

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 authors explore how seizures contribute to cell proliferation and differentiation within the different subregions of the hippocampus and explore its potential influence on the emergence of seizure activity and the development of chronic epilepsy.

For such purposes, they compare three different groups of rats (control group, Kainic acid group, pentylenetetrazole group) with parameters of:

- 1. Neurodegeneration (Nissl's staining, fluorojade B staining, TUNEL assay)
- 2. Cell proliferation and differentiation (immunohistochemically, using anti-BrdU for GFAP, a glial marker, or calbindin, a neuronal marker)
- 3. Changes in GABAergic neurons, nitrergic neurons, BDNF, and NGF expression.

They observe interesting and valuable findings that may help to understand the factors involved in the process of epileptogenesis.

However, there are some commentaries that may help to improve the quality of the article.

ABSTRACT

I believe there is an important part of the summary missed: **methods**. At the beginning, there is an introductory part (aims), but after that, results are commented on, ending with a conclusion. I strongly recommend adding a <u>subsection of "methods" and trying to give more numerical data in the "results" part, ending with a discussion trying to synthesize the main findings.</u>

Also, when the authors say "onset of seizures and the development of chronic epilepsy", I think they could replace that with the term "epileptogenesis."

Also, they use some **acronyms such as NGF and BDNF** with which not every reader may be familiarized, so I would write down the whole name before using the acronyms. For example, nerve growth factor (NGF).



INTRODUCTION

First paragraph:

- I am not sure if I would say "periodic seizures"; maybe it sounds more accurate to sayspontaneous (unprovoked)
 and unpredictable occurrence of seizures.
- "is difficult to manage and cure": not every patient is difficult to manage, so I would addmay, might (around 30% of patients have refractory epilepsy).
- "it is often observed after acute seizures like status epilepticus, brain injury, tumours...": I think it is an error, but I am not sure whether they refer to: "acute INJURIES/NOXAS", but not seizures (a tumor is not a seizure), or "acute seizures in the setting of "SE, brain injury, etc. Try to clarify that.

Second paragraph:

- Later on during the article, they use several times "DG" in order to talk about the dentate gyrus. Therefore, you should
 add the acronym after that (since it is the first time you mention it): "neurodegenerative changes in the dentate gyrus
 (DG), CA1-CA3 subfields..."
- 4th line: Before "abnormal hippocampal neurogenesis has also emerged...", I would add a connector of contrasting ideas like "**However**," or something like that.

Third paragraph:

• Second line: "about **ifty percent** of newly born cells differentiate into neurons and **fifteen percent** into glial cells": is it correct? Or should it be **fifty/fifty?** - clarify.

MATERIALS AND METHODS

Parameters studied: I would write down the full meaning of BrdU, GFAP, BDNF, and NGF and after that, the acronym in brackets. For example: **Bromodeoxyuridine** (BrdU)...and so on.

RESULTS

- First paragraph/line: "while SRS was absent" Should it be "were absent"? (if plural), just check it.
- Third paragraph: as you have already mentioned 'dentate gyrus'', you could use the acronym "DG" (first and second lines in the same paragraph).
- Page 6: BDNF and NGF expression (Fig. 7)- third line: "similar results WERE WERE obtained" eliminate one
 "were".

DISCUSSION

Second paragraph: "neuronal loss in Dg" -→ correct it: DG (capital letter).



FIGURES AND LEGENDS

I think they are correct and understandable.

REFERENCES

I have noticed that when there are several authors, they mention some of them, but if there are more than six, they use one and "et al". I am not sure which method the authors use, but I would revise it and homogenize it. Normally, you have to write down the names of 6 authors and then "et al" if there are more. (references 3, 6, 8, 11, 15, 20, 21, 25).

Also, usually we use the abbreviation of the journal. Although, as I have said, I am not sure which method the authors are using (not Vancouver). For example, Journal of Neuroscience: J Neurosci.

Reference 17: I miss the pages or the chapter the authors are using or referring to.

Otherwise, I find the article very interesting with worthwhile findings.

Qeios ID: LL3RVS · https://doi.org/10.32388/LL3RVS