Review of: "Impending role of hippocampal neurogenesis in the development of chronic epilepsy following seizures after Kainic acid and Pentylenetetrazol treatment"

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Potential competing interests: No potential competing interests to declare.

The manuscript entitled "Impending Role of Hippocampal Neurogenesis in the Development of Chronic Epilepsy Following Seizures after Kainic Acid and Pentylenetetrazol Treatment," by Dr. Sharma and colleagues, initially presents results that contribute to our understanding of the factors involved in the onset of seizures and the development of chronic epilepsy. Nevertheless, there are a series of important questions that the authors must address in order to improve this work and be accepted for publication in Qeios.

TITLE

I would correct it to:

"Impending Role of Hippocampal Neurogenesis in the Development of Chronic Epilepsy Following Seizures after Kainic Acid and Pentylenetetrazol **Injections in Wistar Rats**".

Explaining - "Treatment" means: "a session of medical care or the administration of a dose of medication." Kainic acid and PTZ are not remedies. "The patient received repeated treatments as needed." In the manuscript, instead of patients, rats are used.

ABSTRACT

"I miss in the abstract values, numbers, percentages, statistics that corroborate the obtained results and refer to the 'impending role of hippocampal neurogenesis.' The authors need to include, at least, the most relevant ones."

I would exchange the word 'animals' for 'rats'.

INTRODUCTION

Animal models of Temporal Lobe Epilepsy (TLE), which most accurately represent this condition, are typically developed using pilocarpine, inducing morpho-functional alterations characteristic of this pathology and, consequently, neurogenesis.

Additionally, researchers have used chemical kindling with kainic acid and PTZ, which is more common in acute epilepsy models. I do not understand why the authors begin the introduction by discussing TLE. Why did they not use pilocarpine?

Please explain.

The researchers state: "It is not yet well understood whether neurogenesis following seizure activity is a contributing factor or a protective mechanism against the development of epilepsy." Why not also consider this same pattern of morpho-functional alterations in experimental lesions in rodents and in epileptic patients, such as sprouting? Why not discuss this histopathological feature as well? The sprouting was observed in the hippocampus of rats injected with kainic acid and PTZ? Please explain.

MATERIALS and METHODS

How many rats were used in this entire study? How many animals were discarded? How many rats died?

Did the 12 rats in the KA group receive this acid? How many animals died in this group?

What is BW?

How many rats died in the PTZ group?

How were the changes in GABAergic neurons measured (dosed, analyzed)?

Did the researchers use parvalbumin?

Why didn't the researchers use the “Abercrombrie Correction” to quantify viable and/or proliferating cells? Please explain in detail how the quantification was done.

Cells were counted in the CA1, CA2, CA3, hilar, and DG subfields. What was the area in mm^2 used for this quantification?

The weight of the two-month-old rats was 150 g, please check?

RESULTS

In this section where treatment referring to kainic acid and PTZ is mentioned, replace it with injection.

What are dispersion of cells and distorted? Please provide a description of the morphological alterations found in the hippocampus.

How do researchers know that cells are undergoing degeneration?

What is mild activation of glial cells?

Researchers describe "some neurons may have regenerated or repaired over time." In which area of the hippocampus was neuronal regeneration observed? How do researchers know there was regeneration? Was there sprouting? Sorry for insisting, it's strange that they didn't observe this histopathological figure. Please explain.

Was there greater and/or lesser susceptibility to initiate and propagate seizures and lesions between the dorsal

and ventral areas of the hippocampus?

It is necessary to include the scale of magnification in the photomicrographs representing the hippocampal regions in Figure 1. If possible, in the same figure, include a photograph/insert with higher magnification/resolution. In this figure, indicate that the images are representative.

Will all apoptotic cells die?

In Figure 2, it is also necessary to include the magnification bar. In fact, in all figures containing photomicrographs, the magnification scale should be included. These are also representative images.

How was the phenotype of the cells defined? Please make it clear in the Materials and Methods section.

What was the method of GABA immunostaining? Please describe.

The level of NGF expression was lower than that observed in the hippocampi of control rats. How much was this quantitatively in %?

There are some data that are only described qualitatively. Whenever possible, researchers should provide values, numbers, %, quantitative data.

DISCUSSION

In the text: "Neuronal loss in DG..." Replace Dg with DG. Check abbreviations throughout the text.

To what extent are the events of seizure crises/neurogenesis observed in the hippocampus modulated by nigral GABAergic mechanisms (substantia nigra pars reticulata)? Reading suggestion: Rodrigues et al., 2004; DOI: 10.1016/j.eplepsyres.2004.02.001.

Will the proliferated and differentiated cells not die if the rats were sacrificed over a longer period, with long-term observation?

I'm not sure if this journal has the section 'Conclusion' separated in its articles. If so, please include it.