Author's response to reviews

Title: Modified constraint-induced movement therapy or conventional occupational therapy following injection of Botulinum toxin-A to improve bimanual performance in children with hemiplegic cerebral palsy: A randomised controlled trial methods paper

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Version: 2 Date: 13 April 2010

Author's response to reviews: see over
Thank you for your feedback on this manuscript. Below we have included each comment by the reviewer in bold followed by our responses indicating where we have made changes. We have also made minor grammatical corrections as required.

An exhaustive introduction gives a good picture of the background and problems in the treatment of spastic cerebral palsy. Similarly, the methods section is very wide and broad and includes a lot of discussion. Every effort to abridge the text would be welcomed to make it easier for the reader to follow the thinking of the authors.

We acknowledge the length of the paper and have removed a section of the introduction to make it easier for the reader to follow our argument and purpose in presenting this manuscript. This has reduced the introduction length from 9 pages to 6 pages. Some paragraphs have been reordered to facilitate flow of the argument following these changes.

In relation to the Methods section, this trial is the first trial to evaluate the effects of two specific forms of movement-based intervention following upper limb injection of Botulinum toxin-A. More specifically, this is the first trial to comprehensively describe and evaluate a bimanual occupational therapy protocol. While bimanual training approaches within occupational therapy are common, they have not been reported in scientific literature in sufficient depth to enable either replication, or adequate understanding of the intervention methods used. We acknowledge the length of the methodological description but believe that this level of detail is required to enable therapists to understand the exact nature of the interventions being evaluated. Given that therapy interventions are often inadequately described, this paper provides a unique opportunity for therapists providing interventions to children with hemiplegic cerebral palsy to access an important resource. Therefore, we propose to leave the comprehensive descriptions of the two movement-based interventions in the manuscript. Where possible we have revised the wording to cover this content as clearly and succinctly as possible.

Another feature is subheadings. They are definitely too many, because the text goes to pieces, and they are not in rank order by font sized or type.

We agree with the number of subheadings and have removed many of them, as appropriate.
The paper has been formatted using the recommended BMC Neurology Microsoft Word template. This includes the formatting for level of headings. We agree that when using this formatting template, the headings do not appear different but we have followed the specified guidelines. We are happy to be guided further in this area as needed.

There are several hypotheses in the study, and one can only guess why there are two hypotheses 4; in the Methods, only one hypothesis #4 will be tested.

This was a typographical error and has been amended. Thank you.

The inclusion criteria are followed by another subheading of inclusion criteria, virtually including exclusion criteria. The exclusion criteria should be determined more precisely. For example, was mother tongue other than English, intelligence deficit or other co-morbidity a criterion of exclusion? The source population can hardly be defined but, supposedly, a distance from the hospital (possibly determining the sociodemographic features of the population), financial or other resources of the families, if better/worse than the average, may influence of the capacity of the families (as is in the reviewer's experience). Were the study subjects from the neighborhood of the hospital?

Two subheadings stating “inclusion criteria” was a typographical error and has been amended to read “inclusion criteria” and “exclusion criteria”.

As stated in the manuscript, data collection in this study is now complete. As a result, we cannot alter the exclusion criteria. We acknowledge the comments of the reviewer and will address their questions here but have not made any changes to the manuscript.

1) Children were not excluded if their primary language was other than English. In fact, one child whose primary language was Greek was included in the trial.
2) Children were included if they were “able to attend to tasks and follow simple one stage commands”. If they had a severe intellectual deficit then this would not have been possible and therefore inclusion in the trial would not be possible. A specific intellectual level or ability was not specified in the inclusion/exclusion criteria as this would have been extremely difficult to assess in many of the children aged 18 months.
3) No child was excluded based on co-morbidity.
4) No child or family was excluded based on socio-demographic factors. As stated in the inclusion criteria parents were required to “to commit to an intensive therapy program”. This also referred to a commitment to travel to the hospital twice weekly for intervention. If parents from regions located a distance from the hospital were willing to make this commitment they were able to be included in the trial. Many families drove for over 60 minutes (one way) to attend the intervention sessions.

Was the inter-observer/inter-rater variability checked and how was the method of arriving at consensus, f. ex., in determining the degree of disability in the study subjects assessed for inclusion/exclusion?
The degree of disability for each child was not assessed. To determine eligibility, each child was required to meet all of the specific inclusion criteria as assessed by the Chief Investigator, as stated on page 16. There was no requirement for consensus. This process was categorical in nature; the CI assigned either a yes or no for each criterion. As stated, a diagnosis of spastic hemiplegic cerebral palsy was required to be determined and documented by a medical specialist (i.e. neurologist, paediatrician). For criteria relating to movement of the affected upper limb and following verbal commands, the child either met these criteria or did not. The inclusion criteria where rater reliability can be an issue is the assessment of muscle tone and spasticity. The CI, who has been trained, and in addition has significant clinical experience in administration of these measures and regularly provides teaching to other clinicians on administration and interpretation, conducted each of these assessments.

One basic question is the definition of "hemiplegic cerebral palsy". Were, f.ex., subjects who had quadriplegia with predominantly unilateral spasticity included? Were only subjects with congenital spastic hemiplegia included?

Only subjects with congenital spastic hemiplegic cerebral palsy were included in this trial. We acknowledge the comments of the reviewer and have added “congenital” to the inclusion criteria for clarity.

Amendments had to be made in shortage of study patients. Could any particular causes be determined for the shortage? Unexpectedly many who did not fulfill the criteria? Too many refusals? Too many dropouts during the procedure? Difficulties in finding matchable pairs within the limits of preset age? By the way, were the pairs matched for gender?

As stated in the manuscript, “approval was requested due to the trial being behind schedule due to slow recruitment rates”. Recruitment was slow to reach the required number of 34 children within our estimated time frame, due only to the specific nature of the study population and the limited number of children in the region.

We did not feel it was appropriate to put the results of recruitment in this methods paper. We will include the details of patient flow (CONSORT diagram) in a separate publication reporting the results of this trial. For the purpose of responding to the reviewers questions, of the 58 children with hemiplegic cerebral palsy screened, 35 were eligible to participate. Thirty-five consented and were randomly assigned; seventeen to the experimental group (mCIMT) and 18 to the control group (BOT). After enrollment, one child randomized to the control group withdrew prior to baseline assessment and treatment due to external family stressors. Data were obtained for all participants at 0, 1, 3 and 6 months.

Children were not matched by gender as gender was not considered as a variable that would impact outcome. This has been supported with evidence from other trials.

In the text, there are no references to the table or figures.
The references to the tables and figures are contained in the text. We have highlighted them in this version for easy reference.

Finally, a suggestion. Might the authors consider the option of writing two papers: (1) a literature review on the current status of the treatment of hemiplegic cerebral palsy, and (2) another paper of the methodological plan (with a reference to the former paper)?

This research team has recently published two Cochrane systematic reviews relating to both the use of Botulinum toxin-A in the upper limb in children with cerebral palsy and the use of Constraint-induced movement therapy. We have also previously published a systematic review and one author has been involved in the development of an international consensus statement on Botulinum toxin-A. The team is also aware of the reference cited below which is an updated systematic review of upper limb therapeutic intervention for children with congenital hemiplegia.


We acknowledge the reviewers suggestion as an effective method for reducing the size of the manuscript but feel there is already significant literature relating to the effectiveness of upper limb intervention in children with hemiplegic cerebral palsy. Although lengthy, we feel this manuscript provides essential information to clinicians on the exact nature of these clinically feasible interventions. As stated previously, these details have not been published previously and therefore provide a valuable and unique addition to the literature.

Finally, we would like to highlight an extremely important and frustrating technical issue for this manuscript as we have used an Apple Mac computer and EndNote referencing system. Unfortunately, there is a serious issue when using “track changes” in the Apple version of Word. When track changes exist in the Word document it is not possible to format the references as an error message will continually appear until all the “track changes” have been accepted and removed. We sincerely apologise for this frustrating issue and hope that once you approve the changes you can send it back to us to allow the 30 second process of formatting! We will then immediately return the manuscript.

We trust these responses address the issues and recommendations made by the reviewer and hope that they meet the criteria for publication in BMC Neurology.

Sincerely,

Brian Hoare, on behalf of all authors.