Caloric Restriction Increases Mitochondrial Calcium Uptake Rate and Retention Capacity in Mouse Livers

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INTRODUCTION: Caloric restriction (CR) is a dietary intervention known to extend lifespan, delay the onset of many age related pathological conditions and promote several other benefits in many experimental models. The mechanisms by which CR promotes its effects are not completely understood, but alterations in mitochondrial function are frequently observed in CR models. Since mitochondria can interfere in calcium signaling, and calcium signaling and homeostasis deregulation can lead to many pathological conditions, including some prevented by CR, we sought to evaluate the impacts of CR on mitochondrial calcium handling in mouse liver.

OBJECTIVES: To evaluate the impact of CR on mitochondrial calcium handling in mitochondria isolated from mouse livers.

MATERIAL AND METHODS: Mitochondria from livers of 6 months old swiss mice submitted to 4 months of 40% CR or eating ad libitum (AL) were isolated by differential centrifugation and assayed for maximal calcium uptake before undergoing permeability transition by incubating in a medium with a fluorescent calcium probe (calcium green 5N) and conducting calcium additions at fixed time intervals. Oxygen consumption in state 3, 4 and uncoupled respiration was measured in an Oroboros oxygraph.

DISCUSSION AND RESULTS: Mitochondria from CR animals showed a marked increase in calcium retention capacity (CRC) and uptake rates of the ion. External addition of ATP or loading with ATP equaled both parameters between the two groups. Incubation with the cyclophilin D inhibitor ciclosporin A equaled CRC, but not the uptake rates. ADP, whose transport into the mitochondria is not as efficient as ATP, did not equal CRC. These results suggest an increased basal concentration of adenine nucleotides in the mitochondrial matrix of CR livers. No changes in oxygen consumption were observed in any state.

CONCLUSION: CR increases CRC and Ca^{2+} uptake rates in mouse liver mitochondria in a manner dependent on matrix adenine nucleotide concentration.

Palavra chave: Mitochondria, Caloric Restriction, Calcium, Liver
Patrocínio: FAPESP, REDOXOMA and CAPES