

## **Reply to the Editor.**

Dear Respected Editor/Reviewer

Good day

Thank you very much for the comprehensive review and for your precious time that you spent in reviewing this study. We did the advised changes and answered the queries. All the changes were marked by red colour for easily tracking by the reviewer. The manuscript looks much better with these changes and we tried to improve the language as we can. Thank you gain for your precious assistance.

Here we are replying point by point:

### **The reviewer Comments:**

1. The first appearance of abbreviations such as “ASD, EEG, GERD, IGG” in manuscript without Abstract Part should be stated in detail.

Our Reply: We did the requested changes and revised the whole manuscript for any missed abbreviations. The corrections were marked in red colour.

2. Is there really a definition of “Excitopathy”?

Our Reply: Excitopathy was first described by Scholl, Ute I., et al in 2012 when they describe SeSAME/EAST syndrome (1). This was followed by Ola Abdelhadi et al in 2016 (2) while describing EAST syndrome, which is a tetrad of cardinal features; Epilepsy, Ataxia, Sensorineural deafness, and (a renal salt-wasting) Tubulopathy, hence the acronym EAST syndrome. Excitopathy of postsynaptic terminals is glutamate-mediated and is a reason for synaptopathy that occurs in different places e.g., cochlea causing cochlear synaptopathy.

1. Scholl UI, Dave HB, Lu M, Farhi A, Nelson-Williams C, Listman JA, Lifton RP. SeSAME/EAST syndrome--phenotypic variability and delayed activity of the distal convoluted tubule. *Pediatr Nephrol.* 2012 Nov;27(11):2081-2090. doi: 10.1007/s00467-012-2219-4. Epub 2012 Aug 21. PMID: 22907601.
2. Abdelhadi O, Iancu D, Stanescu H, Kleta R, Bockenhauer D. EAST syndrome: Clinical, pathophysiological, and genetic aspects of mutations in KCNJ10. *Rare Dis.* 2016 Jun 1;4(1):e1195043. doi: 10.1080/21675511.2016.1195043. PMID: 27500072; PMCID: PMC4961265.

3. Some words were misspelled and should be revised. Such as: Increased excitability in the developed brain causes “imapired” plasticity which in turn induces both cognitive deficits. “imapired” should be “impaired”.

Our Reply: Correction was done and marked in red colour.

4. The CONCLUSION PART is a little bit tedious. It will be better if shorter and concise.

Our Reply: Conclusion was reduced as requested.

**Editorial Comments:**

**Language quality:**

We revised the manuscript, correcting any deficiencies and revised by WILEY.

**Reply to *Science editor*:**

Thank you very much.

5 Issues raised: (1) Authors should always cite references that are relevant to their study. Please check and remove any references that not relevant to this study.

**Our Reply:**

We revised the references and removed 2 of them that could be compensated by the other references. All the other references are essential for scientific and ethical consideration. The number of references removed is 55 and 63.

***Reply to the Company editor-in-chief:***

The issue raised:

Before final acceptance, the author(s) must add a table/figure to the manuscript.

**Our Reply:**

We added two tables. The first one summarises the comorbidities in children with autism while the second table describes the Criteria of “Autism Friendly Emergency Department.