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## Reactive oxygen species initiate a metabolic collapse in hippocampal slices: Potential trigger of cortical spreading depression

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### Abstract

Excessive accumulation of reactive oxygen species (ROS) underlies oxidative damage. We find that in hippocampal slices, decreased activity of glucose-based antioxidant system induces a massive, abrupt, and detrimental change in cellular functions. We call this phenomenon metabolic collapse (MC). This collapse manifested in long-lasting silencing of synaptic transmission, abnormal oxidation of NAD(P)H and FADH<sub>2</sub> associated with immense oxygen consumption, and massive neuronal depolarization. MC occurred without any preceding deficiency in neuronal energy supply or disturbances of ionic homeostasis and spread throughout the hippocampus. It was associated with a preceding accumulation of ROS and was largely prevented by application of an efficient antioxidant Tempol (4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl). The consequences of MC resemble cortical spreading depression (CSD), a wave of neuronal depolarization that occurs in migraine, brain trauma, and stroke, the cellular initiation mechanisms of which are poorly understood. We suggest that ROS accumulation might also be the primary trigger of CSD. Indeed, we found that Tempol strongly reduced occurrence of CSD in vivo, suggesting that ROS accumulation may be a key mechanism of CSD initiation. © 2014 ISCBFM All rights reserved.

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