

Review of: "Proton Mechanisms of Neurotransmission and Calcium Signalling for Impulse Initiation, Development, and Propagation"

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Potential competing interests: NA

The manuscript submitted by Molinari G, titled 'Proton Mechanisms of Neurotransmission and Calcium Signalling for Impulse Initiation, Development, and Propagation,' to the journal is of overall good quality. Once these minor comments are removed, it should be accepted for publication.

Minor Comments:

- 1. Proton Mechanisms of Neurotransmission and Calcium Signaling for Impulse Initiation, Development, and Propagation:
- This section could benefit from a clearer delineation of the specific mechanisms and pathways involved in protonmediated neurotransmission and calcium signaling. Providing more detailed explanations and perhaps visual aids could enhance clarity for the reader.

2. The H+/Ca2+ Correlation:

- While the correlation between H+ and Ca2+ in neurotransmission is intriguing, the manuscript should delve deeper into the physiological significance and functional implications of this correlation. Additionally, providing evidence from both in vitro and in vivo studies could strengthen the argument.
- 3. Endogenous Sources of H+ lons, Overlooked Until Now:
- This section presents an interesting premise, but the manuscript should provide robust evidence to support the claim
 that these sources have been overlooked. Including a discussion on previous research and why these sources were
 not adequately addressed could add depth to the argument.
- 4. Pre-synaptic Transmission of the Impulse in Sensory Neurons:
- While the discussion on pre-synaptic transmission is relevant, the manuscript should provide more context on how
 proton mechanisms specifically contribute to impulse transmission in sensory neurons compared to other neuron types.
 Additionally, incorporating findings from relevant studies could bolster the argument.



5. Synaptic Transmission of the Impulse:

This section could benefit from a more structured approach, perhaps by breaking down synaptic transmission into its
key components and discussing how proton mechanisms interact with each step. Additionally, including comparative
analyses with traditional neurotransmission pathways could provide valuable insights.

6. Conclusion:

- The conclusion succinctly summarizes the key findings and insights presented in the manuscript.
- Additionally, one should suggest that avenues for further investigation could be added to the conclusion section.

Overall, the manuscript shows promise in exploring proton mechanisms in neurotransmission and calcium signaling, but it would benefit from clearer organization, more detailed explanations, stronger evidence, and deeper contextualization within the existing literature.

Thanks

Regards