ABSTRACT

Despite advances in research and therapy, cardiovascular diseases are still the leading cause of death worldwide. A closer understanding of the endogenous protective mechanism may improve pharmacological interventions for the treatment of heart diseases. Cold acclimation or hardening has strong potential for reducing cardiovascular risk and the literature shows that it stimulates the β-adrenergic and thyroid systems in tissues. At the same time, the adrenergic system in the heart is one of the main regulators of cardiac activity. However, these signaling pathways have surprisingly not been studied at the protein level in the heart yet, and no studies can be found on the subject matter in current literature. Our results show a reduced infarct size induced by ischemic injury in cold-acclimated rats (CA) at 8 ° C for 5 weeks and then returning to normothermic conditions for 2 weeks (CAR). The aim of this dissertation is to determine, the degree of involvement of the adrenergic system in the myocardium during acclimation after 3 days, 10 days, 5 weeks of CA and subsequent CAR at the level of all three β-adrenergic receptor isoforms (β-ARs) and their signaling pathways. The results show unchanged signaling of β1-AR-Gs-adenylyl cyclase-protein kinase A in the cardioprotective regimes CA and CAR, whose long-term activation is detrimental for cardiomyocytes. An important result is the demonstrated activation of β2-AR-protein kinase B (Akt) in CAR and potentially the activation of β3-AR, which are associated with many cyto- and cardioprotective mechanisms. These results provide a first and unique insight into the molecular mechanism of cold acclimation and its effect on the heart.

Key words: cold acclimation, rat, heart, adrenergic and thyroid signaling