Author's response to reviews

Title: Moderate to Severe Traumatic Brain Injury Self-Reported Long Term Outcomes: A Gender Based Analysis

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Version: 2 Date: 22 September 2010

Author's response to reviews: see over
Dr. Melissa Norton
Editor-In-Chief
BMC Neurology

September 13, 2010

Dear Dr. Norton,

Please find enclosed the revised version of the article ‘Moderate to Severe Traumatic Brain Injury Long Term Outcomes: A Gender Based Analysis.’ We have addressed the concerns from both the editorial office and the reviewers below. In the attached manuscript the changes have been highlighted in yellow.

Sincerely,

Angela Colantonio, PhD
Senior Scientist, Toronto Rehabilitation Institute
Professor, Department of Occupational Science and Occupational Therapy,
University of Toronto
Response to Reviewers

We thank the reviewers for their insightful questions and comments. We have addressed each query below. Changes in the attached manuscript are highlighted in yellow.

Response to Editorial Office

Request 1

*Ethics - Please confirm that appropriate ethical approval was obtained. Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate.*

Thank you for bringing this to our attention. The appropriate ethical review board information has been written in the manuscript.

Methods, Participants, page 5, paragraph 1

Ethics approval was granted from the research ethics boards at the University of Toronto and the Healthsouth Rehabilitation Center.

Request 2

*Please include an Authors’ contributions section before the Acknowledgements and Reference list.*

The requested information has been placed on Page 13.

Author’s Contributions

AC was responsible for the concept, design, coordination of the study as well as data analysis/interpretation and manuscript revisions.

JEH was responsible for data analysis and interpretation as well as the writing and revisions of this manuscript.

GR was responsible for the concept, design, and coordination of the study and manuscript approval.

SC was responsible for the concept, design, and coordination of the study as well as manuscript approval.

KE was responsible for preliminary data analysis and interpretation and manuscript approval.
Responses to Reviewer 1

Major Compulsory Revisions

Request 1

The title should be revised to be more informative to the readers. It should make reference to fact that this is a study of long term functional outcome following moderate to severe TBI using a self report scale.

We agree with the reviewer that a more descriptive title would be beneficial. We did not include the word ‘functional’ because some of the outcomes listed are impairments (e.g. dizziness, headaches) and would not be considered function according to the International Classification of Functioning and Disability.

Title Page:

Moderate to Severe Traumatic Brain Injury Self-Reported Long Term Outcomes: A Gender Based Analysis.

Request 2

The authors report that Bonferroni adjustments were made for the multiple group comparisons (page 8, line 9). However, the next sentence states “Significance level was set at p<0.05 for all comparisons”. This would suggest that a Bonferroni adjustment was not undertaken. No where in the paper (such as next to tables 2 and 3) is any reference made to what the corrected p value was set at, following a Bonferroni adjustment. This should be addressed by the authors and may have implication on the reported significant findings.

The results section and corresponding Tables 2 and 3 depict the results of gender comparisons analyzed without adjustment. To calculate the adjusted p value we considered the correlation/dependency between comparisons as calculations are based on the assumption of independence between comparisons (Sankoh et al 1997; Pavur 1988). The internal consistency of items on the PCL ranges from 0.78 to 0.91; we chose the lowest item correlation of 0.78 for our calculations. When adjustment analysis was used for multiple comparisons the α level was set at p=0.021. We have added this information to the Methods, Results and Discussion section of our paper.

Methods, analysis, page 7, paragraph 1

We also completed analysis for multiple comparisons using Bonferonni’s adjustment with correction for correlation between observations (Pavur, 1988; Sankoh et al 1997). Significance for adjusted differences was set at p≤ 0.02.

Results, page 8 paragraphs 1 and 2
Page 8, paragraph 1: Significantly more men than women reported difficulty setting realistic goals (p<0.02) whereas significantly more women than men reported headaches (p<0.03), dizziness (p<0.03), and loss of confidence (p<0.05).

Page 8, paragraph 2: Men reported sensitivity to noise (p<0.04) and sleep disturbances (p<0.04) as having a greater impact on daily functioning compared to women. Symptoms presenting significantly more of a problem in daily functioning for women compared to men was lack of initiative (p<0.02) and needing supervision (p<0.03).

Table 2, page 15 and Table 3 page 16: added asterisk to p value column to indicate adjusted p value.

Discussion, limitations, page 11, last paragraph

In addition, due to the many comparisons in our study, it is possible that some of our significant differences are spurious; however we did use an adjusted p value to minimize type 1 error.

Request 3

Another limitation that needs to be addressed is that the PCL was developed using a sample of participants with widely varying injury severity levels and whom were primarily three years post injury. Given that this current study includes a longer follow-up period, this difference should be acknowledged.

The participants in our study are described as having, on average, moderate to severe brain injuries and were a minimum of seven years post injury. We agree with the reviewer that these characteristics are not completely equivalent to the sample group used to develop the PCL. However, all ranges of severity from mild to severe are included in our sample (see Table 1, loss of consciousness, less than one hour = 12.1% of total sample). The reviewer brings forth a good observation regarding differences in length of time post injury as well. Though we agree that symptoms and their impact may differ along the chronicity continuum, the terms long-term and or chronic frequently refers to the time frame greater than one year post injury. We have addressed these issues in the limitations section of the manuscript.

Methods, limitations, Page 12, paragraph 1.

Our participants were a minimum of seven years post injury, however the PCL was developed using a sample of individuals three years post injury; there may be differences in symptoms and symptom impact when measured at a later stage of chronicity. Only 12% of our participants were classified as having a mild injury consequently, findings may not accurately represent this sub-population.

Request 4

Reference is made by the authors to use of control group data (page 12, line 23) to minimize specificity errors (i.e. symptoms reported to be due to TBI that exist in general population).
However, this is the first reference to control group data, with no such reported data in the results section.

We thank the reviewer for bringing this to our attention. There was no control group in this study. The sentence was used to illustrate this limitation but was worded awkwardly. This line has been deleted from Methods, limitations section.

**Minor Essential Revisions**

**Request 1**

Consistently throughout the paper, there are examples of awkward wording, sentence structure or spelling mistakes (for example, pg 4 line 8 “know should be known” pg 4 lines 14-16, pg 8 lines 17-19, pg 13, lines 5-6) that detract from the true impact of the paper. The authors are encouraged to seek assistance of an external reader prior to re-submission.

We thank the reviewer for bringing this to our attention and apologize for the editing mistakes. We have made all grammatical corrections.

**Request 2**

There appears to be some confusion regarding references made to papers (for example on page 4 a sentence states “and a recent systematic review [6] supported this finding but for older women only [7].” This would imply the more recent review is denoted as reference 6 but in actual fact it is listed as number 7 in the reference list.

We have reviewed the correspondence between numbered references made within the text and those numbered in the Reference List. Corrections were made for the indicated reference, no other discrepancies were found.

**Discretionary Revisions**

**Request 1**

Additional references on gender differences in functional outcome could be included specifically those that have looked at longer term outcomes.

To illustrate long term functional outcome post TBI, 16 references were used; of those 9 are directly related to gender differences. We feel this does represent the literature on gender and TBI.
Responses to Reviewer 2

Major Compulsory Revisions

Request 1

Since this is a secondary data analysis of a previous study group, it would be helpful for the authors to state what the hypothesis of this study was. Otherwise, it can be interpreted as just searching the previous data for additional "significant" findings.

This study was designed to explore long term outcomes following traumatic brain injury. In addition explanatory factors for outcome were integrated into the hypothesis and included: time since injury, injury severity, gender, and discharge functional status. We have added this information in the Methods section of the paper.

Introduction, page 4, paragraph 2

This study is part of a larger study which was designed to examine long term outcomes post TBI (Colantonio et al 2004). A study objective was to examine the impact of factors such as gender and injury severity on long term outcomes.

Request 2

On page 9 of the manuscript, 2nd paragraph, it is noted that high sex drive was reported in significantly more men (p<0.02), and the reader is referred to Table 2. However, in Table 2, under "High sex drive" has a p value reported of 0.11. The authors need to explain or correct this discrepancy.

We thank the reviewer for bringing this to our attention. Since in the revised copy of the manuscript we only present the adjusted p value, high sex drive (p<0.01) is no longer reported in the results section.

Discretionary Revisions:

Request 1

In order to determine if gender differences in symptoms are the same or different in people who have suffered TBI, a control group of non-injured patients could have been studied who were also administered the PCL. The authors should describe why this was not done.

We agree with the reviewer. We addressed this issue in the Limitations section, page 11.

Discussion, limitations, page 11, last paragraph

A main limitation of this study is the lack of a control group to ensure symptoms reported are due to the TBI and not a reflection of differences seen in the general population.
Request 2

In the Analyses section the authors describe that Bonferonni’s adjustment for multiple comparisons was used in the group differences analyses, and that significance level was set at $p<0.05$. It is not clear from the text or in the tables, if the $p$ values that are reported are Bonferonni adjusted or not. Certainly with the number of comparisons that were made there is a higher likelihood that a chance "significant" difference will be noted.

We have addressed this issue for Reviewer 1. Our response is copied here.

The results section and corresponding Tables 2 and 3 depict the results of gender comparisons analyzed without adjustment. To calculate the adjusted $p$ value we considered the correlation/dependency between comparisons as calculations are based on the assumption of independence between comparisons (Sankoh et al 1997; Pavur 1988). The internal consistency of items on the PCL ranges from 0.78 to 0.91; we chose the lowest item correlation of 0.78 for our calculations. When adjustment analysis was used for multiple comparisons the $\alpha$ level was set at $p=0.02$. We have added this information to the Methods, Results and Discussion section of our paper.

Methods, analysis, page 7, paragraph 1

We also completed analysis for multiple comparisons using Bonferonni’s adjustment with correction for correlation between observations (Pavur, 1988; Sankoh et al 1997). Significance for adjusted differences was set at $p \leq 0.021$.

Results, page 8 paragraphs 1 and 2

Page 8, paragraph 1: Significantly more men than women reported difficulty setting realistic goals ($p<0.02$) whereas significantly more women than men reported headaches ($p<0.03$), dizziness ($p<0.03$), and loss of confidence ($p<0.05$).

Page 8, paragraph 2: Men reported sensitivity to noise ($p<0.04$) and sleep disturbances ($p<0.04$) as having a greater impact on daily functioning compared to women. Symptoms presenting significantly more of a problem in daily functioning for women compared to men was lack of initiative ($p<0.02$) and needing supervision ($p<0.03$).

Table 2, page 15 and Table 3 page 16: added asterisk to $p$ value column to indicate adjusted $p$ values.

Discussion, limitations, page 11, paragraph 1

In addition, due to the many comparisons in our study, it is possible that some of our significant differences are spurious; however we did use an adjusted $p$ value to minimize type 1 error.

Request 3
In the Discussion section, 1st paragraph, the final sentence seems to be a bit overstated. Since the differences reported between men and women who are post TBI are similar in many cases to the gender differences in non-injured people, it is hard to see how a knowledge of the differences will "provide essential information to health care providers and planners for the delivery of comprehensive care...".

We have changes the sentence to a more temperate statement.

Discussion, page 9, 1st paragraph

These differences can provide information to health care providers for the planning and delivery of care for individuals with a TBI.