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Mitochondrial respiratory chain and creatine kinase activities following trauma brain injury in brain of mice preconditioned with *N*-methyl-D-aspartate

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Abstract Traumatic brain injury (TBI) induces glutamatergic excitotoxicity through *N*-methyl-D-aspartate (NMDA) receptors, affecting the integrity of the mitochondrial membrane. Studies have pointed to mitochondria as the master organelle in the preconditioning-triggered endogenous neuroprotective response. The present study is aimed at understanding energy metabolism in the brains of mice after preconditioning with NMDA and TBI. For this purpose, male albino CF-1 mice were pre-treated with NMDA (75 mg/kg) and subjected to brain trauma. Mitochondrial respiratory chain and creatine kinase activities were assessed at 6 or 24 h after trauma. The mice preconditioned and subjected to TBI exhibited augmented activities of complexes II and IV in the cerebral cortex and/or cerebellum. Creatine kinase activity was also augmented in the cerebral cortex after 24 h. We suggest that even though NMDA preconditioning and TBI have similar effects on enzyme activities, each manage their response via opposite mechanisms because the protective effects of preconditioning are unambiguous. In conclusion, NMDA preconditioning induces protection via an increase of enzymes in the mitochondria.

Keywords NMDA preconditioning · Neuroprotection · Trauma brain injury · Mitochondrial respiratory chain · Creatine kinase

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Introduction

The cellular damage that occurs following traumatic brain injury (TBI) constitutes dynamic pathophysiology of the brain in consequence of the combination of primary (unavoidable damage, occurs at the time of injury) and secondary damage (avoidable damage, occurs at variable times after injury). The severity of the secondary injury level over time depends on the degree of mechanical impact [1, 2], and can be classified as mild, moderate or severe [2, 3]. The subsequent cascade of events leading to acute brain injury include glutamatergic excitotoxicity [4], ionic imbalance, ATP depletion, proteolysis and oxidative stress [5]. This set of intracellular outcomes leads to the impairment of synaptic plasticity, with an associated modulation of glutamatergic N-methyl-D-aspartic (NMDA) receptor activity [6] and alteration of subunit NMDA receptors content [7]. Excitotoxicity induced by glutamate involves, at least in part, the elevation of intracellular Ca^{2+} levels through excessive activation of the NMDA receptors [8], which may affect the integrity of the mitochondrial membrane through mitochondrial permeability transition pore opening [9].

Once opened, the mitochondrial membrane pore uncouples oxidative phosphorylation, induces a reduction of ATP levels, disturbs metabolic homeostasis, releases cytochrome *c*, and induces cell death by apoptosis [10].