SUSCEPTIBILITY OF STRIATUM TO 3-NITROPROPIONIC ACID-INDUCED MITOCHONDRIAL PERMEABILITY TRANSITION: A DOSE-DEPENDENT STUDY AND CORRELATION WITH OTHER BRAIN REGIONS AND TISSUES

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The purpose of the present study was to compare the susceptibility of isolated mitochondria from liver, kidney and heart and different rat brain regions (striatum, cortex and cerebellum), regarding to permeability transition pore (PTP) opening evoked by 3-nitropropionic acid (3-NP) and Ca^{2+} ions. In general, isolated brain mitochondria from different regions were more sensitive to 3-NP and Ca^{2+} toxicity than mitochondria from liver and kidney as estimated by decrease in the transmembrane electrical potential and mitochondrial swelling. The comparision of different brain regions revealed that the inhibition of 50% of the mitochondrial succinate-supported respiration elicited by 3-NP resulted in a Ca^{2+}-induced PTP opening, inhibited by cyclosporin A, faster in striatal than in cortical and cerebellar mitochondria. It was verified an inhibition of succinate dehydrogenase activity from the same magnitude in all tissues studied after a 3-NP systemic treatment. Interestingly, isolated forebrain mitochondria obtained from rats systemically treated with 3-NP showed a more pronounced susceptibility to Ca^{2+}-induced PTP opening when compared to control rats. We propose that the increased susceptibility of rat striatum to 3-NP-induced neurodegeneration could be in part explain by a region-specific susceptibility to PTP opening together with increase vulnerability of this brain region to glutamate receptors-mediated cytosolic Ca^{2+} influx.

Supported by *FAPESP* and *CNPq*.