PRIOR EXERCISE INDUCES CARDIOPROTECTION AGAINST ISCHEMIA-REPERFUSION INJURY: CONTRIBUTION OF THE INTRACELLULAR AXIS PKCEPSILON-ALDH2

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Introduction and objectives: Ischemic preconditioning protects the heart against sustained ischemia and reperfusion (I/R) injury. This process is dependent on the translocation of protein kinase C isoform epsilon (PKCε) from cytosol to mitochondria and subsequent phosphorylation of cardiac mitochondrial aldehyde dehydrogenase 2 (ALDH2). Similar to ischemic preconditioning, previous physical exercise induces cardioprotection against I/R. However, the cellular mechanisms involved in this process have not been elucidated. Thus, we aim to understand the molecular aspects involved in cardioprotection induced by exercise against the insult of I/R in mice. Materials and methods: We submitted C57BL6 mice (wild type-WT) and protein kinase Cε knockout mice (PKCεKO) to a protocol of aerobic exercise training on treadmill for seven following days. 24 hours after the last session of exercise hearts were excised and retrograde perfused using a Langendorff apparatus. Analyzed variables: Infarct size (triphenyltetrazolium chloride staining), release of hydrogen peroxide (H₂O₂) in isolated mitochondria, PKCε translocation (western blotting in total lysate and mitochondrial fraction) and ALDH2 activity in cardiac lysate. Results and conclusions: Our results demonstrate that seven days of physical exercise on treadmill protects against I/R injury (myocardial infarction size: control 50±2% vs exercised 31±4%, p<0.05). The exercise-mediated cardioprotection was paralleled by increased PKCε protein level in both total lysate and mitochondrial fraction as well as elevated ALDH2 catalytically activity. Of interest, exercise did not protect PKCε KO mice against I/R injury, further supporting a PKCε mechanism for exercise-induced cardioprotection. No differences were found in the H₂O₂ release after training in WT and PKCεKO groups. These results reveal for the first time the crucial role of the axis PKCε-ALDH2 during exercise-induced cardioprotection against ischemia/reperfusion injury. Acknowledgements: FAPESP. Key Words: physical exercise, PKCε, cardioprotection.