BRAIN MITOCHONDRIAL DYSFUNCTION IN SEPSIS

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Sepsis is a systemic inflammatory condition that may evolve into multiple organ dysfunction. Evidences indicate that a deregulation of mitochondrial oxygen metabolism contributes decisively to the pathogenesis of this disease. Here, we investigated the changes in mitochondrial functions in the brain during sepsis. Non-lethal sepsis was induced by coecal ligation and puncture (CLP) in adult Swiss mice for 24h. Brain homogenates from septic mice had increased oxygen consumption rate in the absence of ADP (state 4), affecting both respiratory control ratio and ADP:O ratio, suggesting an uncoupling of oxidative phosphorylation. Isolated brain mitochondria from CLP mice had a significant delay in the time of membrane potential (??m) repolarization after ADP addition, showing that ??m is being dissipated during sepsis. Moreover, the activity of complex IV, and not other mitochondrial complexes, was partially inhibited in the brain of septic animals. Measurements of mitochondrial ROS production induced by succinate revealed that CLP brain failed to diminish ROS production after the addition of ADP. Together, these data indicate that mitochondrial dysfunctions such as uncoupling and impairment of complex IV activity occur in the brain during sepsis and may play an important role in the pathogenesis of this condition.

Key words: Brain, mitochondria, sepsis.
Support: CNPq, Faperj, FUJB.