Author's response to reviews

Title: The relationship between spasticity in young children (18 months of age) with cerebral palsy and their gross motor function development

Authors:

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Author's response to reviews: see over
Dear Sir, Madam,

On behalf of my co-authors I would like to submit our revised manuscript, entitled ‘The association of initial spasticity in young children (18 months of age) with Cerebral Palsy on their gross motor function development’ for online publication in BMC Musculoskeletal Disorders.

We recognize most of the comments and feel that the referees’ recommendations are constructive and have contributed to improve the quality of the manuscript. In this letter, we will clarify how we revised the manuscript based on the comments, questions and suggestions of the reviewers. The revised manuscript has been uploaded, and all changes have been highlighted in yellow.

I hereby declare that all authors have read the final version of the manuscript and agree to it being submitted for publication. There are no ethical, financial, personal or any other conflicts of interest.

Thank you very much for your willingness to consider our paper. We sincerely hope that you will find our manuscript suitable for publication.

Yours sincerely,
On behalf of Olaf Verschuren, Laura van Riel and Marjolijn Ketelaar,

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Reviewer 1: (Mintaze Kerem Gunel)

Background
The authors should state how their methods are better suited to answer the somewhat unsettled and disputed question about to evaluate the influence of initial spasticity in the lower limbs of young children (under the age of two years) with CP on their development in gross motor function in one year? Because, children with cerebral palsy are growing up during one year so the authors also should explain this condition and how is the effectiveness on your study results? How can this study answer if any findings are a result of children of spastic?

Reply: We agree with reviewer 1 that the title and research question, i.e. to evaluate the influence of initial spasticity on gross motor function, is hard to answer. This study analyses the relationship between spasticity and the development of gross motor function. We have changed the title and the research question throughout the manuscript. See also our reply to the comments of reviewer 3.

We need information about “initial spasticity for young children with cerebral palsy?

Reply: We agree with the reviewer that this is important information. Unfortunately, there is little information on spasticity in young children with CP, except from a recent study published by Hagglund and Wagner that is mentioned in the last paragraph of the discussion section (reference 29 in the original manuscript, now reference 30 in the revised manuscript). We hope that our study may be an important piece in the puzzle of our knowledge about spasticity (see comments reviewer 4). We strongly advocate for longitudinal studies to look at the role of spasticity and its relationship with gross motor development.

Procedure
Authors declared as “All assessments were performed by a team of trained Research assistants with a background in physiotherapy, movement sciences or medicine”. Although GMFM and Modified Tardieu Scale are still inter-reliable methods, must be explained the reason of the measure which is performed by different researchers. The authors need to indicated why did prefer Modified Tardieu Scale for assessment of spasticity and GMFM for motor development?

Reply: The assessments were done by a team of trained research assistants for pragmatic reasons. The participants were recruited from 10 centres over a period of 3 years (see the methods section). All assessors were trained in the measures and followed the study protocol to standardize the assessment. The reliability and validity of the GMFM for children with CP has been reported and is mentioned in the methods section. To monitor the reliability of the GMFM, all of the assessors were tested using a criterion test videotape. We have added this information to the procedure section. The preference for the Modified Tardieu Scale and its psychometric properties is stated in the methods section under spasticity and discussed as a limitation of the study in the in the discussion section (3rd paragraph).
Participation
More information should be provided about the subjects? Etc. demographic information, IQ degree, environment and family factors are??
Participant’s knowledge must be related manuscripts Tables.
Including Table I: Dysknetic subject is participated in this study? Why?

Reply: We refrained of reporting extra characteristics of the study population as the purpose of this study was to examine the relationship between initial spasticity and gross motor development only. We agree with the reviewer that future studies should take other factors into account (see the last but one paragraph of the discussion section).
We included all participants aged 18 months from the PERRIN CP 0-5 study with complete data on the GMFM and spasticity (n=50). These children were classified according their predominant type of motor impairment following the SCPE classification system (See Table 1).
Children with a dyskinetic subtype may have spasticity in the muscle groups of the lower limbs. Please note that the reliability and validity of the diagnosis of CP and the classification of CP subtypes have not been established yet, for children under the age of 4 in particular. (Gainsborough M, Surman G, Maestri G, Colver A, Cans C. Validity and reliability of the guidelines of the surveillance of cerebral palsy in Europe for the classification of cerebral palsy. Dev Med Child Neurol 2008: 50: 828-831.)

Discussion
The authors need to discuss the other factors that effective on growing children with cerebral palsy.
In first paragraph, the authors need to talk about environment and family factors?
The authors investigated only three muscle/muscles group in the lower extremities. The authors need to discuss why select only this muscles and how they present as “spasticity situation” on cerebral palsy and how is the effect “motor development”?

Reply: We agree with reviewer 1 that the original title and research question would require a discussion in which the reviewer’s questions are discussed. This study, however, analyses the relationship between spasticity and the development of gross motor function. In other words we looked at the relationship only; we did not study the causality of this relationship nor the question how spasticity in three muscle groups would influence gross motor development. We have changed the title and the research question throughout the manuscript. See also our reply to the first comment of reviewer 1 and the comments of reviewer 3.
Reviewer 2: Sam Pierce

Minor essential revisions

Introduction:
1) Page 3, paragraph 2: I would acknowledge that there are alternate definitions of spasticity that have been proposed (such as the SPASM group's definition).

Reply: We acknowledge that the spasticity is often inconsistently defined and poorly measured. We have now made reference to a very recent paper by Malhotra et al (July 2009) in which the most recent definition by the members of the SPASM consortium is mentioned. We feel that we have stated clearly how we defined spasticity in our study (velocity dependent resistance) and that the measure used, i.e. Modified Tardieu Scale, is congruent to this definition.

2) Page 3, final paragraph: I don't think that this paragraph & figure is essential to the manuscript. I would remove this and go right into your purpose statement which you have set up nicely from your introduction.

Reply: We have deleted this paragraph from the introduction as most of it duplicates with the discussion. We have now made reference to the figure in the discussion section. Figure 1 has become Figure 2, and consequently Figure 2 is now Figure 1.

Methods:
1) Page 5, last paragraph: Table 1 was never referred to in your description of subjects.

Reply: We have now made reference to Table 1 in the second paragraph of the Methods section.

2) Page 8, Paragraph 1, sentence 2: It appears that the sentence was cut off since it leads with the reference number as the subject of the sentence.

Reply: The reviewer is correct. We have completed the sentence.

Statistical analysis:
1) You note that you did a linear regression analysis but never report the results of the regression. Also, you would need to establish that your Spasticity Total Score is Interval level data to do a linear regression unless you are doing a non-parametric version of some sort.

Reply: We have deleted this part from our statistical analysis section as we did not perform a linear regression.

Results:
1) I believe that the data from the children with hempliegia should be removed from the analysis since the data from their "unaffected"/less affected limb would have been included in Total Spasticity Score. By including these children, you may have invalidated your results. You could choose not to do this but then you
should discuss your rationale for including the children with hemiplegia in your analysis (which would probably include difficulty with making the dx in young children, the data which shows the "unaffected" side is really not unaffected, etc) and discuss how the results of your study may have been affected by including this data in your analysis.

Reply: We think that we should not exclude children with unilateral spastic CP (hemiplegia) from the analysis for the reasons suggested by the reviewer. We have made a statement in the statistical analysis section and added a comment on the effect of including children with unilateral CP in the analysis in the discussion section (page 12, last paragraph).

Discussion:
1) Page 11: I feel you need to acknowledge that you have no data on the reliability of the Spasticity Total Score with young children with CP.

Reply: We have acknowledged this in the discussion section.

2) Page 12, Paragraph 1: How do you know that you have an adequate sample size for a correlative design? If you did a power analysis, please report it.

Reply: We have not done a power analysis and deleted the text on sample size in the discussion.

References:
1) The Boyd reference (19) was incorrect since it came from a supplement.

Reply: The reference is now correct.
Reviewer 3: Gunnar Hagglund

This is a well designed study, and the subject is of clinical importance. I have, however, three major comments:

1. The study analyses the correlation between spasticity and the development of gross motor function. A significant correlation does not mean that a higher level of spasticity is the cause of impaired improvement in gross motor function, it could be a coincidence. I would suggest changing the title to “The relationship (or association) between initial spasticity...” In the last paragraph of the Background I would accordingly suggest changing the word “influence” to “relationship”.

Reply: We fully agree with the reviewer and have changed the title and research question throughout the manuscript.

2. In Statistical methods the authors writes that a linear regression analysis was performed. I think it is correct to do so, but the result of the analysis is not presented. The results of the statistical analysis is only presented as Rho

Reply: We have deleted this part from our statistical analysis section as we did not perform a linear regression (See also comment of reviewer 2).

3. In the statistical analysis the GMFM Change Score was used as dependent variable and the Spasticity Total Score as independent variable. It seems more correct to use the Spasticity Total Score as dependent variable, and I think this calculation should be done and presented.

Reply: We have deleted this part from our statistical analysis section as we did not perform a linear regression (See also comment of reviewer 2).
Reviewer 4: Reidun Jahnsen

Following minor essential revisions are suggested for the authors to consider:

1. The purpose of the present study was to evaluate the influence of initial spasticity in young children with cerebral palsy (CP) on their development of gross motor function in one year. The research question embedded in this purpose is clear. To my knowledge this has not been studied before in a longitudinal design, and the study therefore may be an important piece in the puzzle of our knowledge about the relationship between spasticity and the development of motor function in CP, with potential implications for clinical practice. The introduction gives a good overview of this specific part of the field with new and representative references, and thereby giving good reasons for the need for studies like the present. One detail; the first sentence in the second paragraph should specify that: “Motor impairment in CP can be classified…”

Reply: We thank reviewer 4 for the positive feedback. We have changed the text.

2. The methods are appropriate for the purpose of the study and well described. The study sample is 50 children from the PERRIN CP - 0-5 study, consisting of the examination of gross motor function (GMFM 66) and spasticity in the adductors, hamstrings, and gastrocnemius in children with CP 18 months of age and one year later. Data are analysed with appropriate statistical methods related to a well validity- and reliability tested instrument, (GMFM 66), and one clinical assessment tool, which is considered to be the most reliable way of assessing spasticity in children with CP. The authors did a thorough job, creating a rough ordinal scale of spasticity to differentiate between the three actual muscle groups’ impact on motor function. However, the description of this process on page 8 is unclear because of a misprint and an incomplete sentence after the one starting with: “The first level of the spasticity scale….” Except for this, enough details on the study group and methods are given. It is reason to believe that the study provides representative results which can be generalised.

3. The data are sound; taken from the PERRIN CP - 0-5 study in the Netherlands, and can be controlled in their central database. The parents signed written consent, and the study was approved by the Ethics Committee of the University Medical Centre Utrecht

4. The manuscript follows relevant standards of reporting, and tables and figures are clear visualisations of the results, making it easier for the reader to follow the steps of the analysis.

5. The discussion and conclusion are well supported by the data. Hopefully this study is only the first one in a series of longitudinal studies on the impact of spasticity on development of gross motor function, contractures and deformities in the long term in persons with CP.

6. Limitations of the work are clearly stated, such as, the lack of an inter-rater reliability study on the MTS.
7. The authors acknowledge clearly other researchers’ work which they are building upon, e.g. the use of Figure 1.

8. The title and abstract are clear reflections of the content of the paper.

Reply comment 2-8: We thank reviewer 4 for her positive feedback.

9. I am not a native English speaking person, but in my opinion the article is readable and well written. However, there are some misprints that should be corrected e.g. was/were (methods and discussion), mixing present tense and imperfect in the same sentence (methods), misspelling of dyskinetic (results), inconsistent use of small and capital letters, and inconsistent use of cerebral palsy and CP in the abstract.

Reply: We have checked the text for errors, misspelling and consistency.