Reviewer's report

**Title:** Duplication involving GABA receptor genes accounts for paradoxical response to antiepileptic drugs in Isodicentric 15 syndrome.

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**Reviewer:** Pasquale Striano

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This is a case report on epilepsy worsening in adult individual with isodicentric 15 syndrome (IDIC-15) after the introduction of pregabalin. The authors speculate that the clinical worsening effect can be due to the duplicated 15q11–13 region that includes genes encoding the #5 (GABRA5) and #3 - #3 (GABRB3) receptor subunits.

- The case description and the discussion of their findings can be significantly improved. In particular, description of seizure semiology and EEG findings during the clinical evolution of the patient would be useful.

- Epilepsy worsening due to the use of some anticonvulsants is a well known phenomenon. The literature on this topic needs to be addressed more in detail. For instance, there is much literature on a derivative of pregabalin, i.e., gabapentin that may also induce life-threatening status epilepticus in some cases.

- The 15q11–13 region that includes 2 GABA genes is of special interest. Notably, microdeletions at this position have been described in individuals with intellectual disability, autism spectrum disorder, and even epilepsy (Dibbens et al., Hum Mol Genet. 2009;18:3626-31). These data could improve the discussion of the genetic rearrangement found in the patient reported by Di Rocco et al.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests