INVOLVEMENT OF MITOGEN-ACTIVATED PROTEIN KINASES (MAPKS) DURING TESTICULAR ISCHEMIA-REPERFUSION INJURY IN NUCLEAR FACTOR-κB KNOCK-OUT MICE

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We investigated the patterns of ERK 1/2 and JNK activation in NF-κB knockout (KO) mice subjected to testicular torsion.
KO and normal littermate wild-type (WT) animals were subjected to testicular ischemia followed by 24 h reperfusion (TI/R). Sham testicular ischemia-reperfusion mice served as controls. ERK 1/2 and JNK expression by western blot analysis, Tumour Necrosis Factor-α (TNF-α) expression (RT-PCR and western blot) and a complete histological examination were carried out.
TI/R caused a greater increase in phosphorylated form of ERK 1/2 in KO mice (25 ± 3 integrated intensity; 18 ± 3 integrated intensity; respectively) than in WT animals (15 ± 2 integrated intensity; 10 ± 1 integrated intensity; respectively) in either the ischemic testis and the contralateral one. By contrary, active form of JNK was completely abrogated in both testes of KO mice (0.1 ± 0.02 integrated intensity; 0.3 ± 0.01integrated intensity; respectively), while WT animals showed a significant activation of this kinase in both testes (10 ± 2 integrated intensity; 8 ± 1integrated intensity; respectively). TNF-α expression was markedly reduced in KO mice (3 ± 0.6 n-folds/β-actin; 5 ± 1 integrated intensity;) when compared to WT mice (14 ± 2 n-folds/β-actin; 18 ± 3 integrated intensity) either at the mRNA and the protein level. Finally TI/R-induced histological damage was markedly reduced in KO mice. Our data indicate that NF-κB plays a pivotal role in the development of testicular ischemia-reperfusion injury and suggest that, in the absence of the transcriptional factor, the up-stream signal JNK may be abrogated while ERK 1/2 activity is over-expressed.