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Changes in the Pattern of Activation of Sap Kinases during Ischemia/Reperfusion after Thyroxine Administration in Isolated Rat Hearts: Possible Mechanism of Thyroxine Induced Cardioprotection

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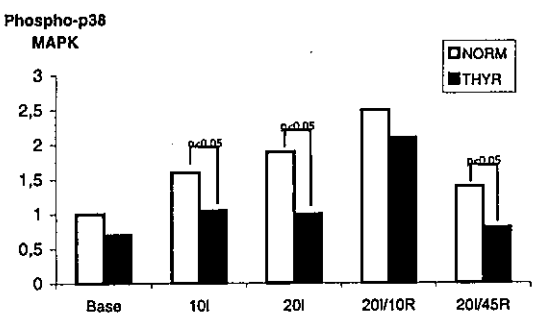
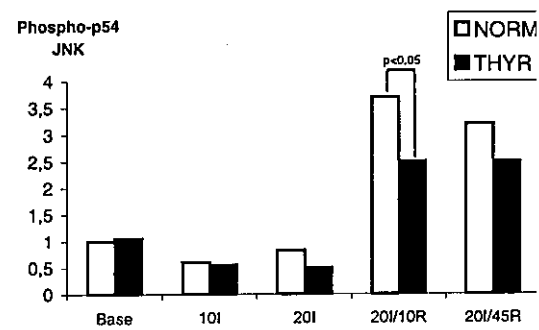
AIM

The sustained activation of SAPK (Stress Activated Protein Kinases), such as p38 MAPK and JNK, has been shown to induce apoptosis in the heart during ischemia-reperfusion. Previous studies have shown that long-term thyroxine administration protects the heart against ischemia. Aim of this study was to investigate whether thyroxine induced cardioprotection is associated with changes in the pattern of activation of SAPK during ischemia-reperfusion in isolated rat hearts.

METHODS

Hyperthyroidism was induced in Wistar rats by L-thyroxine administration (25μg/100g body weight) for 14 days (THYR), while normal animals treated with normal saline served as controls (NORM). Isolated rat hearts were perfused in a Langendorff mode. Normal and hyperthyroid hearts were subjected to: 1) 15 min stabilization, NORM (Base), n=4 και THYR(Base), n=5. 2) 15 min stabilization and 10 min global, zero-flow ischemia (I), NORM(10I), n=5 και THYR(10I), n=5 3) 15 min stabilization and 20 min of I NORM(20I), n=5 και THYR(20I), n=4, 4) 15 min stabilization, 20 min of I and 10 min reperfusion (R), NORM(20I/10R), n=5 και THYR(20I/10R), n=5. 5) 15 min stabilization, 20 min of I and 45 min reperfusion (R), NORM(20I/45R), n=5 και THYR(20I/45R), n=4. Postischaemic recovery of left ventricular developed (LVDP) pressure was expressed as % of the initial value (LVDP%). Phosphorylated and total p38 MAPK, and JNK were measured by Western blot analysis





RESULTS

LVDP% was 61.5 (6.6) for THYR(20I/45R) and 42.7 (4.9) for NORM(20I/45R) hearts, $p<0.05$. The pattern of activation of SAPK is shown in the following figures.

CONCLUSIONS

Thyroxine induced cardioprotection is associated with changes in the pattern of activation of SAPK during ischemia/reperfusion in the isolated rat heart model.