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.

This paper examines the alterations in neurons associated with epileptogenesis in two pharmacological models of temporal lobe epilepsy. The authors used well-known models of kainate- and PTZ-induced epilepsy in Wistar rats.

The introduction is too short and does not adequately address the problems being studied. I suggest giving an overview of both kainate-induced epilepsy and PTZ-induced epilepsy, focusing on neuronal mechanisms of epileptogenesis.

Kainate-induced epilepsy. Systemic application of kainate, acting specifically via GluK1 kainate receptors, can cause locomotor arrest and induce myoclonic behavioral seizures and electrographic seizure discharges in the basolateral amygdala and hippocampus. Kainate-induced epilepsy is characterized by epileptogenesis, which involves 3 processes: reactive gliosis, neurodegeneration, and neurogenesis.

1. Reactive gliosis was not covered by the research, but the authors used glial markers (anti-BrdU or GFAP). I recommend better defining the aim to mark glial cells.
2. Neurodegeneration is a key feature of epileptogenesis. This process is characterized by the loss of neurons and glial cells. The authors differentiate between apoptosis and necrosis, which are complex processes that need more attention.
3. Neurogenesis, the generation of new neurons, is a fascinating process when combined with epileptogenic neurodegeneration (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8714646/ and others). Please be aware that persistent neurogenesis was observed in C57BL/6J mice during epileptogenesis, potentially to compensate for the ongoing neurodegeneration (https://pubmed.ncbi.nlm.nih.gov/27100347/).

This current paper aimed to examine neurodegeneration and neurogenesis. I recommend stating this in the Introduction.

PTZ (pentylenetetrazol) is an excitotoxic drug that produces seizures by causing excessive calcium influx into neurons, leading to cell death. PTZ-induced seizures can lead to apoptotic neurodegeneration. This also needs to be mentioned.

The brain tissue was examined in two narrow periods: 48 hours and 6 weeks after the KA-induced status epilepticus model and PTZ-induced kindling. Please provide an explanation in the introduction for why these time periods were chosen.

The problem of neurogenesis during epileptogenesis is fascinating and deserves a better introduction.

The authors used various markers, such as anti-BrdU, GFAP, NADPH-d, BDNF, NGF. Please clarify the intended use of each marker.

In addition, I suggest specifying each type of staining of brain slices, including Nissl staining, Fluorojade B staining, and TUNEL assay. Be aware that ***Fluoro-Jade B*** stains all degenerating neurons regardless of a specific insult or mechanism of cell death.

I highly suggest adding a distinct "Conclusions" section that summarizes the main points of the provided information.