Reviewer’s report

Title: A novel compound mutation in GLRA1 cause hyperekplexia in a Chinese boy- a case report and review of the literature

Version: 0 Date: 25 Jul 2017

Reviewer: Márta Széll

Reviewer's report:

This is a well-written paper on the genetic background of an extremely rare monogenic disease. These reports are absolutely needed to unravel the genotype-phenotype associations in rare monogenic diseases. Analyzing and reviewing the literature is the next step in this process. This is why papers like Yang et al submitted have high importance in clinical genetics.

I arranged a list of major comments and suggestions and a list of minor comments and suggestions.

MAJOR COMMENTS AND SUGGESTIONS:

Title:

I suggest to modify the title: … - a case report and a review of the literature

Abstract and Background

Well written parts, I have no suggestions.

Case presentation

1. Why did you need the approval of the ethics committee for a routine molecular genetics diagnostic procedure? This is not an experimental process which would need the permission of an ethical committee. But if this is the case in China, of course, I accept this sentence.

2. Did the authors perform the NGS procedure by themselves? If not, please indicate what the name of the service company is. The same applies for the direct capillary sequencing for the validation of the NGS identified mutations.

3. Is there any connection between the target(s) of clonazepam and the glycine transmission system? If yes, please add 1-2 sentences about at the relevant part of the paper.
Results:

1. Do we have any data on the mode of heredity of the 2 novel mutations mentioned at Page 8 row 10? Dominant? Recessive? If there are no data about them, you should tell that the papers that first described these mutations could not define it.

Discussion and conclusions

1. Please delete the sentence at Page 9 row 9. It is obvious and no need to emphasize it in a paper like this.

2. The same applies for the last sentence of the first paragraph on page 10. Please delete this sentence or re-phrase it. My suggestion would be: This suggests that these recessive mutations of the GLRA1 gene in a compound heterozygote state are pathogenic and cause hyperekplexia.

Tables and Figures:

1. Please delete (%) from the heading of the second column of Table 2. You show only numbers but no percentages in this column.

2. I suggest to show Table 3 as a Supplementary material.

3. Figure 2: please re-phase the explanation of the color code. Regions harboring mainly recessive mutations AND Regions harboring mainly dominant mutations

MINOR POINTS AND SUGGESTIONS:

Page 2 row 4: … most of the mutations…

Page 4. row 14: … most of the mutations…

Page 4. row 14: … mutation loci and hyperekplexia phenotype.

Page 5. row 4: … for about 13 years. He was born and had an unremarkable antenatal and birth history. In the neonatal period…

Page 6 row 10: After genetic counselling with a clinical geneticist…
Page 9, row 19: … likely to be dominant pathogenic mutations

Page 10 row 20: … the ER control system, they are transported…

Page 10 row 21: Please delete „an attack could occur”.

Page 11 row 1-6: Please use autoantibody instead of antibody

Page 11 row 7: hyperekplexia (no capital is needed when you write the name of the disease)

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

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3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

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If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

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