Author's response to reviews

Title: Evaluation of the muscle strength and motor ability in type II and III spinal muscle atrophy children treated with valproic acid

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Author's response to reviews: see over
Dear Dr. Editor,

Thank you for giving us the opportunity to address the comments of the referee in addition to what we have changed in the first version of the manuscript. As you can see below, all the major and minor points were answered, and we believe that the manuscript is now much better. All new information or changes added to the text are in red color. About the quality of the English, we might submit this version of the paper to Scientific Writing and Editing Services from the BMC for language correction, and we will pay for the expense.

Thank you very much again,

Sincerely,

Illora Aswinkumar Darbar

Reviewer’s report Major points:

1.) The authors have corrected the definition of SMA III (initial manifestation after 18 months instead of after 10 months as in the original version of the manuscript). Can we be sure that this has not changed the relative numbers of the patients in this study (see Table 2). Can the authors confirm that no patient needed to be reclassified as SMA type II who was classified as SMA type III in the 1st version of the manuscript?

We have checked the age of onset of the disease in all patients and we can confirm that no patient needs to be reclassified.

2.) The RESULTS chapter contains the sentence: "All 22 patients achieved the 20 mg/kg/d of the VPA serum concentration in the period of the study". 20 mg/kg/d is NOT a serum concentration, but the applied VPA dose. Since it was claimed in the MATERIALS AND METHODS chapter that the VPA serum concentrations were measured at 6 and 12 months, it should be easy to provide these data, if not in detail at least by stating that VPA serum levels were in all cases "between ... and ..." for the duration of the study.

We included in the text: “In all 22 patients the serum concentration of VPA was between 40-100 mg/dL in the period of the study”

3.) Since 5 patients gained weight, it would be helpful to know how much this was in the individual cases expressed as BMI centiles changes. The patients were growing children; simply quoting mean weight and height does not give any information.
We agree with the referee and we corrected this information in the text. Reviewing our data, only 3 patients gained weight during the treatment with VPA according to the IBC measurement.

4.) I do not understand the data from table 3: why is there a negative sign for all values, if (DISCUSSION) "we noted a better score in the second and fourth, but not in the fifth evaluation"? What about the third evaluation?

Negative value means that the value of the first evaluation is lesser than the values of the subsequent evaluations. However, this was statistically significant only for second and fourth evaluation. As we have discussed in the text maybe this occurred due to the oscillation of the medication effect.

5.) As in my previous comment: the data from table 4 have still not been explained.

We agree that the data in this table was confused. In the last column the p value is the result of the comparison of the first evaluation with the other evaluations, and in this case the p values were not statistically significant for both groups (younger and older than 6 years of age). A new line with p values comparing both groups in each evaluation was also added in this table. We also added a legend in this table explaining the meaning of the p values from the last line and last column.

We have added a new table in the paper (named table 3) in which we included the comparison of the measurement of the HFMS in 2 SMA groups (type II and III) separately, and in the last column we can see that the p value was statistically significant only in the type II group. There is a legend in this table explaining the meaning of the p values from the last line and last column. This new information was added in the abstract, results, discussion and conclusion sections of the paper.

Table 2 from the previous version was removed in this new version of the paper.

Minor points:

As in my previous comment, please change "Hammersmith Function Motor Scale" throughout the text, tables and even the reference (no. 21!) to Hammersmith Functional Motor Scale".

It was corrected.

As in my previous comment, please use consistently "." rather than "," to indicate decimal positions.

It was corrected.
In the BACKGROUND section, third page, last sentence: instead of "Brichta et al. 2003" it should be "Brichta et al. 2006"

It was corrected

In the DISCUSSION section, second page, last sentence: instead of "Swoboda et al. 2007" it should be "Swoboda et al. 2009"

It was corrected