Author's response to reviews

Title: "Neurofeedback and ADHD children and adolescent A clinical randomized controlled trial: parents report"

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Version: 2 Date: 18 May 2012

Author's response to reviews: see over
Comments from Editor, Referee 1, Referee 2 and their revisions

Dear Mrs Catherine Olivo,

The manuscript has been now revised according to the requests from the Editor and Referee 1 and 2. The comments have been addressed in revised manuscript and provided giving a point-by-point response to the concerns as requested.

1. Language:

EDITOR

- Copyediting: After reading through your manuscript, we feel that the quality of written English needs to be improved before the manuscript can be considered further. We advise you to seek the assistance of a fluent English speaking colleague, or to have a professional editing service correct your language. Please ensure that particular attention is paid to the abstract.

- For authors who wish to have the language in their manuscript edited by a native-English speaker with scientific expertise, BioMed Central recommends Edanz.

Manuscript has been edited by Edanz BioMed Central and particularly attention has been paid to the abstract.

REFEREE 1

- Manuscript needs reviewed and edited by someone more fluent in use of English
language;
-there are a number of awkward sentences and use of words throughout (e.g., “auditive” feedback [rare usage], alfa for alpha). Also, there is mixed use of NF and NFT. Choose one and be consistent.

See the answer above about editing. Use of words (auditive, alfa) has been edited. The use of NF/NFT has been done as consistent.

2. Title page

EDITOR

Title page: Please include a title page at the front of your manuscript file. It should contain, at minimum, the names, institutions, countries and email addresses of all authors, and the full postal address of the submitting author.

These have been done as requested from Editor.

3. Abstract

REFEREE 1

-Last sentence needs editing to indicate that the values are compared to what?

These have been done according to referee 1.

4. Introduction

REFEREE 1

-Spacing of lines and paragraph construction needs editing.

These have been corrected as requested.

-Reference the Lubar and Othmers protocols.

The two references have been applied.

5. Method

EDITOR
- In particular, the authors need to provide more details about the neurofeedback treatment and medication dosing/titration.  
Details about the treatments have been given.

**REFEREE 1**

- Subjects – should refer to and discuss the consort flow chart at this point in method.  
*Discussion has been done i Methods.*

- Likewise could move the IRB process to here (children assent? Not consent), not at end of statistics description.  
*IRB has been moved to Methods.*

- Statement regarding “almost half confirmed their participation” doesn’t match the 91 – what does that statement means?  
*This has been described under Methods/subjects now.*

- The ADHD diagnostic assessment paragraph really needs editing with more procedural details.  
*ADHD paragraph has been edited now according to the request.*

- Inclusion should state how IQ was assessed and with what instrument with reference.  
*Assessment for IQ has been edited including the reference.*

- What were the exclusion criteria?  
*The exclusions criteria were mental retardation, free school children (under 6 years) and I addition to hyperactivity not being ADHD.*

- Should “Dropped out” be part of subject section and consort chart?  
*This has been done according to referee 1.*

- Neurofeedback – need to include more information about “targeted frequencies” and “specific conditions we tried to address specific to the individual”. That statement makes one think everybody could have been treated differently?  
*More information was included about target frequencies and the statement has been edited.*
- How would one replicate your procedure? Need to be a lot more specific about what drove
the decisions made and how addressed.

This has been edited according to referee 1.

-Evaluation of effect of treatment – were the raters (and who were they? Clinician,
parent, teacher, self, etc.) blinded to treatment?

The paragraph has been edited as requested.
The raters were not blinded to treatment.

-Footnote 3 in Table 1 suggests only based on parent score. That needs to be stated in the
methods and unfortunately is not as good as using blinded trained clinician raters combined
with blinded school reports.

This has been stated in the methods.

REFEREE 2

-The details of treatment with MPH (e.g. dosing range; form of medication) need
to be more fully described and the presence or absence of titration of children on
MED dose over the 30 sessions must be described. For example, the MTA study
found that only 25% of children treated in an outpatient setting with MPH showed
significant improvement vs. 57% of children who were clinically titrated on MPH
dose.

No titration regarding medication was done. Refer to the point 5 /Editor

6. Statistic

EDITOR

-As Professor Hughes pointed out, the data can be analyzed in a more satisfactory manner by
using a mixed between and within ANOVA, or by a linear mixed effect model than by paired
T-tests.

See above.

-Using either of these approaches will also enable the authors to ascertain whether age or
gender are meaningful covariates.
Even if this question is not central for the study target the analysis was done. Unfortunately, the lack of power in the adjusted GLM makes it difficult to make a decision.

- Instead of (or in addition to) presenting change scores the authors should present effect size measures for the various treatments. This will better enable readers to compare effects of NFT with and without meds to other published treatments. For an accurate determination of effect size in a mixed between/within study design I refer them to equation 8 in: Morris, S. B., & DeShon, R. P. Combining effect size estimates in meta-analysis with repeated measures and independent-groups designs. Psychological Methods, 2002, 7(1): 105-125.

These effect size scores for the pre-post treatment changes were added and refered to Morris, SB.

**REFEREE 1**

-“Basic methods…” needs to be more specific.

This has been done according to the referees 1

- Not sure one tests for “change scores vanishing”; can’t prove a null hypothesis.

Due to the method change this point gets obsolete.

- Instead of paired t-test and change scores, one could use a repeated measure ANOVA (allows for covarying age, gender and IQ) or mixed model random regression. It appears that a “completer” analysis was conducted?

The original analysis is replaced by a GLM for repeated measures.

- Are the scores in Table 2 the change score? Or the raw score?

Both the raw and the correct change scores have been added

- The use of scores without labeling is very confusing. It is not clear where the p-values in Table 2 for Treatment group comparisons come from.

Due to the method change this point gets obsolete.

- Are they based on a post-hoc after the ANOVA?

Post-hoc-tests were added but did not find any significant difference between the treatments.
- Your Bonferroni doesn’t appear to be correct as described in statistical section. 

_Due to the method change this point gets obsolete._

- In table 2, you did at least 12 one sample (paired/dependent) t-tests. It would be better if the pre test values of Table 1 were in Table 2 so one can see a direct comparison with the post values (and based on raw scores rather than change scores). 

_This is part of the changed analysis._

- The statistical tests need to be explicitly clear that there are between group comparisons (with a post hoc for ANOVA model), and within group comparisons. 

_This is part of the changed analysis._

- A simple bar graph of pre-post scores for each group might be more helpful than current Figure 2, but Figure 2 is good. 

_Due to doubling the figure has been removed._

- Table 1. Needs work regarding footnote 3 (see above). Are these the baseline (T1) scores? If so, needs to be part of title. Superscript 2 on gender is incorrect based on footnote. How does one do an ANOVA on dichotomous gender? Need to use Chi-square 

_The explanation is corrected._

### 7. Results, discussion, conclusion

**REFEREE 1**

- Both sections are very brief and lacking in details. No consideration of what the results really mean or what may explain the findings for attention.

_The results section has been upgraded._

_We did a major check of all procedures and data and obtained an error in the data transfer leading to a wrong table 2. These errors are fixed and the findings for attention were an_
artifact of the data errors. The abstract, results, discussion and conclusion have been updated according to that.

-And a more thorough integration and comparison to prior studies would be better.  
*This has been done according to referee 1.*

-What are the clinical ramifications?  
*The lower change of the multimodal approach in our study has been discussed as a possible but not confirmed ramification.*

**EDITOR**
- Results should be presented in a straightforward manner ? showing pre and post-treatment scores on the rating instrument by group.  
*This has been done according to editor.*

**8. Figures**

**EDITOR**
- Figure titles: All figures must have a figure title listed after the references in the manuscript file. The figure file should not include the title or number (e.g. Figure 1... etc.).  
*This has been done according to editor.*

- The figures are numbered automatically in the order in which they are uploaded. For more information, see the instructions for authors:  
[http://www.biomedcentral.com/info/ifora/figures](http://www.biomedcentral.com/info/ifora/figures).  
*This has been done according to editor.*

**REFEREE 1**
- Figure 1. What does “Not accepted” mean and need to include somewhere the various reasons for not accepted. Similarly, what are the reasons for “dropouts”?  
*Figure 1 has been upgraded after the request from referee 1.*

- Figure 2. “Rate” scale, word is rating.
Figure 2 is removed after the request from referee 2.

REFEREE 2
- Figure 2 should be removed as the information is duplicated in table 2.

Figure 2 is now removed.

It would be helpful to have a better understanding of why children dropped out of the study and specifically how many out of each group. For example, was the drop out higher for MED or NFT groups?

In the upgraded figure 1 the association between the two time points has become clearer such that it is obvious now that the drop out per randomization group is the difference of the participant numbers for each time point.

9. Tables

- Table 1. Needs work regarding footnote 3 (see above). Are these the baseline (T1) scores? If so, needs to be part of title. Superscript 2 on gender is incorrect based on footnote. How does one do an ANOVA on dichotomous gender? Need to use Chi-square.

This has been done according to referee 1.

10. Text

REFEREE 2

- Page 6, 2nd paragraph line 1; remove extra “and,”

This has been done.

- Page 13, Discussion, 2nd paragraph comma missing between “gender intelligence”.

This has been done.

- Page 18, ref 15. Change ADDH to ADHD.

This has been changed.
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-Page 19, ref 23. http://www.thoughttechnology.com/bioinf.htm does not appear to work as a link, please correct and provide more information about the company.

Web address has been corrected and more information about company has been given according to request from referee 1.

11. Journal style

EDITOR

-Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals). It is important that your files are correctly formatted.

Manuscript has been revised according to the journal style.

12. COVER LETTER

EDITOR

-We would be grateful if you could address the comments in a revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

Cover letter giving a point-by-point response is provided.

-We look forward to receiving your revised manuscript by 19 May 2012.

The revised manuscript has been submitted by 19 May 2012.

Best regards

Nezla Duric