Conclusion — EPO improves post-ischemic cardiac function recovery in insulin resistance but not in diabetic rat hearts. Survival signalling pathways seem to be impaired in presence of diabetes.

F006
CRITICAL ROLE OF ERK1/2 IN ERYTHROPOIETIN-MEDIATED CARDIOPROTECTION COMPARED WITH ISCHEMIC POSTCONDITIONING
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Background — Erythropoietin (EPO) and ischemic postconditioning (IPost) have been shown to attenuate myocardial reperfusion injury.

Aims: This study compared the mechanisms of the acute cardioprotective effect of EPO and IPost and tested whether they share similar signalling pathways in isolated rat hearts, focussing on phosphatidylinositol 3-kinase (PI3K)/Akt and ERK1/2 pathways.

Methods — Hearts were subjected to 25 min global ischemia followed by 30 min of reperfusion. 7 groups were tested: control (no intervention); IPost (3 cycles of 10 sec reperfusion/10 sec ischemia at the onset of reperfusion); EPO (1000 UI/kg, at the onset of reperfusion); EPO+IPost- or EPO-treated hearts exhibited significantly improved left ventricular function reflected by an increase in post-ischemic recovery of left ventricular developed pressure (LVDP) and improved contractility (dP/dtmax) and relaxation (dP/dtmin) indexes throughout the reperfusion period compared with control hearts. EPO showed better LVDP than IPost at 30 min reperfusion (73.18±10.23 mmHg vs. 48.11±7.92 mmHg, p<0.05); ii) up-regulation in PI3K/Akt, ERK1/2 and GSK-3β signalling.

Results — IPost- or EPO-treated hearts exhibited significantly improved left ventricular function reflected by an increase in post-ischemic recovery of left ventricular developed pressure (LVDP) and improved contractility (dP/dtmax) and relaxation (dP/dtmin) indexes throughout the reperfusion period compared with control hearts. EPO showed better LVDP than IPost at 30 min reperfusion (73.18±10.23 mmHg vs. 48.11±7.92 mmHg, p<0.05); ii) up-regulation in PI3K/Akt, ERK1/2 and GSK-3β signalling.

Conclusion — EPO and IPost share similar intracellular cardioprotective pathways. EPO exhibits better cardioprotective effects than IPost against reperfusion injury leading to great hopes in EPO as a pharmacological agent of postconditioning. This increased resistance to myocardial ischemia induced by EPO seems to be mediated by an enhanced phosphorylation of ERK1/2.

F007
MODULATION OF THE STAT3 PATHWAY BY TRANSIENT ANOXIA AND OXIDANT STRESS IN A FETAL HEART MODEL
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Purpose — The Janus Kinase 2 / Signal Transducer and Activator of Transcription 3 (JAK2/STAT3) pathway is involved in protection of the adult heart against ischemia/reperfusion. STAT3 activation can result from phosphorylation on two sites: tyrosine 705 by JAKs and serine 727 mainly by Mitogen-Activated Protein Kinases (MAPKs). We have previously shown that, under basal conditions, STAT3 is inhomogeneously distributed and phosphorylated in atria, ventricle and outflow tract of the embryonic heart. However, to what extent the JAK2/STAT3 pathway contributes to the response of the developing heart to transient oxygen lack or oxidant stress remains unknown.

Methods — Hearts isolated from 4-day-old chick embryos were studied in vitro. In a first series of experiments, hearts were submitted to anoxia (30min) and reoxygenation (80min) with or without the antioxidant MPG (1mM) to determine the role of reoxygenation. The time course of STAT3 phosphorylation on tyrosine (P-Tyr) and on serine (P-Ser) of adult rat hearts was determined by immunoblotting on ventricles removed at specific time points. In a second series of experiments, hearts were exposed to H2O2 (1mM, 1h) and STAT3 phosphorylation (P-Tyr and P-Ser) was assessed in atria, ventricle and outflow tract.

Results — In the ventricle, P-Tyr STAT3 was unchanged during anoxia but increased upon reoxygenation, reaching a peak (eightfold) after 1h and returning to baseline after 80min. P-Ser STAT3 slightly increased (x1.7) only after 1h of reoxygenation. The peak of P-Tyr STAT3 was abolished by MPG. Exposure to H2O2 increased significantly P-Tyr STAT3 only in the ventricle (twofold) but had no effect on P-Ser STAT3 whatever the investigated region. Moreover, H2O2 suppressed atrial activity in 50% of the hearts and atroventricular conduction in 70% of the hearts.

Conclusions — In the anoxic-reoxygenated ventricle of the embryonic heart STAT3 activation i) is ROS-dependent, ii) requires specific phosphorylation on tyrosine site and iii) is probably independent of MAPKs. STAT3 could also contribute to the protection of the developing heart submitted to oxidant stress or transient anoxia.

F008
ADAPTATION DE L’ÉNERGÉTIQUE MITOCHONDRIALE CARDIAQUE CHEZ LA SOURIS EN RÉPONSE À L’HYPoxie Chronique
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La compréhension des mécanismes physiologiques ainsi que leur retentissement global sur l’énergétique cardiaque en réponse à l’hypoxie chronique nécessite l’étude intégrée de modèles expérimentaux développant les symptômes adaptatifs observés lors des pathologies pulmonaires.