**Reviewer’s report**

**Title:** Clinical features and genetic analysis of two siblings with Startle disease in an Italian family: a case report.

**Version:** 0  **Date:** 12 Feb 2019

**Reviewer:** Éliane Chouery

**Reviewer's report:**

I highly appreciated the request to review this paper. I have carefully reviewed it. This work must be reconsidered for these points:

1- Language needs the oversight of a native English speaker.

2- Abstract section:

- citing the mutation or the results should be after citing the methods.
- in the abstract authors should state the modes of inheritance of startle disease to make the abstract complete
- the conclusion of the abstract should mainly focus on the clinical heterogeneity in the same family. the conclusion should be rewritten.

3-background:

line 28 authors should be more clear and develop all mode of inheritance due to mutations in GLRA1 gene.

4- case presentation:

all the clinical part should be rearranged in a chronological way for each patient separately and including the mother. The age of patients at time of examination should be stated too.

- to add full name of ExAC and url accession for all used databases.
- the mutation p.R299X is already reported, the authors should develop in the main text where this mutation was reported and if it was reported in a recessive or dominant inheritance manner.
- Authors should explain why did they chose to do NGS while sequencing the gene GLRA1 by Sanger is more quick and less expensive knowing that mutations in Startle disease accure in 80% of affected patients.

- authors should put the result of each experiments after describing each protocol in a logic way.
- authors should state the MAF of the second mutation identified p.D98E according to ExAC or other databases.

5- A paper published recently in 2017 in BMC medical genetics by Zhiliang yang et al. describes in an excellent manner a correlation between genotype and phenotype in startle disease. Authors should rely on this paper and interpret their findings in order to arrange more their discussion.

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.

Unable to assess

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

No

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:

Not suitable for publication unless extensively edited

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