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 manuscript aims to elucidate the role of hippocampal neurogenesis in the progression to chronic epilepsy following induced seizures by kainic acid (KA) and pentylenetetrazol (PTZ). The study presents an in-depth analysis of neurodegeneration, cell proliferation, and neurogenesis post-seizure and attempts to correlate these phenomena with the development of chronic epilepsy.

Major Comments:

1. The methodology section lacks comprehensive details on the criteria for animal selection and the specifics of the seizure induction process and quantification (Racine scale?). Additionally, there is insufficient explanation regarding the choice of doses for KA and PTZ treatments and administration via, which is crucial for understanding the study's applicability and reproducibility. Clarifying these aspects would significantly enhance the methodological rigor.
2. 2- The statistical analysis is not thoroughly detailed. For instance, the manuscript does not specify the statistical tests used for each set of data or justify the choice of these tests. Moreover, there seems to be a lack of discussion on the assumptions of each statistical test and whether the data met these assumptions. A more detailed statistical methodology and analysis section is needed to ensure the validity and reliability of the conclusions drawn.
3. The manuscript utilizes a systemic model of seizure induction via intraperitoneal injection of Kainic acid (KA) and Pentylenetetrazol (PTZ). Given the known systemic toxicity and adverse effects associated with these chemical models, it is standard practice to opt for intracerebral treatments to reduce dose and systemic toxicity. The authors need to justify their specific choice of a systemic model for this study, considering the potential impact on the study's outcomes and animal welfare.
4. The method of quantifying cell numbers per slice as presented raises significant concerns. Standard practice in histological studies involves normalizing cell counts to a standard metric, typically the number of positive cells per area (μm^2), to account for variations in tissue section thickness and size. The lack of normalization to such a metric calls into question the accuracy and reliability of the presented data. The authors are urged to reanalyze their results using standardized metrics and revise their statistical analysis accordingly.
5. The images provided suffer from low resolution, lack of focus, and absence of scientific rigor. Notably, they do not include scale bars, compromising their scientific validity. Furthermore, many of the quantification graphs are not accompanied by corresponding illustrative images, casting doubt on the data's integrity. The Fluoro Jade B images fail

to display specific cellular morphology, and several images appear to contain artifacts that may not represent cells. Additionally, panoramic magnifications to identify the tissue and study area are missing. The authors must address these significant issues by providing high-quality, well-processed images that adhere to scientific presentation standards.

6. The presentation of the western blot data lacks scientific appropriateness. To meet the standards of scientific publication, it is essential to include the full membrane images and ensure that the figure is edited and presented in a scientifically accurate manner. The current presentation undermines the credibility of the data and necessitates revision.

Minor Comments:

1. While the introduction provides a reasonable overview of the field, it could be enhanced by including more recent studies that have investigated similar themes. This would help to situate the study within the current research landscape more effectively. The introduction and literature review could be enhanced by incorporating more detailed discussions on the use of intracerebral vs. systemic models in epilepsy research. This would provide a clearer rationale for the study's methodological choices and situate it within the broader research context.
2. The discussion section should more thoroughly address the limitations of the study's methodology, particularly the choice of systemic models and the potential implications for the findings. Additionally, considering alternative interpretations of the data and how they might align with or diverge from existing theories of epilepsy would enrich the manuscript's analysis.
3. Some figures and tables are not as clear or informative as they could be. Improving the quality and presentation of these visual aids would aid in the reader's understanding and interpretation of the data.
4. The manuscript contains several typographical and grammatical errors that detract from its overall professionalism. A thorough proofreading is recommended to correct these issues.