PHYSICAL EXERCISE AS A FORM OF NON-ISCHEMIC „CONDITIONING“: POTENTIAL MOLECULAR MECHANISMS OF CARDIOPROTECTION

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Although ischemic preconditioning (IPC) is the most robust adaptive intervention protecting the heart of all animal species against ischemia/reperfusion (I/R) injury, its application in humans is limited to elected operations due to technical requirements, such as chest opening, short-term duration and unpredictable occurrence of AMI. However, other forms of “conditioning” do not require invasive intervention.
We explored preventive interventions applied *in vivo* aimed to increase cardiac resistance to I/R prior to AMI *ex vivo* using non-invasive approach in the adult male Wistar rats: voluntary exercise-induced PC (EPC). For EPC, adult male animals were placed in the cages equipped with wheels for free running, while control sedantary animals stayed in the standard cages. At the beginning and the end of the protocol, heart structure and function was evaluated by ECHOcardiography and except reduced body weight did not reveal functional changes. After 2 weeks, the efficacy of EPC was tested in the Langendorff-perfused hearts exposed to 30 min global ischemia/2 hrs reperfusion, focused on the postischemic recovery of function, arrhythmogenesis and extent of lethal injury (infarct size, IS/AR, TTC staining). In parallel groups, heart tissue samples were obtained for the investigation of the levels and activity of several proteins involved in “pro-survival” RISK cascade. EPC significantly reduced contractile dysfunction, IS size and the incidence and severity of reperfusion arrhythmias. Protective effects were associated with a significant up-regulation of selected pro-survival RISK proteins, such as PKB, PKCε, eNOS, anti-apoptotic and anti-oxidative effects. Beneficial effects of sub-chronic free running suggest its potential in the management of ischemic heart disease.

Grants Slovak Grant Agency VEGA SR 2/0104/22, 1/0016/20, APVV-19-0540, APVV-20-0242.