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Pathological stimuli-induced remodeling of rat heart mitochondrial membranes: positive role in processes of myocardial adaptation
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Purpose: Mitochondria (MIT) from hearts of rats with acute streptozotocin (STZ)-diabetes (DIA) and hearts subjected to remote preconditioning induced by limb ischemia (R-PC) exhibited functional re-modeling of membranes followed by a cascade of changes reflecting a dynamic equilibrium between the pathological processes and the processes of endogenous protection (EP). Aim of the study was to investigate the effects of R-PC and PC - induced acute diabetes mellitus (DM), on the biophysical and biochemical properties of cardiac MIT.

Methods: Male Wistar rats (220 ± 20g) were used in the experiment. DIA was induced by a single dose of STZ, (65 mg/kg, i.p.). R-PC was induced by 3 series of 5 min. ischemia and 5 min. reperfusion. Hearts were rapidly excised, perfused in the Langendorff mode and exposed to 30 min. global ischemia and 40 min reperfusion. MIT were isolated by means of differential centrifugation combined with protease treatment. Mg2+-dependent and 2, 4-dinitrophenol - stimulated ATPase activity was determined by estimation of Pi liberated from ATP splitting. Membrane fluidity (MF) of isolated MIT was assessed by measuring fluorescence anisotropy of 1,6-diphenyl-1,3,5-hexatriene. Content of oxidized isoforms of the coenzyme Q (CoQ9-ox and CoQ10-ox) in the MIT was assessed by means of HPLC and the content of conjugate dienes (CD) was determined spectrophotometrically at 230 nm.

Results: MIT from acute (8 days) DIA hearts exhibited significantly (p < 0.05) elevated MF and Mg2+-ATPase activities. An increase in MF was also observed in R-PC and it remained present even after ischemia and post-ischemic reperfusion. Free radicals created in heart MIT in the time course of development of the DIA left the MIT membrane without inducing any considerable increase in the amount of CD or decrease in fluidity of the lipid bilayer. On the other hand, the increase in oxidized forms of the CoQ9-ox and CoQ10-ox in the MIT membrane occurred in sense of the old paradigm that radicals-induced oxidative changes in components of the respiratory chain are at least co-responsible for its malfunction in diabetes.

Conclusions: Our findings confirmed that the changes in properties and function of MIT membranes associated with DIA- and R-PC-induced remodeling are intimately involved in increased ischemia-tolerance of the myocardium. Grants: VEGA 2/0101/12, APVV 0102-11, KEGA 003 UK-4/2012.