

<https://doi.org/10.70200/RX202401036L>

## REDOX REGULATION OF NEUROVASCULAR COUPLING BY NITRIC OXIDE TO IMPROVE COGNITION IN AGING AND NEURODEGENERATION

João Laranjinha<sup>1\*</sup>, João Gonçalves<sup>1</sup>, Cátia Lourenço<sup>1</sup>

<sup>1\*</sup>Center for Neurosciences and Cell Biology and Faculty of Pharmacy, University of Coimbra, Portugal, [laranjin@ci.uc.pt](mailto:laranjin@ci.uc.pt)

The physicochemical properties of nitric oxide (NO) as an intercellular messenger, in particular the way it conveys information via volume signaling, translate into advantages of communication in the brain. This becomes apparent when considering neurovascular coupling (NVC), the tightly temporal and spatial functional communication between active neurons and local blood microvessels. That the brain is energetically expensive given its mass and that increased neuronal activity in a region of the brain is associated with a local increase in blood flow (CBF) has been known since the XIX century. In turn, the association between CBF dysregulation and cognitive decline has been consistently established in older adults (brain aging, neurodegenerative diseases, type II DM) and lab rodent models but the neurobiological links are poorly understood. I will discuss the notion that neuronal-derived NO is the key mediator of NVC in the hippocampus and that impairment of NVC is an early and likely causative event leading to cognitive decline. The premise is that by rescuing the functionality of NVC then cognitive enhancement should be observed. This will be experimentally supported on basis of a diet-driven redox mechanism, involving the interaction of nitrite with ascorbate released from active neurons. Data suggest that an operational NVC, allocating energy resources according to neuronal activity, is a most fundamental biochemical process that underlines biological organization to support cognition.

*Supported by project 2022.05454.PTDC (<https://doi.org/10.54499/2022.05454.PTDC>).*