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The spatial and temporal relationship between oxidative stress and neuronal degeneration in 3-nitropropionic acid model

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ABSTRACT

The current study investigates the role of oxidative stress and calcium homeostasis in the development of selective striatal lesions in metabolic impairment model caused by 3-nitropropionic acid (3NP). In this report, we examined the distribution of oxidative stress markers and the production of mitochondrial reactive oxygen species in the presence of 3NP in male Sprague-Dawley rats. Protein oxidation was assessed using 3-nitrotyrosine immunoreactivity, while DNA oxidative damage was evaluated by poly (ADP-ribose) polymerase-1 activity. The Reactive Oxygen Species (ROS) production was determined in isolated mitochondrial from striatum and cerebellum of two age groups following 3NP and variable calcium concentration. The results demonstrate that increased 3-nitro-tyrosine level is the most robust in the striatum and the least evident in the cerebellum following 4 days of 3NP treatment. No significant change in the levels of poly ADP-ribosylated proteins was observed, likely due to a rapid PARP-1 cleavage as detected by the appearance of 50 kDa necrotic fragment. In mitochondrial isolates, there was no immediate increase in mitochondrial ROS following 3NP in either striatum or cerebellum; however, calcium addition resulted in a concentration dependent increase in reactive oxygen species in striatal mitochondria of the older animals. These results suggest that in aging, mitochondria become more susceptible to the generation of ROS in conditions that cause a concurrent compromised in mitochondrial calcium concentration. This finding implicates mitochondria dysfunction as a key cellular target in pathological states that are associated with metabolic impairment. The results also reinforce the notion that mitochondrial function in the striatum and cerebellum respond differently to the aging process, which may explain the variable regional vulnerability in 3NP model.

KEYWORDS

Energy Impairment; 3-Nitropropionic Acid; Oxidative Stress; Neurodegeneration

Cite this paper

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