Author's response to reviews

Title: Effectiveness of functional splinting and the Cognitive Orientation to Occupational Performance (CO-OP) approach in children with Cerebral Palsy and Brain Injury: Two randomised controlled trial protocols

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Author's response to reviews: see over
To Whom It May Concern:

Re: Revisions to manuscript 2579059611231906. Effectiveness of functional splinting and the Cognitive Orientation to Occupational Performance (CO-OP) approach for children with cerebral palsy and brain injury: Two randomized controlled trial protocols

Thankyou for your consideration and peer review of the above study protocol manuscript, the reviewers comments are much appreciated and will make a significant contribution to improving the quality of this protocol and the overall study being conducted. Please find below the reviewers comments, followed by responses to each comment. The amended manuscript, with recommended changes, is attached.

Reviewer 1

The assumptions which sample size calculation was based on need some clarifications:

1. The sample size calculation is based on the study by Iona Novak "Occupational Therapy Home Programs for Cerebral Palsy: Double-Blind, Randomized, Controlled Trial", why should this type of intervention be the reference for sample size calculation? Why assuming an effect size of 0.9? It is not clear.

Although the Novak study may not appear to be the ideal study on which to base sample size calculation, we were unable to locate a more appropriate alternative. In seeking to locate a previously conducted study relevant to the population and intervention of the current study on which to base sample size calculations, we were unable to locate other studies that involved 3 parallel groups, cerebral palsy and brain injury (including all typographies of cerebral palsy), and that utilized the Canadian Occupational Performance Measure as the primary outcome measure.

The effect size of 0.9 was determined based on calculating a cohen effect size, utilizing Novak's mean of experimental group minus mean of control, divided by the standard deviation (5.4 – 3.2 / SD), which gave a value of 0.9. This data were not reported in the Novak article, however obtained directly from the author. The available data were then inputted into a sample size calculator, as shown below:
2. In addition, the study by Novak et al, focused only among children with CP. Children post TBI probably will increase sample variability. This has to have an effect on sample size.

The proposed trial is a pragmatic trial, designed to provide advice for selecting an intervention in a clinic where children with neurological impairment present for therapy. We have powered to account for two covariates, however it is not possible to recruit the number required to power the sample for another covariate. We acknowledge that the variability among children with CP and brain injury will lead to variability in the sample, and should have been accounted for in sample size calculations. Unfortunately, due to the current challenges being experienced with recruitment, and the time-limited nature of the study (as it is being completed as part of Ms Jackman’s PhD), we do not feel it is realistic to retrospectively increase the sample size to allow for increased variability.

3. Can you please clarify the calculations "...effect size of 0.9, power analysis for the three groups...", Performing simple calculations reveal different numbers.

*Please see justification for sample size in response to point 1.*

4. Assuming that MACS levels associate with outcomes means that this component need to be addressed during sample size calculation.

*We acknowledge that varying MACS levels will lead to increased variability in the sample, and should have been taken into account. As identified in point 2, we do not feel it is realistic to power the sample based on a greater number of covariates.*

5. A Block randomization method seems to useful method for creating comparable groups based on for example participants’ pathology, CP or TBI.

*Thankyou for this feedback and suggestion. Please note that recruitment and treatment for this study has begun, as such the randomization process would be impacted upon if we were to change the randomization method at this point during the trial.*

6. Statistical methods:

- Please clarify, what will be the method for "treating" drop outs: intention to
treat method or per protocol?

Thank you for pointing this out, please note that this statement has been updated and now reads:

“Data from all randomized participants will be analysed on an intention to treat basis. Where outcome data are unavailable, previous scores will be carried over for analysis”.

- It is not clear, which statistical test will be used for each study aim. Please add the specific potential tests.

Additions have been made to the statistical methods paragraph, and now reads:

“Participant attributes will be analysed using descriptive and inferential statistics to assess baseline comparability among the 3 treatment groups. Comparison of differences between the 3 groups in the randomised controlled trial will be analysed using multiple regression analysis, with statistical significance set at p<0.05). Data from all randomised participants will be conducted on an intention to treat basis. Where outcome data are unavailable, previous scores will be carried over for analysis. Statistical analysis for RCT1 will be conducted using 2 group comparisons on all participants, based on the box and blocks test (T1 vs T2). Statistical analysis for RCT2 will be conducted on an intention-to-treat basis at assessment at 2 weeks (T3) and 10 weeks (T4). Primary analyses at T3 and T4 compared to (T1) baseline scores, analysing between group differences will be based on the COPM and GAS scores. Secondary analysis will use the same data analytical methods for scores on the BBT and range of motion.”

7. Study hypothesis:

What is the supportive evidence for this study assumption? I am sorry but this is not clear.

Thank you for pointing this out. As discussed in the background section, under “functional hand splints combined with task-specific training’, there are differing views in clinical practice about how these interventions work, although there is currently no reliable evidence to inform practice. This hypothesis is based on the theory discussed and referenced within the abovementioned paragraph. Additional references have been added to this section.

Hypotheses 2 has been removed from the protocol

Some other points:

8. The CO-OP approach implementation among children post TBI seems to be problematic.

We agree that, depending on type of injury and resulting limitations a child with a brain injury may experience, the CO-OP approach may be challenging. Indeed, this may also be the case in cerebral palsy. We have tried to limit this through the
inclusion/exclusion criteria of the study, which acknowledges the attributes a child must display in order to undertake CO-OP. Many children with brain injury exhibit the difficulties with motor planning for which the CO-OP approach was devised to address. Initial investigations regarding the use of CO-OP for children with brain injury found that it was effective in leading to goal achievement, and a critically appraised topic found that “there is emerging evidence to support the use of the CO-OP approach to improve the functional performance of children with ABI; however, more research is required to determine the specific components of a cognitive approach that influence improved functional outcomes, and whether or not this approach can generalize to activities beyond those specifically targeted in therapy”. This study seeks to contribute to the existing evidence base.

9. The motor performance and functional abilities of children post TBI are different from the more typical appearance of children with CP and in addition is quite variable with this group of children.

We agree that there is much variability in the presentation of children with a brain injury, as well as children with a diagnosis of CP. Despite this variability, there are many commonalities; CP and brain injury are both non-progressive neurological conditions whose symptoms are a result of an insult to the brain; both may result in disorders of movement, as well as learning difficulties, visual deficits and behavioral concerns.

Please note that changes have been made to the inclusion criteria (full response to follow under reviewer 2 comments) to ensure participants eligible for this study display similar characteristics in regard to hand function, cognition and behavior.

10. Do the COPM is an appropriate tool for assessing children post TBI? The MACS?

The COPM is a standardized goal setting and measurement tool that was developed for all diagnostic groups, therefore is just as reliable in brain injury as in CP.

The MACS is not standardized for children with brain injury. This is noted under the measures section of the protocol, however the authors felt that it is an appropriate tool for describing how a child with brain injury typically uses there hands, in order to capture a demographic picture of the participants hand function, regardless of whether they have a diagnosis of CP or brain injury. The MACS will be used only to collect diagnostic information, not as an outcome measure. We have attempted to reflect this within the protocol with the following statement:

“Although not developed for children with brain injury, the MACS is an appropriate tool to enable a consistent classification of hand function in all participants of the present study, and as such will be used to describe hand function in participants with brain injury as well as those with cerebral palsy.”

11. The age span seems to be quite large.

The age range is large. Given that functional hand splints, and task-specific motor training interventions are utilized among a broad age range of children with
neurological conditions, we did not wish to limit participation to a smaller age range. The authors also felt a broad age range would improve the potential to recruit the required number of participants for this trial.

12. Severity of the injury, uni or bilateral involvement, cognitive and behavioral skills description, all need to be assessed.

Thankyou for identifying this. Demographic information collected from each participant initially will include information regarding severity of injury (GMFCS and MACS) and specific diagnosis (including which limbs are affected and type of motor impairment). Demographic information regarding behavior and cognition will also be collected during baseline assessment (formal diagnoses eg. ASD/ADHD/intellectual impairment, as well as informal concerns in these areas identified by parents).

Added to the protocol, under measures section: “cognition and behavior”.

13. Would not it be better to include only children with CP?

There is a significant evidence base to guide occupational therapy (OT) practice in the CP population. There is a significant lack of evidence to guide OT practice in the brain injury population, and many therapists working in brain injury base their clinical decisions on the CP evidence, for lack of better guidance. However, conducting adequately powered trials in brain injury is almost pragmatically impossible. In seeking to conduct a reliable RCT to guide practice in brain injury, we did not feel it was realistic to recruit the number of participants with a brain injury required for a successful RCT. Given the commonalities in clinical presentation among children with CP and brain injury, we felt that including children with CP would enable recruitment of sufficient numbers to fulfill the study criteria. The authors feel there are enough similarities in the presentation of children with CP and brain injury, that it is not unreasonable to combine these diagnostic groups for clinical research. This is reflected in paragraph 2 of the background.

Reviewer 2

1. Inclusion criteria: Further detail around inclusion/exclusion criteria for children with brain injury is warranted. It would be important to clarify how long post brain injury these children are as presumably if they have acquired an injury and are less that 12 months post insult, their status may not be stable. This would be a potential confound. Also, many children who acquire a brain injury during childhood may have good resolution of physical function, but residual cognitive/behavioural difficulties alone. Presumably children with brain injury included in this study would present with some degree of upper limb impairment. This would need to be stated in the inclusion criteria.

Thankyou for this feedback, and identifying the need to clearly define inclusion criteria. Inclusion criteria has been amended:
• Diagnosis of cerebral palsy or brain injury (minimum 12 months post injury)
• Age 4-15 years
• Manual Abilities Classification System (MACS) level I – IV
• Goals related to improving hand function
• Impaired hand function as a result of the neurological condition
• Sufficient language, cognitive and behavioral skills to set goals, interact with the therapist and participate within a group context (according to CO-OP guidelines)
• Parents able to commit to a two week block of therapy

Minor typographical/editorial points

Background: page 1, paragraph 1. Please support statement "... task-specific training to improve hand function is well supported..." with reference please.

Thankyou for identifying this omission. Supporting references have now been inserted.

Page 1, please review whether international classification of functioning should be capitalized.

Now reads International Classification of Functioning, Disability and Health (ICF).

Page 4. There is no referencing supporting statements made in the paragraph "Functional hand splints combined with task-specific training.

References have now been added throughout this paragraph. Please note that due to the lack of reliable evidence regarding functional splints, and how functional splints interact with motor training interventions, the theories discussed in this paragraph are based on published clinical experience and expert opinion, rather than high level evidence.

Page 4: COPM, GAS and MACS are abbreviated and have not been spelt out in full prior to this.

Amendments made to include full title prior to abbreviations

Box and Blocks Test: please review whether this assessment title should be capitalized throughout the paper.

Amendments made to capitalize Box and Block Test throughout paper

Could the authors please comment on the potential practice effect of doing the repeated Blocks and Box Test within 1 hour of each other.

No literature regarding the practice effects of repeated Box and Block Tests could be located by the authors. Consideration was given to the fact that there may be
some practice effect, however, in seeking to investigate the immediate effect of a hand splint, it was necessary to re-assess hand function within such a timeframe. Alternative hand function measures were considered, however most presented similar concerns in regard to potential practice effect. Given that change data will be compared directly between the 2 groups in RCT1, and we will not be looking at point change data for individual interventions, we hope that any potential practice effect would be present in both groups, eliminating the impact of practice effect on the outcomes.

The following statement has been added to the protocol to reflect this: “it is unknown whether repeating the Box and Block Test within a 1 hour timeframe will have a practice effect”

Thankyou for the valuable feedback from the reviewers, and for accepting the amended protocol. Please do not hesitate to contact me should any additional information be required.

Sincerely,

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