "May" and "can" are redundant - delete "may."

Lines 51-52: The information in this one-sentence paragraph is redundant with Page 15, Lines 8-10, "Capo-Ante et al. found significantly..."

Line 58: Use the acronym "AI."

Response:

*Lines 5-6 have been rewritten, and the scope of this study was on objective markers for brain injury as now mentioned in the text.

*Lines 11-12 this has been changed.

*Line 16-24, we consider median to be the most appropriate measure. The testing was done twice. We have therefore not made changes here, except for adding and rewriting the second sentence concerning NPC of mTBI patients. "just within.." have been added.

*Line 30, 45, 46, 58 have been changed

*Line 33 we considered this but do not consider a change merited.

*Line 51-52 this is now only mentioned once.

//Page 15.

Line 24: Replace "minor trauma" with "orthopaedic."

Line 29: Delete "studies."

Line 33: Provide references.

Line 38: The word "minor" is not needed here.

Lines 42-44: The sentence needs a word or phrase to clarify its relationship to the last sentence of the previous paragraph. Consider replacing "where" with "in which." Delete "was expressed as latency distribution." Specify "several" as "four."

Lines 48-49: Remove "distribution" because "increased distribution" does not make sense. Also remove the two "mean"s.

Lines 55-58: Consider adding "having" in the first sentence so it reads, "The strength of our study is having two control groups." "Confound" is a transitive verb and needs an object. The authors should discuss specific insights derived from implementing this design. Otherwise, consider stating the point in INTRODUCTION.

Response:

*Line 24, 29, 38, 42-44, 48-49 and 55-58: English language and presentation issues have been corrected.

*Line 33 references have been provided as required.

//Page 16.

Lines 9-10: The statement is design-related, and the authors have justified the sample size. If an expected findings was not made because of unanticipated problems, discuss these specific problems as limitations.

Line 19: Please specify "several aspects."

Line 24: Change "selected" to "selective."

Response:

Unexpectedly, we did not find a statistically significant difference in saccades between the mTBI and control groups, which might be due to the low sample size, and thus a possible type II error. This is now discussed in the limitation section.

Reviewer: 3

Reviewer Name: Alexandre Reynaud

Institution and Country: McGill University, Canada

Please state any competing interests: None declared

Please leave your comments for the authors below

In general, the study is clean and well designed. The hypothesis and methods are clear and sound. However two major issues are the lack of clarity in the presentation of the results and a lack of discussion of the implications of the findings, in particular on stereo vision. A lot of tests have been performed but only a part of the results are reported in only 3 figures and 2 unclear tables. The paper would benefit greatly of a more thorough analysis, looking at correlations between all the measures performed.

Furthermore, I think the paper would greatly benefit of reporting clearly the acquired data in readable figures, and in particular in showing more individual data as we know that TBI data can be highly variable.

For instance pages 10,11,12: lots of data are reported in the text without appearing in any table or figure, I think it would be easier to process if it was reported in a table or graph.

In general it would be very useful to see individual data, and in particular for non-significant differences.

Response: We recognize that there are a lot of data in this study. In our attempt to keep structure in the paper we chose to focus on the statistically significant findings. We are happy to report all data, perhaps in an appendix, if that is a common request by the journal. The journal also requires using no more than up to 5 figures/tables for readability.

Fig1: which criterion was used to determine outliers ? was the analysis performed excluding them in p11 ?

Response: No, outliers were not excluded from the analyses.

Table 2 and its description are very confusing, why not making a figure ?

Maybe a scatterplot baseline/follow up, with different colors/symbols for groups and diagnosis

Response: Thanks for this suggestion. We have considered other options for presenting the data but for now we would like to suggest keeping the table since we think a graph covering all these aspects may be quite complex to interpret. We are of course willing to discuss any further suggestions.

Comment: Given the numerous abbreviations used, I would suggest to add a glossary at the end of the article

Response: we have discussed this, and we removed LOC, PTA and ACRM.

Comment: There is no report on stereo acuity data whereas the authors say it was measured on 8-42. In fact I think it would be interesting to discuss the implications of the observed symptoms on stereo vision?

Response: Thanks for this suggestion. We have added information in Results to read as follows: "Regarding stereo vision, all non-injured controls performed 60 seconds of arc or better at both test occasions. In the orthopaedic group three subjects performed 120-240 at baseline and two of these performed similarly at follow up (one missing). A contrasting finding was that one third (n=5) of the mTBI patients showed crude level of stereo acuity at baseline (120-240) whilst at follow-up, all but one (subject 14, TNO 120), performed 60 or better."

And in the discussion we have added to read as follows:

"One third of the mTBI patients showed deficient levels of stereo acuity at baseline (120-240), whilst at follow-up, all but one performed normally, i.e. 60 or better. These findings may suggest that the visual processing of disparity was affected particularly in the mTBI group. Based on the improvement in stereo acuity we may speculate that underlying factors, i.e. inadequate or inefficient vergence and/or accommodative function, affecting the ability to resolve and detect stereo disparity improved with time. It has been shown that stereo acuity is affected both at vergence- and accommodative disorders and that it can be improved after treatment (Rutstein & Daum, Schadt et al 2013)."

Comment: The discussion on page 15 lacks a bit of substance and should flow a bit better

Response: Thank you for your valuable comment. We have made changes in the discussion in order to improve the presentation.

Comment: The interesting correlation observed between the CISS score and positive fusional vergence should be discussed

Response: Thank you for your valuable comment. We have changed and added text in order to discuss this, as follows:

"We found that mTBI patients had significantly more visual symptoms as measured by CISS score than orthopaedic and non-injured controls. Our findings about reporting visual disturbances at near work after mTBI are consistent with previous studies.(13)"

We found a significant correlation between CISS score and PFV at near in the mTBI group. This may appear somewhat unexpected since the PFV was normal at the group level. We could however not find similar correlations for the other groups. The symptom score (CISS) was significantly higher in mTBI than in the control groups. This may be an indication that most mTBI patients were indeed able to perform normally on the PFV but at a greater effort (causing symptoms). It has been suggested that binocular functions are performed less efficiently after injury and therefore more likely to cause symptoms. Objective recordings of vergence eye movement have indicated this (Scheimann et al 2017)."

Comment: The CISS and RPQ scores improvement at follow up might just be due to habituation, this should be discussed

Response: We have added in Discussion section to read: One of the reasons for improvement of self-rated symptom scores might be lack of interest or habituation in filling out a questionnaire.

Minor points:
6-20 in to

Response: The english language has been corrected.

Comment: testing periods are inconsistent between 2-29 7-53 and 10-13

Response. Thank you for this comment. We have clarified the testing periods in the Results section, and we have added a sentence to read as follows: "In order to minimize drop outs, we extended the planned follow-up time."

8-9 and 9-50: "data will be reported separately" why not combining everything in one unified article ?

Response: This project was conducted to investigate medical, visual and neuropsychological aspects of mTBI from a rehabilitation perspective. The target group of readers is therefore different for the different aspects. Gathering all data in one article would reduce readability of the manuscript. Therefore the issues were divided into several articles, according to the intended readership.

Comment: 9-13: 5mm, please report in degrees

Response: Done (0.5 degrees)

Comment: 9-21: I think the antisaccade condition should come before the self-paced one for clarity

Response: OK, done

Comment: 10-35 non-injured

Response: OK, done

Comment: 11-22 11-48 and figures captions: "min and max excluding outliers" is unclear, it could be interpreted as min and max, excluding outliers. please rephrase

Response: OK, done

Comment: 11-44 "The higher the negative value"

Response: OK, clarified

Comment: 14-4 than

Response: OK, changed

14-58 sentence not clear Response: OK, clarified as follows: "The accommodative amplitude was significantly lower in mTBI compared to controls at baseline. It then recovered to a certain degree at follow-up, but six mTBI patients still presented with deviations meeting the diagnostic criteria for accommodative insufficiency. "

Comment: 15-18 theirs

Response: OK, changed

Comment: 16-25 selective?

Response: OK, clarified

Comment: Reviewing ethics committee and adequacy with the declaration of Helsinki should be mentioned

Response: We added the sentence "The study adhered to the tenets of the Helsinki Declaration" within the section "Ethics approval", at the end of the manuscript.

VERSION 2 – REVIEW

REVIEWER	Nabin Joshi SUNY College of Optometry, USA
REVIEW RETURNED	30-Oct-2017

GENERAL COMMENTS	Thank you for making the changes as suggested. The changes in my opinion, are adequate. Thank you for undertaking a prospective study in mTBI, which shows some natural recovery in objective measurements. However, symptoms did persist in many patients, and the need some form of remediation should also be highlighted, especially in this subset..
-------------------------	---

REVIEWER	Jun Maruta Assistant Clinical Professor Department of Rehabilitation Medicine Icahn School of Medicine at Mount Sinai USA
REVIEW RETURNED	25-Oct-2017

GENERAL COMMENTS	<p>[General comments]</p> <p>I still found the manuscript to be problematic. To some degree, the authors seem to have lost sight of the forest for the trees while revising. Mainly, I am concerned that the Kruskal-Wallis test and ANOVA may have been used without a clear purpose, given that the first objective of the study is to compare mTBI patients with control subjects, rather than to detect a difference across the three groups involved. If these statistical tests are deemed appropriate, a finding of a difference among the groups should be followed up with an appropriate post-hoc test, rather than proceeding to multiple two-group comparisons. I think that the overall presentation can still be much improved by organizing RESULTS/DISCUSSION to concisely echo the stated objectives. There are still some passages that do not seem to be expressed in correct English. Also, "mTBI" seems to be incorrectly used in some places to refer to people rather than a condition.</p> <p>[Specific comments] //Title.</p>
-------------------------	--

	<p>The title is awkward. In particular, "Swedish" seems misplaced. Consider "Longitudinal changes in oculomotor function in young adults with mild traumatic brain injury in Sweden - an exploratory prospective observational study," or "Longitudinal changes in oculomotor function in young adults with mild traumatic brain injury - a prospective observational exploration in Sweden."</p> <p>//Page 2, ABSTRACT. Objectives: The first objective seems to contain two ideas. Consider specifying them as "1) whether visual disturbances can be...compared to controls, 2) whether such objectively demonstrated disturbances change over time." Outcome measures: Use a parallel construction, e.g. "Visual examination including..." and "Symptom assessment using..." Results: Reorganize so that the findings echo the stated objectives. Change "significantly" to "statistically." Remove the p-values because what is compared is unclear. Conclusion: Change "There are" to "There were."</p> <p>//Page 5. Line 6: Define the acronym "mTBI" – Also change "mild traumatic brain injury" (Lines 11-13) to "mTBI." Lines 8-9: "Oculomotor" and "eye movements" are redundant. Rephrase. Also, insert a comma after "eye alignment." Line 11: Change "a possible correlate" to "possible correlates." Line 14: Consider changing "promising, yet preliminary" to "preliminary but promising." Line 18: Change "...after mTBI, but..." to "...after mTBI; however, ..." Line 22: Change "visual networks" to "vision-related networks." Lines 24-26: Consider changing "Visual impairments of different kinds have been found in several studies with prevalence up to 70 percent in a cohort of patients with..." to "Various visual impairments with a prevalence up to 70 percent have been found in patients with..." Line 33: Remove the space in "follow- up." Insert a hyphen in "vision related." Lines 37-38: The sentence seems redundant with Lines 8-13. Regardless, it needs "The" in front of "ability" and a comma in front of "and." The comma in front of "can" is not needed. Lines 40-45: The term "vergence" should be used when discussing different (as opposed to near) viewing distances. Consider re-writing the sentence as "Convergence is a nasalward eye movement for near vision. Insufficient convergence is one of the most frequently described oculomotor changes after head injury." Line 47: Remove the comma after "vision)" and add a closing parenthesis and a comma after "near work."</p> <p>//Page 6. Lines 3-10: The meaning or significance of the two sentences are not clear. Line 21: Insert "or" in front of "blurred." Lines 23-24: Insert a hyphen between "vision" and "based." Line 33: Delete "to be." Line 44: Delete "a group of." Line 46: Delete the comma between "saccades" and "executed." Line 51: Delete the comma between "environment" and "and."</p> <p>//Page 7. Lines 8-10: Change "...important to control for...after trauma, and</p>
--	---

	<p>allow..." to "...important for controlling for...after trauma to allow..."</p> <p>Lines 12-19: See comments re ABSTRACT – Objectives</p> <p>Line 23: Consider adding a phrase to distinguish the present subset study from the stated parent study (both are described as a prospective controlled observational study).</p> <p>Line 25: Change "a large emergency department of a general hospital" to "an emergency department of a large general hospital."</p> <p>Lines 26-33: Move this passage under a new heading "Inclusion criteria."</p> <p>Lines 33-35: Were the groups matched for age by design or as a result. Consider moving this passage to RESULTS.</p> <p>Lines 37-40: Consider moving this passage under "Data collection."</p> <p>Lines 43-50: Consider moving this passage after the second sentence of METHODS. Change "10 individuals" to "10 persons" and "would be needed in each group" to "per group were needed" so consistent expressions are used within the paragraph.</p> <p>Lines 53-58: The passage does not appear to be correctly presented - perhaps "(i) acute brain injury...; (ii) one or more of...; and (iii) Glasgow Coma Scale...?"</p> <p>//Page 8.</p> <p>Lines 8-10: Delete "of mTBI."</p> <p>Line 19: Change "and GCS<13" to "with GCS<13."</p> <p>Lines 44-45, Table 1: Add n and (%) for consistency.</p> <p>//Page 9.</p> <p>Lines 3-8: Consolidate this passage with "Inclusion criteria" (see comment re Page 7, Lines 26-33).</p> <p>Lines 9-10: Move this passage to the first paragraph of METHODS or under "Data collection."</p> <p>Lines 19-21: Change ", in the subacute phase, (trauma patients 7-10 days after the trauma)" to "(for trauma patients, 7-10 days after the trauma)." Clarify the difference between the follow-up assessment plan and the actual output.</p> <p>Line 28: Change "The mTBI and patients with" to "Patients with mTBI or." See General comments re the use of the term "mTBI."</p> <p>Line 31: Insert a comma after "At baseline and follow-up."</p> <p>Line 45: Change "valid and reliable instrument, which" to "validated and reliable instrument that."</p> <p>Lines 55-58: Use a complete sentence.</p> <p>//Page 10.</p> <p>Line 42: Reviewer 3's comment was not followed up completely as "0.5°" is still missing.</p> <p>//Page 11.</p> <p>Line 14: Clarify what ANOVA was used for.</p> <p>Lines 18-21: Move the passage under "Assessments" (perhaps after structural and functional MRI).</p> <p>Lines 25-27: It was by design that 15 subjects were included in each group. Move this passage to METHODS.</p> <p>Lines 34-54: Move this passage to METHODS. See comments re Page 9, Lines 19-21. Also, see General comments re the use of the term "mTBI." "17 mTBI and 82 orthopaedic controls" reads like "17 mTBI controls and 82 orthopaedic controls." Change the passage to "17 mTBI and 82 orthopaedic subjects." Similarly, Change "88% of mTBI patients and 64% of orthopaedic controls" to "88% of mTBI and 64% of orthopaedic subjects."</p> <p>//Page 12.</p> <p>Lines 4-8: Please determine if the Kruskal-Wallis test is needed.</p>
--	--

	<p>Lines 36-38, 48-50: Specify the test used and the terms of interaction (e.g. group by time). From my point of view, a paired t-test is the most appropriate tool for the stated objective.</p> <p>//Page 13.</p> <p>Lines 7-11: My previous comment was not addressed sufficiently. That is, the sentence is grammatically incorrect, and "...reduced positive fusional vergence...was...marginally reduced..." is semantically incorrect. I think what is meant is "...reduced positive fusional vergence...was found in four mTBI patients and four orthopaedic controls. None of the non-injured controls had reduced fusional vergence." Clarify.</p> <p>Lines 14-22: Specify the statistical tests used.</p> <p>Lines 26-33: Specify the statistical tests used. Add a word or phrase after "performed," e.g. "at the level of." Add "(lower)" after "better." Insert a comma after "120-240 at baseline." Remove the subject ID, which is not relevant. "TNO" is undefined.</p> <p>Line 48: Specify the statistical test used.</p> <p>Line 56: Insert a comma after "12 patients."</p> <p>//Page 14.</p> <p>Lines 48-52: Summarize the findings echoing in a parallel manner the specific study objectives listed in Page 7.</p> <p>//Page 15.</p> <p>Line 3: Remove the hyphen from "brain-injury."</p> <p>Line 6: Change "recall bias, biopsychosocial" to "recall bias and biopsychosocial."</p> <p>Line 8: Change "also are" to "are also."</p> <p>Line 11: Change "scope for" to "scope of." "Objective measures" of what? Specify ("measures of the severity of mTBI," or perhaps "measures of an injury after a suspected one"?).</p> <p>Line 26: I dispute that the authors' response to my previous comment. I once again visited the Capo-Ante et al. paper and found the reporting of the mean rather than the median. Regarding the interpretation of the data, I am not an ophthalmologist or optometrist, and therefore not in any position to suggest following either von Noorden & Campos or Scheiman & Wick. However, the way the two reference books were contrasted previously was awkward, and I suggested a solution as "may or may not be considered clinically meaningful (cite both books)," which the authors accepted. Thus, clearly, now the sentence "On the other hand, according to established criteria for CI, any NPC greater than six cm is considered insufficient" is unnecessary.</p> <p>//Page 16.</p> <p>Line 3: Change "In accordance to previous studies" to "In agreement with a previous study."</p> <p>Lines 13-16: Change "To our knowledge there is quite limited research available" to "We know little." Add "in accommodation" (or another specifying term) after "spontaneous improvement."</p> <p>Line 23: Clarify who needs to be aware of possible accommodative disorders, or rewrite the sentence.</p> <p>Line 29: Specify the unit of measure.</p> <p>//Page 17.</p> <p>Lines 48-49: Delete "To our knowledge there are no another published reports..." The sentence is not informative and also grammatically incorrect.</p>
--	--

REVIEWER	Alexandre Reynaud Université McGill, Canada
REVIEW RETURNED	27-Oct-2017

GENERAL COMMENTS	<p>The authors partially followed the suggestions of the reviewers. I definitely think the manuscript would really benefit of presenting more data and in a more intelligible way. The authors reported slightly different versions in their response document and in the manuscript, and even if minor mentioned they made some suggested changes but in fact didn't apply them. I don't get why the authors are so reluctant at following advices which only purpose is to make the article more clear. As a reviewer I feel very offended by this behaviour.</p> <p>I still think it would be worth showing this data, maybe merging some figures together or indeed, as suggested, in an appendix/supplementary document.</p> <p>Non exhaustively, for instance at least the results of the visual examination and stereo acuity should appear, preferably in the manuscript.</p> <p>It is clearly stated in Fig1 caption, and clearly visible on the figure : "The x's indicate outliers". If they were included in the analysis there is no reason to mark them on the figure. Please explain</p> <p>Generally, I still think that most tables and figures should be reformatted to provide more data, in a more intelligible way.</p> <p>Still. There are still a lot of abbreviations, I don't think it is a big effort to just add a glossary at the end</p> <p>So the actual values must also appear in the abstract, introduction, and methods too. not the planned ones</p> <p>Some paragraphs have been deleted, it would have been practical to illustrate it clearly. It would also have been useful to number lines in the .doc document. There are still a few english mistakes here and there.</p>
-------------------------	--

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Nabin Joshi

Institution and Country: SUNY College of Optometry, USA Please state any competing interests:

None declared

Please leave your comments for the authors below

Comment: Thank you for making the changes as suggested. The changes in my opinion, are adequate. Thank you for undertaking a prospective study in mTBI, which shows some natural recovery in objective measurements. However, symptoms did persist in many patients, and the need some form of remediation should also be highlighted, especially in this subset.

Response: Thank you. We agree that there is a need for further research on treatment methods in case of persistent symptoms after mTBI and to establish if these interventions are effective. From the visual functioning point of view we have highlighted the need of intervention when appropriate, e.g. spectacle lenses for near work and/or vision therapy. This is discussed in "Future recommendations".

Reviewer: 2

Reviewer Name: Jun Maruta

Institution and Country: Assistant Clinical Professor, Department of Rehabilitation Medicine, Icahn School of Medicine at Mount Sinai, USA Please state any competing interests: None declared

Please leave your comments for the authors below

[General comments] I still found the manuscript to be problematic. To some degree, the authors seem to have lost sight of the forest for the trees while revising.

Thank you for your effort in assisting us in improving this manuscript. We have made several further changes in the manuscript to make it easier to read. We have made it clear in the objectives that there are two separate control groups, reorganized the results and discussion to concisely echo the stated objectives, and changed the presentation of Inclusion and Exclusion criteria.

Mainly, I am concerned that the Kruskal-Wallis test and ANOVA may have been used without a clear purpose, given that the first objective of the study is to compare mTBI patients with control subjects, rather than to detect a difference across the three groups involved. If these statistical tests are deemed appropriate, a finding of a difference among the groups should be followed up with an appropriate post-hoc test, rather than proceeding to multiple two-group comparisons.

Response: Thank you for the comment. We have had a new consultation with a statistician and after further consideration still consider these tests to be appropriate, as discussed below. We did receive a recommendation to present U value instead of z value when presenting statistics from Man Whitney U test.. And the appropriate change has been made.

We have clarified now that the first objective of the study was to compare mTBI group with two control groups: orthopaedic control group and non-injured control group. Regarding the statistical test used, repeated measures ANOVA and Kruskal-Wallis tests were performed in order to avoid several paired t-tests, that could increase the risk of type I error. A post-hoc test was conducted only if ANOVA or Kruskal- Wallis test showed statistical significance. Repeated measures ANOVA is the test, which can analyse repeated measurements (on several occasions) in several groups in one and the same analysis. There were two post-hoc tests used: Holm-Bonferroni (following ANOVA) and Man-Whitney U test (following Kruskal-Wallis test).

Comment: I think that the overall presentation can still be much improved by organizing RESULTS/DISCUSSION to concisely echo the stated objectives.

Response: Thank you for a very helpful suggestion. We have now re-organised RESULTS and DISCUSSION to concisely echo the stated objectives, and at the same time improved readability by rewriting several parts of the RESULTS.

Comment: There are still some passages that do not seem to be expressed in correct English.

Response: The manuscript has been edited and corrected by native English speaker.

Comment: Also, "mTBI" seems to be incorrectly used in some places to refer to people rather than a condition.

Response: Thank you for pointing this out. We have made necessary changes.

[Specific comments]

//Title.

The title is awkward. In particular, "Swedish" seems misplaced. Consider "Longitudinal changes in oculomotor function in young adults with mild traumatic brain injury in Sweden - an exploratory prospective observational study," or "Longitudinal changes in oculomotor function in young adults with mild traumatic brain injury - a prospective observational exploration in Sweden."

Response: Thank you, as suggested, we have changed the title as follows:

"Longitudinal changes in oculomotor function in young adults with mild traumatic brain injury in Sweden - an exploratory prospective observational study".

//Page 2, ABSTRACT.

Objectives: The first objective seems to contain two ideas. Consider specifying them as "1) whether visual disturbances can be...compared to controls, 2) whether such objectively demonstrated disturbances change over time."

Response: Thank you for suggesting this important clarification.

We have specified the first two study objectives as suggested:

"1) whether visual disturbances can be demonstrated with objective measures more often in patients with mild traumatic brain injury (mTBI) than in orthopaedic controls and non-injured controls, 2) whether such objectively demonstrated disturbances change over time".

Outcome measures: Use a parallel construction, e.g. "Visual examination including..." and "Symptom assessment using..."

Response: Thank you, we have changed to "visual examination including..." (page 2, line 13)

Results: Reorganize so that the findings echo the stated objectives.

Response: We agree that this is important, thank you. We have now reorganized the results section as suggested.

Change "significantly" to "statistically."

Response: Thank you for the suggestion to change "significantly" to "statistically". We considered that this might be a little unclear to the reader, and therefore we have chosen to retain both terms. So, the text now reads "statistically significantly". (page 2, line 23)

Remove the p-values because what is compared is unclear.

Response: We have removed all p values from the ABSTRACT.

Conclusion: Change "There are" to "There were."

Response: We have changed as suggested. (page 2, line 27)

//Page 5.

Line 6: Define the acronym "mTBI" – Also change "mild traumatic brain injury" (Lines 11-13) to "mTBI."

Response: We have changed as suggested. (page 5, lines 2-3 and line 6)

Lines 8-9: "Oculomotor" and "eye movements" are redundant. Rephrase. Also, insert a comma after "eye alignment."

Response: Thank you for this valuable comment, we have rephrased and made changes as suggested. (page 5, lines 4-6)

Line 11: Change "a possible correlate" to "possible correlates."

Response: Thank you, we have changed as suggested. (page 5, line 5)

Line 14: Consider changing "promising, yet preliminary" to "preliminary but promising."

Response: Thank you, we agree and have changed as suggested. (page 5, line 7)

Line 18: Change "...after mTBI, but..." to "...after mTBI; however, ..."

Response: We have changed as suggested. (page 5, line 9)

Line 22: Change "visual networks" to "vision-related networks."

Response: Thank you, we have changed as suggested. (page 5, line 11)

Lines 24-26: Consider changing "Visual impairments of different kinds have been found in several studies with prevalence up to 70 percent in a cohort of patients with..." to "Various visual impairments with a prevalence up to 70 percent have been found in patients with..."

Response: We have changed as suggested. (page 5, lines 13-14)

Line 33: Remove the space in "follow- up." Insert a hyphen in "vision related."

Response: We have changed as suggested. (page 5, line 17)

Lines 37-38: The sentence seems redundant with Lines 8-13. Regardless, it needs "The" in front of "ability" and a comma in front of "and." The comma in front of "can" is not needed.

Response: Thank you, we have rephrased the sentence, and we have made changes accordingly. (page 5, lines 19-20)

Lines 40-45: The term "vergence" should be used when discussing different (as opposed to near) viewing distances. Consider re-writing the sentence as "Convergence is a nasalward eye movement for near vision. Insufficient convergence is one of the most frequently described oculomotor changes after head injury."

Response: Thank you for pointing this out, we have rewritten the sentences as suggested. (page 5, lines 21-23)

Line 47: Remove the comma after "vision)" and add a closing parenthesis and a comma after "near work."

Response: We have made changes as suggested. (page 5, lines 23-24)

//Page 6.

Lines 3-10: The meaning or significance of the two sentences are not clear.

Response: We agree with this comment. We removed these two sentences.

Line 21: Insert "or" in front of "blurred."

Response: We have made this insertion as suggested. (page 5, line 31)

Lines 23-24: Insert a hyphen between "vision" and "based."

Response: We have made this insertion as suggested. (page 6, lines 1-2)

Line 33: Delete "to be."

Response: We have made this change as suggested. (page 6, line 8)

Line 44: Delete "a group of."

Response: We have made this change as suggested. (page 6, line 14)

Line 46: Delete the comma between "saccades" and "executed."

Response: We have made this change as suggested. (page 6, line 15)

Line 51: Delete the comma between "environment" and "and."

Response: We have made this change as suggested. (page 6, line 18)

//Page 7.

Lines 8-10: Change "...important to control for...after trauma, and allow..." to "...important for controlling for...after trauma to allow..."

Response: We have made this change as suggested. We have made changes as suggested. (page 6, line 25)

Lines 12-19: See comments re ABSTRACT – Objectives

Response: Thank you for pointing this out. We have made changes as suggested. (page 6, lines 28-30)

Line 23: Consider adding a phrase to distinguish the present subset study from the stated parent study (both are described as a prospective controlled observational study).

Response: Thank you for the comment. We have rewritten the sentence to clarify that this is a first article from this prospective controlled observational study. We aim to report cognitive and fatigue measures as well as imaging findings in another article. (page 7, lines 2-4)

Line 25: Change "a large emergency department of a general hospital" to "an emergency department of a large general hospital."

Response: We have made the change as suggested. (page 7, line 4)

Lines 26-33: Move this passage under a new heading "Inclusion criteria."

Response: Thank you for this suggestion. We have rewritten this section with, as suggested, a new heading "Inclusion criteria", and in order to be consistent, we also changed the presentation of exclusion criteria.

Lines 33-35: Were the groups matched for age by design or as a result. Consider moving this passage to RESULTS.

Response: Thank you. We excluded the sentence about age matching in the Methods section, and clarified that age between 18 and 40 years was an inclusion criteria for all groups. (page 7, line 12)

Lines 37-40: Consider moving this passage under "Data collection."

Response: Thank you, we agree that moving this passage under "Data collection" improve clarity, and have made the change as suggested. (page 9, lines 2-4)

Lines 43-50: Consider moving this passage after the second sentence of METHODS.

Response: Thank you, this change also improves clarity. We have moved the passage about power calculation after the second sentence in METHODS as suggested. (page 7, lines 6-10)

Change "10 individuals" to "10 persons" and "would be needed in each group" to "per group were needed" so consistent expressions are used within the paragraph.

Response: We have made the change as suggested. (page 7, lines 6-10)

Lines 53-58: The passage does not appear to be correctly presented - perhaps "(i) acute brain injury...; (ii) one or more of...; and (iii) Glasgow Coma Scale..."?

Response: Thank you for pointing this out, we have clarified the text to read: "mTBI is an acute brain injury resulting from mechanical energy to the head from external physical forces. Operational criteria for clinical identification include: (i) 1 or more of the following...." (page 7, lines 17-21)

//Page 8.

Lines 8-10: Delete "of mTBI."

Response: We have changed as suggested. (page 7, line 25)

Line 19: Change "and GCS<13" to "with GCS<13."

Response: In order to improve readability, we have removed this sentence which was tautologous since the inclusion criteria stated "...GCS score of 13-15..." (page 7, lines 23-24)

Lines 44-45, Table 1: Add n and (%) for consistency.

Response: We added "n" and "%" as suggested, and for consistency, removed "%" from type of trauma figures. (page 8, Table 1)

//Page 9.

Lines 3-8: Consolidate this passage with "Inclusion criteria" (see comment re Page 7, Lines 26-33).

Response: Thank you for this suggestion. We have reorganised the inclusion section with a new sub-heading "Inclusion criteria" in the METHODS. We have rewritten this passage and moved a part of this sentence to "Data collection". (page 9, lines 4-5)

Lines 9-10: Move this passage to the first paragraph of METHODS or under "Data collection."

Response: We have moved this sentence to "Data collection". (page 9, lines 5-6)

Lines 19-21: Change ", in the subacute phase, (trauma patients 7-10 days after the trauma)" to "(for trauma patients, 7-10 days after the trauma)."

Response: Thank you for your comment, we have rewritten this sentence as suggested. (page 9, lines 11)

Clarify the difference between the follow-up assessment plan and the actual output.

Response: Thank you for this valuable comment. We have clarified the difference between the assessment plan and actual output in Abstract as well as in Methods. (page 2, lines 17-18 and page 9, lines 13-18)

Line 28: Change "The mTBI and patients with" to "Patients with mTBI or." See General comments re the use of the term "mTBI."

Response: Thank you for the comment. We have made the change as suggested. (page 9, line 22)

Line 31: Insert a comma after "At baseline and follow-up."

Response: We have made the change as suggested. (page 11, line 3)

Line 45: Change "valid and reliable instrument, which" to "validated and reliable instrument that."

Response: We have made the change as suggested. (page 11, line 11)

Lines 55-58: Use a complete sentence.

Response: Thank you for this comment. We have changed "giving" to "gives" to make a complete sentence. (page 11, line 17)

//Page 10.

Line 42: Reviewer 3's comment was not followed up completely as "0.5°" is still missing.

Response: Thank you for pointing that out, now we have changed as suggested (0.5 degrees). (page 10, line 27)

//Page 11.

Line 14: Clarify what ANOVA was used for.

Response: Thank you for the comment. We have now clarified this in the "Data analysis". The two-way repeated measures ANOVA was used for analysing the within-subject factors (baseline vs. follow-up) and the between subject factor (effect of group). (page 11, lines 22-24)

Lines 18-21: Move the passage under "Assessments" (perhaps after structural and functional MRI).

Response: We have moved this text, as suggested, to after the description of imaging in the section on "Data collection". The "Assessments" section is reorganised, to be consistent with study objectives. (page 10, lines 1-4)

Lines 25-27: It was by design that 15 subjects were included in each group. Move this passage to METHODS.

Response: Thank you for this suggestion, we have moved this text accordingly. (page 9, lines 4-5)

Lines 34-54: Move this passage to METHODS. See comments re Page 9, Lines 19-21.

Response: Thank you, we have moved this text to METHODS as suggested. (Page 9, lines 13-18)

Also, see General comments re the use of the term "mTBI." "17 mTBI and 82 orthopaedic controls" reads like "17 mTBI controls and 82 orthopaedic controls." Change the passage to "17 mTBI and 82 orthopaedic subjects." Similarly, Change "88% of mTBI patients and 64% of orthopaedic controls" to "88% of mTBI and 64% of orthopaedic subjects."

Response: Thank you, we agree that it is a relevant point. We have changed the text accordingly. (page 9, lines 29-30)

//Page 12.

Lines 4-8: Please determine if the Kruskal-Wallis test is needed.

Response: Thank you for this valuable comment. Kruskal-Wallis tests were performed for comparison of ordinal data between three groups. The use of two control groups is now clarified early in the manuscript, that is, in the first objective of the study.

Lines 36-38, 48-50: Specify the test used and the terms of interaction (e.g. group by time). From my point of view, a paired t-test is the most appropriate tool for the stated objective.

Response: We have specified the statistical methods in "Data analysis" and described interaction effect of the group and over time (baseline vs. follow-up) in the RESULTS section.

//Page 13.

Lines 7-11: My previous comment was not addressed sufficiently. That is, the sentence is grammatically incorrect, and "...reduced positive fusional vergence...was...marginally reduced..." is semantically incorrect. I think what is meant is "...reduced positive fusional vergence...was found in four mTBI patients and four orthopaedic controls. None of the non-injured controls had reduced fusional vergence." Clarify.

Response: Thank you for pointing this out. We have rewritten this part of the RESULTS and clarified that there was no significant difference in fusional vergence at the group level at any time point.

Lines 14-22: Specify the statistical tests used.

Response: We have used the ANOVA to analyse the results of saccade performance and this now is clarified in the RESULTS section. (page 13, line 1-5)

Lines 26-33: Specify the statistical tests used.

Response: Results of stereo acuity are presented with descriptive statistics.

Add a word or phrase after "performed," e.g. "at the level of." Add "(lower)" after "better." Insert a comma after "120-240 at baseline." Remove the subject ID, which is not relevant.

Response: Thank you for these comments, we agree and have rewritten the section on stereo acuity in RESULTS. Subject ID has been removed. (page 13, lines 4-9)

"TNO" is undefined.

Response: Thank you for pointing this out. TNO - test for stereoscopic vision (The Netherlands Organisation for Applied Scientific Research), is now defined in the attached List of abbreviations. (page 22)

Line 48: Specify the statistical test used.

Response: We have specified that the statistical test used was the Wilcoxon signed ranks test. (page 13, lines 20)

Line 56: Insert a comma after "12 patients."

Response: We have rewritten this part of the RESULTS and removed this sentence.

//Page 14.

Lines 48-52: Summarize the findings echoing in a parallel manner the specific study objectives listed in Page 7.

Response: Thank you for this valuable comment that makes the manuscript more readable. We have re-organised the DISCUSSION to summarize the findings in our study. We have identified and shortened some sections in the DISCUSSION that were repetitive. (pages 15-16)

//Page 15.

Line 3: Remove the hyphen from "brain-injury."

Response: We have made this change as suggested. (page 16, line 25)

Line 6: Change "recall bias, biopsychosocial" to "recall bias and biopsychosocial."

Response: Thank you for this comment. We have rewritten this sentence. (page 16, lines 20-21)

Line 8: Change "also are" to "are also."

Response: We have changed this as suggested. (page 16, line 22)

Line 11: Change "scope for" to "scope of."

Response: We have removed this sentence and rewrote this section.

"Objective measures" of what? Specify ("measures of the severity of mTBI," or perhaps "measures of an injury after a suspected one"?).

Response: Thank you for this important comment. We have rewritten this section and removed this sentence.

Line 26: I dispute that the authors' response to my previous comment. I once again visited the Capo-Ante et al. paper and found the reporting of the mean rather than the median.

Response: We have changed "median" to "mean". (page 14, line 31)

Regarding the interpretation of the data, I am not an ophthalmologist or optometrist, and therefore not in any position to suggest following either von Noorden & Campos or Scheiman & Wick. However, the way the two reference books were contrasted previously was awkward, and I suggested a solution as "may or may not be considered clinically meaningful (cite both books)," which the authors accepted. Thus, clearly, now the sentence "On the other hand, according to established criteria for CI, any NPC greater than six cm is considered insufficient" is unnecessary.

Response: We agree. The sentence has been removed accordingly.

//Page 16.

Line 3: Change "In accordance to previous studies" to "In agreement with a previous study."

Response: We have changed this as suggested. (page 14, line 16)

Lines 13-16: Change "To our knowledge there is quite limited research available" to "We know little." Add "in accommodation" (or another specifying term) after "spontaneous improvement."

Response: We have made these changes as suggested. (page 14, lines 22-23)

Line 23: Clarify who needs to be aware of possible accommodative disorders, or rewrite the sentence.

Response: We have rewritten this sentence and moved it to the "Future recommendations". (page 17, lines 22-24)

Line 29: Specify the unit of measure.

Response: We have added a specification of the unit as "seconds of arc". (page 15, line 19)

//Page 17.

Lines 48-49: Delete "To our knowledge there are no another published reports..." The sentence is not informative and also grammatically incorrect.

Response: We have removed this sentence.

Reviewer: 3

Reviewer Name: Alexandre Reynaud

Institution and Country: Université McGill, Canada Please state any competing interests: None declared

Please leave your comments for the authors below see attached file

Comment: The authors partially followed the suggestions of the reviewers. I definitely think the manuscript would really benefit of presenting more data and in a more intelligible way. The authors reported slightly different versions in their response document and in the manuscript, and even if minor mentioned they made some suggested changes but in fact didn't apply them. I don't get why the authors are so reluctant at following advices which only purpose is to make the article more clear. As a reviewer I feel very offended by this behaviour.

Response: Thank you for your further comments. We are grateful for the reviewers' new suggestions and previous comments, and apologise that a couple of the previous points had been missed in the first revision. These have now been addressed.

In order to improve intelligibility, the article has been restructured in view of this and other reviewers' comments.

A list of abbreviations is now included at the end of the manuscript.

The method of data presentation has been changed, again to improve intelligibility: table 2 has been removed and the data instead presented in a new figure, 3ab.

Earlier response: We recognize that there are a lot of data in this study. In our attempt to keep structure in the paper we chose to focus on the statistically significant findings. We are happy to report all data, perhaps in an appendix, if that is a common request by the journal. The journal also requires using no more than up to 5 figures/tables for readability.

Comment: I still think it would be worth showing this data, maybe merging some figures together or indeed, as suggested, in an appendix/supplementary document.

Non exhaustively, for instance at least the results of the visual examination and stereo acuity should appear, preferably in the manuscript.

Response: Thank you for your comments and we agree that there was room for improvement regarding clarity of the tables and figures.

We have therefore removed table 2 and instead added a new figure (Figure 3 a, b). Results of stereo acuity are presented in a new, specific section in the results. Furthermore, we have thoroughly discussed different options for showing individual data. Whilst we agree with the principles of benefits of data sharing, we must also work within the ethical approval for the study, which approved reporting of data at the group level. With a small data set we must also consider privacy issues, there being some risk of identifying individuals as age, sex, and hospital attended are all included in the data set. We have therefore applied to the ethical review board for permission to release data regarding the optometric measures, with age and sex removed to protect privacy. Once ethical approval for data sharing is received, we can make this data available. As this is likely to take some time, we have added a phrase to the manuscript "further data may be available from the authors. Please contact the corresponding author". (page 18, lines 21-22)

Fig1: which criterion was used to determine outliers? was the analysis performed excluding them in p11 ?

Earlier response: No, outliers were not excluded from the analyses.

Comment: It is clearly stated in Fig1 caption, and clearly visible on the figure : "The x's indicate outliers". If they were included in the analysis there is no reason to mark them on the figure. Please explain

Response: Thank you for pointing this out. We have removed the outlier indicators in figure 1 and 2 and adjusted the figure legends accordingly. (page 21, lines 26-33)

Comment: Table 2 and its description are very confusing, why not making a figure ?

Maybe a scatterplot baseline/follow up, with different colors/symbols for groups and diagnosis

Earlier response: Thank you for this suggestion. We have considered other options for presenting the data but for now we would like to suggest keeping the table since we think a graph covering all these aspects may be quite complex to interpret. We are of course willing to discuss any further suggestions.

Comment: Generally, I still think that most tables and figures should be reformatted to provide more data, in a more intelligible way.

Response: Thank you for this valuable comment. We now have replaced Table 2 with a new figure 3, which we hope will make the data easier to comprehend.

Comment: Given the numerous abbreviations used, I would suggest to add a glossary at the end of the article

Earlier response: we have discussed this, and we removed LOC, PTA and ACRM.

Comment: Still. There are still a lot of abbreviations, I don't think it is a big effort to just add a glossary at the end

Response: Thank you, we do agree, this is a relevant suggestion. We have now attached List of abbreviations at the end of the manuscript. (pages 22-23)

Comment: testing periods are inconsistent between 2-29 7-53 and 10-13

Response. Thank you for this comment. We have clarified the testing periods in the Results section, and we have added a sentence to read as follows: "In order to minimize drop outs, we extended the planned follow-up time."

Comment: So the actual values must also appear in the abstract, introduction, and methods too. not the planned ones.

Response: We are grateful for this comment. Deviation from the planned testing periods was due to difficulties getting hold of the patients. We now have clarified actual testing periods in Abstract and in Methods. However, we have not added testing periods in Introduction since this is not mentioned in previous version of the manuscript.

9-13: 5mm, please report in degrees

Response: Done (0.5 degrees)

Comment: No, you didn't

Response: Thank you for pointing this out, we are very sorry that we missed adding this in our previous version of the manuscript. Now we have added 0.5 degrees. (page 10, line 27)

Comment: Some paragraphs have been deleted, it would have been practical to illustrate it clearly. It would also have been useful to number lines in the .doc document. There are still a few english mistakes here and there.

Response: Thank you for these comments. We have added line numbers in the manuscript and highlighted the changes in the manuscript by using the Track changes mode in the .doc(x) document. The manuscript has been edited and corrected by native English speaker.

VERSION 3 – REVIEW

REVIEWER	Jun Maruta Assistant Clinical Professor Department of Rehabilitation Medicine Icahn School of Medicine at Mount Sinai USA
REVIEW RETURNED	12-Dec-2017

GENERAL COMMENTS	<p>[General comments] The presentation can still be improved. The pronoun "this" is often used ambiguously--clarifying what "this" refers to may improve the logical flow between sentences. Some abbreviations are introduced unnecessarily--those that are not used, used only once, or used only in a table should be removed from the text and/or the accompanying list. Overall, the manuscript should be more carefully proofread. See specific comments, although the list will not be exhaustive.</p> <p>[Specific comments] //Page 2, ABSTRACT. Results: The criteria for including specific results are not clear. Consider removing the sentence about saccade performances, or add the results of visual acuity and stereo acuity measures. (Line 40) Change "compare" to "compared." (Lines 40-42) Provide a point of reference. For example, "Six out of 13...at follow-up compared to..."</p> <p>//Page 5. Line 7: Remove the comma after "(mTBI)." Lines 14-19: The sentence is awkward. "Sufficient" and "enough" are redundant. Consider rewriting the sentence as "Although measurement of oculomotor functions appears useful in detecting changes after mTBI, the current evidence does not have a sufficient strength to inform clinical guidelines." Line 28: Remove "several." Line 56: Change "Fusion vergence" to "Fusional vergence" so the term is used consistently.</p> <p>//Page 6. Lines 3-4: Change "an otherwise healthy population with vision-based symptoms" to "a population with vision-based symptoms who are otherwise healthy." Line 22: Change "in the subacute stage, and also as part of" to "in the subacute stage and in a later stage as part of."</p> <p>Line 26: Change "shift" to "can direct." A saccade does not always direct the gaze to the area of interest, e.g. intrusive saccade during ocular pursuit, saccades in darkness, anti-saccades, quick phases of nystagmus. Line 43: Remove the comma after "orthopaedic injury." Lines 43-46: The sentence is awkward. Consider re-writing it as "The orthopaedic group allows evaluation of brain injury-specific</p>
-------------------------	---

	<p>effects by controlling for non-specific effects of pain and distress after trauma."</p> <p>//Page 7. Line 17: Change "needed" to "judged necessary." Line 24: Change "All study participants were 18-40 years of age" to "Study participants needed to be between 18 and 40 years of age." Line 37: Change "include" to "included." Line 56: The abbreviation "CT" is not defined until Page 9. The meaning of "on clinical indication" is not clear in the context of inclusion criteria--consider removing the phrase.</p> <p>//Page 8. Lines 8 and 11: Use a consistent structure ("Did not require surgery," "Did not have traumatic injury").</p> <p>//Page 9. Lines 5-8: Change "Inclusion" and "included" to "Subject recruitment" and "enrolled," respectively. Insert a comma after "15 orthopaedic controls." Lines 24-33: When neuropsychological testing and visual assessment took place on separate days, which day was used to calculate the median and range? Specify (e.g. "The median time between injury and baseline visual assessment was..."). Lines 35-37: The one sentence paragraph seems misplaced. Consider incorporating it with the previous paragraph, perhaps after the sentence about extension of testing time frames. Lines 44 & 46: "HADS" or "FSS" is not used subsequently.</p> <p>//Page 10. Line 25: Remove "The" from "The expected accommodative amplitude was defined..." Line 26: Add "The deviation from expected amplitude was scored." Lines 40-44: The list is awkwardly constructed. Consider re-writing the passage as "We used three test paradigms: (1) pro-saccades; (2) anti-saccades; and (3) self-paced saccades... In the pro-saccade paradigm,...to the left or right of the cross. The performance was characterized with mean latency and positional gain. In the anti-saccade paradigm,... The performance was characterized with..."</p> <p>//Page 11. Lines 17-20: Remove the sentence as its relevance is not clear.</p> <p>//Page 12. Line 12: The sentence seems misplaced. Consider moving it immediately after "Neither required surgery." Line 17: Specify the terms of interaction. For example, re-write the sentence as "A significant effect of interaction between group and test occasions was found in the ANOVA..." Line 18: Remove "ensuing." Lines 25-28: Re-write the sentence as "Six out of 13 patients with mTBI met the diagnostic criteria for AI at follow-up, whereas..."</p> <p>Lines 37-38: The sentence does not seem to reflect what an ANOVA would show. Lines 39-44: Re-write the passage as "The ANOVA showed a significant interaction effect (...), and the post-hoc analysis showed a significant difference in the mTBI group between baseline and follow-up (p=...) with improvement at follow-up (Figure 2)." Line 52: Change "The analysis of fusional vergence" to "The</p>
--	---

	<p>ANOVA on fusional vergence."</p> <p>//Page 13. Lines 3-4: Use a parallel structure--change "whilst..." to "whilst one patient showed a reduced level at follow-up." Line 10: Please tell us if the groups were different. Lines 13-20: Move "(ANOVA)" from the last sentence to the first sentence of the paragraph.</p> <p>//Page 14. Line 6: Change "between" to "among." Lines 8-19: Please report the scores. Lines 29, 32, 53, etc.: Remove "significant/significantly"--the study found a difference based on statistical significance, rather than a significant difference. Lines 34-39: Clarify what "This" is. Replace "six patients" with "almost half of the patients. Delete the second sentence ("This corresponds to..."). Line 42: Remove "persisting," which is redundant with "in the long term." Lines 49-53: Re-write this passage as "The finding of non-significant differences in NPC among groups is in contrast to that by Capo-Aponte and co-workers."</p> <p>//Page 15. Line 12: Remove "motor." Line 17: Change "sensory-motor" to "sensorimotor." Lines 18-21: Clarify what is meant by "the actual test condition for NPC" (the push-up method used in the current study?). Remove "must." Line 22: Clarify what "This" is. The sentence seems to read "convergence effort involves voluntary effort." Lines 32-34: Change "all but one performed normally" to "only one showed deficiency." Clarify what is contrasted. Line 37: Insert "in the acute stage" after "in the mTBI group." Line 46: Remove "several."</p> <p>//Page 16. Line 17: Insert "correlation" after "This." Line 20: Clarify what "This" is. Line 25: Clarify what "this" is.</p> <p>//Page 17. Lines 5-6: Remove the commas. Line 34: Change "needs" to "need." Line 48: Remove the comma. Line 51: Change the passage to "...further evaluation. Accommodation insufficiency could be..."</p>
--	---

REVIEWER	Alexandre Reynaud McGill University, Canada
REVIEW RETURNED	18-Dec-2017
GENERAL COMMENTS	I am glad the authors finally followed the reviewers recommendations. I think the manuscript is much improved and I would only suggest that the authors extend the figure 3 caption and

	description in order to make it more intelligible
--	---

VERSION 3 – AUTHOR RESPONSE

Reviewer: 2

Reviewer Name: Jun Maruta

Institution and Country: Assistant Clinical Professor, Department of Rehabilitation Medicine, Icahn School of Medicine at Mount Sinai, USA

Please state any competing interests: None declared

Please leave your comments for the authors below

[General comments]

The presentation can still be improved. The pronoun "this" is often used ambiguously--clarifying what "this" refers to may improve the logical flow between sentences.

Some abbreviations are introduced unnecessarily--those that are not used, used only once, or used only in a table should be removed from the text and/or the accompanying list. Overall, the manuscript should be more carefully proofread. See specific comments, although the list will not be exhaustive.

Response: Thank you for your suggestions how to improve the flow of the manuscript. Please see below the responses to specific comments related to the use of word "this". The list of abbreviations is shortened.

[Specific comments]

//Page 2, ABSTRACT.

Results: The criteria for including specific results are not clear. Consider removing the sentence about saccade performances, or add the results of visual acuity and stereo acuity measures. (Line 40)

Response: Thank you for this valuable comment. We have changed the sentence about saccade performance and included stereo acuity measures. (page 2, lines 19-20)

Change "compare" to "compared." (Lines 40-42)

Response: Thank you for pointing this out, we changed as suggested.

Provide a point of reference. For example, "Six out of 13...at follow-up compared to..."

Response: Thank you for your suggestion. The comparative information you proposed to include in ABSTRACT, is presented in the RESULTS (page12, lines 16-19). Since number of words in ABSTRACT is limited, the addition of this information would exceed this limit.

//Page 5.

Line 7: Remove the comma after "(mTBI)."

Response: We have made this change as suggested.

Lines 14-19: The sentence is awkward. "Sufficient" and "enough" are redundant. Consider rewriting the sentence as "Although measurement of oculomotor functions appears useful in detecting changes after mTBI, the current evidence does not have a sufficient strength to inform clinical guidelines."

Response: We have rewritten the sentence as suggested (page 5, lines 7-10).

Line 28: Remove "several."

Response: We have made the change as suggested and removed "several". (page 5, line 15)

Line 56: Change "Fusion vergence" to "Fusional vergence" so the term is used consistently.

Response: We have made the change as suggested to "Fusional vergence" (page 5, line 31)

//Page 6.

Lines 3-4: Change "an otherwise healthy population with vision-based symptoms" to "a population with vision-based symptoms who are otherwise healthy."

Response: Thank you. We have changed "an otherwise healthy population with vision-based symptoms" to "a population with vision-based symptoms who are otherwise healthy." (page 6, lines 1-2)

Line 22: Change "in the subacute stage, and also as part of" to "in the subacute stage and in a later stage as part of."

Response: We have changed "in the subacute stage, and also as part of" to "in the subacute stage and at a later stage as part of." (page 6, line 12)

Line 26: Change "shift" to "can direct." A saccade does not always direct the gaze to the area of interest, e.g. intrusive saccade during ocular pursuit, saccades in darkness, anti-saccades, quick phases of nystagmus.

Response: Thank you for the valuable comment. We have changed "shift" to "can direct". (page 6, line 14)

Line 43: Remove the comma after "orthopaedic injury."

Response: We have made the change as suggested.

Lines 43-46: The sentence is awkward. Consider re-writing it as "The orthopaedic group allows evaluation of brain injury-specific effects by controlling for non-specific effects of pain and distress after trauma."

Response: We have changed this sentence as suggested. (page 6, lines 24-26)

//Page 7.

Line 17: Change "needed" to "judged necessary."

Response: We have changed "needed" to "judged necessary". (page 7, lines 9-10)

Line 24: Change "All study participants were 18-40 years of age" to "Study participants needed to be between 18 and 40 years of age."

Response: Thank you, we have been advised that this particular form of words sounds a little clumsy, and would prefer, "For all study participants, age between 18 and 40 years was a necessary criterion for inclusion."

Line 37: Change "include" to "included."

Response: We have made the change as suggested. (page 7, line 19)

Line 56: The abbreviation "CT" is not defined until Page 9. The meaning of "on clinical indication" is not clear in the context of inclusion criteria--consider removing the phrase.

Response: We consider it important, as a part of the definition of the study population, that it is clear to the reader how the upper end of mild traumatic brain injury was defined. A clinically assessed need for a CT-brain was part of this process. We have rephrased this criterion in the interests of clarity as follows:

"CT of the brain performed on the basis of clinical need, as assessed by the ED doctor." (page 8, lines 1-2)

//Page 8.

Lines 8 and 11: Use a consistent structure ("Did not require surgery," "Did not have traumatic injury").

Response: We agree in principle, but the formulation "did not have traumatic injury" is clumsy in English. We have therefore changed the text to: "Individuals who had not suffered traumatic injury and who answered an advert recruiting to the study. (page 8, line 8)

//Page 9.

Lines 5-8: Change "Inclusion" and "included" to "Subject recruitment" and "enrolled," respectively. Insert a comma after "15 orthopaedic controls."

Response: We have made the change as suggested. (page 9, lines 3-5)

Lines 24-33: When neuropsychological testing and visual assessment took place on separate days, which day was used to calculate the median and range? Specify (e.g. "The median time between injury and baseline visual assessment was...").

Response: Thank you for pointing this out. Initially, the timing of the neuropsychological assessment was reported by counting days between the injury and the baseline or the injury and the follow-up assessment. Now we re-calculated median and range between the injury and the baseline visual assessment and the injury and the follow-up visual assessment, and clarified this as suggested. (page 9, lines 16-20)

Lines 35-37: The one sentence paragraph seems misplaced. Consider incorporating it with the previous paragraph, perhaps after the sentence about extension of testing time frames.

Response: Thank you, we have made the change as suggested. (page 9, lines 15-16)

Lines 44 & 46: "HADS" or "FSS" is not used subsequently.

Response: Thank you, we have clarified that anxiety and depression was assessed using HADS and fatigue was assessed using FSS. (page 9, lines 26-26)

//Page 10.

Line 25: Remove "The" from "The expected accommodative amplitude was defined..."

Response: We have made the change as suggested. (page 10, line 19)

Line 26: Add "The deviation from expected amplitude was scored."

Response: Thank you, we prefer "... was calculated", instead of "... was scored". (page 10, line 19)

Lines 40-44: The list is awkwardly constructed. Consider re-writing the passage as "We used three test paradigms: (1) pro-saccades; (2) anti-saccades; and (3) self-paced saccades... In the pro-saccade paradigm,...to the left or right of the cross. The performance was characterized with mean latency and positional gain. In the anti-saccade paradigm,... The performance was characterized with..."

Response: Thank you, we have changed accordingly. (page 10, lines 28-33 and page 11 lines 2-8)

//Page 11.

Lines 17-20: Remove the sentence as its relevance is not clear.

Response: We removed this sentence.

//Page 12.

Line 12: The sentence seems misplaced. Consider moving it immediately after "Neither required surgery."

Response: Thank you, we moved that sentence as suggested. (page 12, lines 6-7)

Line 17: Specify the terms of interaction. For example, re-write the sentence as "A significant effect of interaction between group and test occasions was found in the ANOVA..."

Response: Thank you for valuable comment. We have made the change as suggested (page 12, lines 10-11)

Line 18: Remove "ensuing."

Response: We have made the change as suggested. (page 12, line 12)

Lines 25-28: Re-write the sentence as "Six out of 13 patients with mTBI met the diagnostic criteria for AI at follow-up, whereas..."

Response: Thank you, we have rewritten the sentence and added comparative information. (page 12, lines 16-20)

Lines 37-38: The sentence does not seem to reflect what an ANOVA would show.

Response: We have removed the sentence.

Lines 39-44: Re-write the passage as "The ANOVA showed a significant interaction effect (...), and the post-hoc analysis showed a significant difference in the mTBI group between baseline and follow-up (p=...) with improvement at follow-up (Figure 2)."

Response: Thank you, we have rewritten the passage as suggested. (page 12, lines 23-25)

Line 52: Change "The analysis of fusional vergence" to "The ANOVA on fusional vergence."

Response: We have made the change as suggested. (page 13, line 1)

//Page 13.

Lines 3-4: Use a parallel structure--change "whilst..." to "whilst one patient showed a reduced level at follow-up."

Response: We have made the change as suggested. (page 13, lines 4-5)

Line 10: Please tell us if the groups were different.

Response: We have added information that there was no statistically significant difference between the groups and test occasions. (page 13, lines 4-5)

Lines 13-20: Move "(ANOVA)" from the last sentence to the first sentence of the paragraph.

Response: We have made the change as suggested. (page 13, line 13)

//Page 14.

Line 6: Change "between" to "among."

Response: We have made the change as suggested. (page 14 , line 8)

Lines 8-19: Please report the scores.

Response: We have added median value of RPQ sum of symptoms score at baseline and at follow-up. (page 14, lines 15-16)

Lines 29, 32, 53, etc.: Remove "significant/significantly"--the study found a difference based on statistical significance, rather than a significant difference.

Response: Thank you for valuable comment. We have changed "significant" till "statistically significant" as suggested.

Lines 34-39: Clarify what "This" is. Replace "six patients" with "almost half of the patients. Delete the second sentence ("This corresponds to...").

Response: We have clarified and changed to "accommodative amplitude". We have replaced "six patients" with "almost half of the patient", and deleted the second sentence. (page 14, line 25-26)

Line 42: Remove "persisting," which is redundant with "in the long term."

Response: We have made the change as suggested. (page 14, line 29)

Lines 49-53: Re-write this passage as "The finding of non-significant differences in NPC among groups is in contrast to that by Capo-Aponte and co-workers."

Response: We have made the change as suggested. (page 15, line 2-3)

//Page 15.

Line 12: Remove "motor."

Response: We have made the change as suggested. (page 15, line 12)

Line 17: Change "sensory-motor" to "sensorimotor."

Response: We have made the change as suggested. (page 15, line 15)

Lines 18-21: Clarify what is meant by "the actual test condition for NPC" (the push-up method used in the current study?). Remove "must."

Response: We have clarified this as suggested and removed "must". (page 15, line 16-17)

Line 22: Clarify what "This" is. The sentence seems to read "convergence effort involves voluntary effort."

Response: We have removed the sentence since we consider that it is not necessary.

Lines 32-34: Change "all but one performed normally" to "only one showed deficiency." Clarify what is contrasted.

Response: We have made the change as suggested and added cut-off value for normal stereo acuity. (page 15, lines 25-26)

Line 37: Insert "in the acute stage" after "in the mTBI group."

Response: We have made the change as suggested. (page 15, line 27)

Line 46: Remove "several."

Response: We have made the change as suggested (page 15, line 32)

//Page 16.

Line 17: Insert "correlation" after "This."

Response: We have made this insertion as suggested (page 16, line 15)

Line 20: Clarify what "This" is.

Response: We have changed "This" to "the elevated symptom score". (page 16, line 17)

Line 25: Clarify what "this" is.

Response: We have clarified that "this" concerns the association between symptoms and inefficient vergence performance. (page 16, line 20-21)

//Page 17.

Lines 5-6: Remove the commas.

Response: We have made the changes as suggested.

Line 34: Change "needs" to "need."

Response: We have made the change as suggested. (page 17, line 25)

Line 48: Remove the comma.

Response: We have made the change as suggested.

Line 51: Change the passage to "...further evaluation. Accommodation insufficiency could be..."

Response: Thank you, we have made the change as suggested. (page 18, line 5)

Reviewer: 3

Reviewer Name: Alexandre Reynaud

Institution and Country: McGill University, Canada

Please state any competing interests: none declared

Please leave your comments for the authors below

Comment: I am glad the authors finally followed the reviewers recommendations. I think the manuscript is much improved and I would only suggest that the authors extend the figure 3 caption and description in order to make it more intelligible

Response: Thank you for your suggestion, we have extended the Figure 3 caption to read as follows: Figure 3. The association between CISS score and the presence of accommodative or convergence insufficiency in patients with mTBI, orthopaedic controls and non-injured controls. The findings at baseline and at follow-up are presented in a two-by-two matrix.