Review of: "Catecholaminergic Neuron Electron Transport (CNET): A Neural Signaling Mechanism"

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Potential competing interests: No potential competing interests to declare.

The paper proposes a novel neural signaling mechanism for action selection and initiation, called the Catecholaminergic Neuron Electron Transport (CNET) mechanism. The CNET mechanism is based on the observation that ferritin can store and release electrons. Ferritin is a protein that forms nanoparticles of iron oxide, which can act as a reservoir of electrons. The electrons can be released from ferritin by a variety of mechanisms, including the interaction with other molecules, such as hydrogen peroxide.

The CNET mechanism is proposed to work as follows:

- Dopamine is chemiexcited in large SNc dopamine neurons, producing high-energy triplet electrons.
- The triplet electrons are stored in ferritin structures in the neurons.
- The triplet electrons can tunnel through ferritin structures and reach other neurons.
- The triplet electrons can promote action potentials in the other neurons.
- The action potentials can then be used to select and initiate an action.

The CNET mechanism is a proposed explanation for how action selection and initiation might work in the brain. It is based on a number of observations about the properties of ferritin and dopamine, and it is consistent with what is known about the neural circuitry of the basal ganglia. However, more research is needed to confirm that the CNET mechanism is actually involved in action selection and initiation.

Paper Strengths

The paper is well-written and well-organized. It is based on a solid understanding of the relevant literature, and it is clearly presented. The author provides a strong theoretical framework for the CNET mechanism, and they discuss the potential implications of the mechanism for understanding action selection and initiation. In summary:

- The paper provides a clear and concise explanation of the CNET mechanism, including its proposed mechanism and its potential role in action selection and initiation.
- The paper presents a strong theoretical framework for the CNET mechanism, drawing on evidence from a variety of fields, including neuroscience, physics, and chemistry.
- The paper provides compelling evidence from a variety of sources to support its proposed role in action selection and initiation, including evidence from animal models and human studies.

Paper Weaknesses

The paper is limited by the lack of direct experimental evidence for the CNET mechanism. The author relies on indirect evidence, such as the observation that ferritin can store and release electrons, and the observation that dopamine can be chemiexcited. While this evidence is suggestive, it is not definitive. More direct experimental evidence is needed to confirm that the CNET mechanism is actually involved in action selection and initiation. In summary:

- The paper does not provide direct evidence from in vivo studies to support its proposed role in action selection and initiation.
- The paper does not address the potential for the CNET mechanism to be involved in other neural functions, such as cognition or emotion.
- The paper does not provide a detailed explanation of how the CNET mechanism could be integrated into existing models of basal ganglia function.

Specific Recommendations

- The author should conduct further experiments to directly test the CNET mechanism. For example, they could use electrophysiological techniques to measure the effects of dopamine on action potentials in neurons that contain ferritin. They could also use electron microscopy to visualize the movement of electrons between ferritin structures.
- The author should also consider the potential role of other molecules in the CNET mechanism. For example, they could investigate the role of hydrogen peroxide and other ROS in the release of electrons from ferritin. They could also investigate the role of other signaling pathways in the regulation of the CNET mechanism.
- Investigate the potential for the CNET mechanism to be involved in other neural functions, such as cognition or emotion.
- Develop a more detailed model of how the CNET mechanism could be integrated into existing models of basal ganglia function.
- The author should also consider developing a computational model of the CNET mechanism. This model could be used to simulate the behavior of the mechanism under different conditions, and it could help to identify the key factors that regulate the mechanism.

Conclusion

Overall, the paper "Catecholaminergic Neuron Electron Transport (CNET): A Neural Signaling Mechanism" is a well-written and thought-provoking proposal for a novel neural signaling mechanism. The paper presents a strong theoretical framework for the CNET mechanism and provides compelling evidence from a variety of sources to support its proposed role in action selection and initiation. However, the paper also raises some important questions that need to be addressed in future research. I believe that the CNET mechanism is a promising area of research and I look forward to seeing more work on this topic in the future.

I hope this feedback is helpful.