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 examine the role of neurogenesis in two different models of epilepsy, e.g., kainite- and PTZ-induced rat models. They consider the latter type as kindling. They examine two different survival times after epilepsy induction, 48 hours and 8 weeks. The analysed parameters are numerous, from the number of cells to different neurochemical markers, degenerating processes, and neurogenesis. The consequence (at least one of them) is that neurogenesis and seizure genesis are not related. The questions examined are very interesting, but I have severe concerns about the manuscript.

1. There are no methodological descriptions about the applied reactions and materials. What reactions were applied? What primary and secondary antibodies, in which concentrations, how they were visualized? Tunel reaction? BRdU reaction? How was the GABA reaction executed with these protein immunoreactions? GABA needs high glutaraldehyde fixation, proteins need low glutaraldehyde fixation. No data provided about the fixation protocol at all, e.g., were the rats perfused? Only pieces of information are provided in the figures' legends or in the discussion. Please provide an honest and detailed description of the methods.
2. Why was calbindin used for neuronal labelling? It is sensitive to epileptic seizures, or excitotoxicity, especially in KA-induced models (Magloczky et al., 1993, 1995). This way, since the authors used double staining of the neurons with calbindin and other markers, it is not clear whether the calbindin staining disappeared or the cells. NeuN could have been a more stable neuronal marker. BTW, what double staining? There is no data about this reaction in the manuscript.
3. No description about the examined parameters—what are they and what do they label?
4. Kainate receptors are most abundant in the CA3 region of the hippocampus. A systemic injection of it will overexcite the CA3 pyramidal cells, causing cell death in the CA3 and in the DG. Other cells will be excited by the CA3 pyramidal axons, in the DG antidromically, and in the CA1 by the axons. However, this activation will cause severe sprouting of excitatory and inhibitory fibres, and this can be the main cause of the refractory seizures, with the loss of hilar and other interneurons. Authors may find plenty of papers about it.
5. Figure 7 does not show the changes written in the legend. Usually, figure legends are very poor and do not provide sufficient information.
6. The discussion is poor and sometimes contains false interpretation. E.g., the authors often speak about the number of seizures, as if there are more seizures in KA models than in PTZ or less, at different time points, but the number of seizures was not examined, if I understood well.

In summary, the manuscript is interesting, but the evidence is poorly demonstrated, the methods are missing, and the interpretation in the discussion is loose.

Maglóczky, and T.F. Freund (1993): Selective neuronal death in the contralateral hippocampus following unilateral kainate injections into the CA3 subfield

Neuroscience 56(2): 317-336,

Zs. Maglóczky, and T.F. Freund (1995): Delayed cell death in the contralateral hippocampus following unilateral kainate injection into the CA3 subfield

Neuroscience, 66: 847-860