

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 manuscript entitled "Catecholaminergic Neuron Electron Transport (CNET): A Neural Signaling Mechanism" from Chris Rourk suggests that electron transport in dopaminergic and noradrenergic neurons could contribute to neuronal activity. The author presents data on the behavior of metal ions such as iron in the generation of electrons that could transfer energy over short distances. However, it does not present data showing that this energy can affect neuronal activity. He only presents theoretical conjectures. Therefore, I think this work should be considered as a possible hypothesis. In addition, I have some comments:

Page 3, third paragraph. The manuscript does not present strong evidence that dopamine metabolism may generate triplet electrons that can provide energy between neurons.

Page 4, last line and page 5. Although the presence of iron in some neurons has been demonstrated, it is difficult to believe that the energy produced by its electrons is capable of generating an action potential.

Page 5, second paragraph. Chemiexcitation, a higher-energy process involving melanin, transfers energy to DNA creating mutagenic substances. However, It is difficult to think that this energy can contribute to neuronal activity and cellular synchronization because it should be well organized within the neuron so that its energy could be added.

Page 8, second paragraph. I know that mitochondrial calcium signaling is important in calcium homeostasis. But, mitochondrial calcium does not participation in "the ignition and propagation of calcium action potentials.

Page 8, third paragraph. It is possible that "large SNc dopamine neurons generate high-energy triplet electrons that are stored in somatic ferritin"; however, there is no proof that "these electrons are available to move between soma". Therefore, data must be provided that demonstrate its contribution to neuronal communication.

Page 8. 3. The triplet electrons can tunnel through ferritin between soma. The generation of triplet electrons has been demonstrated in materials but not in neurons.

Page 14. where is figure 8?

Page 16, second paragraph. There is no evidence that these electrons can generate calcium action potentials.

Page 17, second paragraph. The sentence "Endogenous H₂O₂ also regulates the excitability of dopamine neurons ..." should include a reference such as Avshalumov et al. 2005.

Page 17, 5.c. Ryanodine receptors (RyR) release calcium in response to ROS, which can contribute to the generation of calcium action potentials. What is the relationship of the electron transport with the modulation of the Ryanodine receptors?

In conclusion, the author hypothesizes that electron transport can contribute to the control of cellular activity; however, there is no evidence that this energy is sufficient to produce intracellular changes and even less so between neurons.