https://doi.org/10.70200/RX202401020D

NITRITE MITIGATES OXIDATIVE BURST IN ISCHEMIA/REPERFUSION IN BRAIN SLICES

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Nitrite is the typical byproduct of nitric oxide (•NO) autooxidation in biological systems. However, certain circumstances favor its reduction "back" to the signaling free radical, providing a non-enzymatic route for the synthesis of •NO. In pathophysiological conditions such as ischemia/reperfusion (I/R), where low oxygen availability limits nitric oxide synthase activity, nitrite reduction to •NO may allow protective modulation of mitochondrial oxidative metabolism and thus reduce the impact of I/R on brain tissue. In the current study, we used high-resolution respirometry to evaluate the effects of nitrite in an *in vitro* model I/R using hippocampal slices. We found that reoxygenation was accompanied by an increase in oxygen flux, a phenomenon that has been coined "oxidative burst". The amplitude of this "oxidative burst" was decreased by nitrite in a concentration-dependent manner. These results support the notion that nitrite mediates a decrease in the hyper-reduction of the electron transport system during ischemia, decreasing the accelerated oxygen consumption that characterizes the reoxygenation phase of I/R that has been associated with an increase in oxidant production. Additionally, a pilot in vivo study in which animals received a nitrate-rich diet as a strategy to increase circulating and tissue levels of nitrite also revealed that the "oxidative burst" was decreased in the nitrate-treated animals. These results may provide mechanistic support to the observation of a protective effect of nitrite in situations of brain ischemia.