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论文

ErbB信号与蛋白激酶B在快速起搏所致猴心衰心肌细胞损伤中的作用

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摘要:

为了研究ErbB受体与蛋白激酶B在心力衰竭发生机制中的作用，建立快速起搏诱导恒河猴心力衰竭模型。采用颈总动脉插管技术，测定左心室最大压力上升速度($LVdp/dt_{max}$)、左心室舒张末期压(LVEDP)、左心室收缩末期压(LVSP)等血流动力学指标；采用电化学发光免疫测定法观察脑钠肽(BNP)含量；采用RT-PCR方法测定$ErbB_2$、蛋白激酶B(PKB)、Bcl-xl mRNA表达水平；采用Western blotting检测蛋白激酶B活性(phospho-PKB，即磷酸化蛋白激酶B蛋白水平)及凋亡相关基因Bcl-xl的蛋白水平。快速起搏诱导心力衰竭模型恒河猴心肌收缩能力显著下降，心衰标志物脑钠肽水平明显上升($P<0.05$)。与对照组比较$ErbB_2$，PKB及Bcl-xl mRNA表达水平明显下降($P<0.05$)，同时心肌组织蛋白激酶B活性显著下降，Bcl-xl蛋白水平也明显下降($P<0.05$)。快速起搏所致猴心衰心肌细胞损伤的机制可能与$ErbB_2$、下游蛋白激酶B、凋亡抑制基因Bcl-xl表达水平下降及蛋白激酶B活性下降有关。

关键词： 心力衰竭 细胞凋亡 $ErbB_2$受体 蛋白激酶B

Effects of ErbB signal and protein kinase B on monkey cardiocyte apoptosis induced by rapid pacing

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Abstract:

This study is to investigate the roles of neuregulin receptor $ErbB_2$ and protein kinase B (PKB) in pacing-induced heart failure of rhesus monkey. Rapid pacing was used to induce heart failure in rhesus monkey. Aorta intubatton was used to perform hemodynamic measurements, 17 days after pacing. *n*-Terminal pro-brain natriuretic peptide (BNP), one of the most important molecular marker of heart failure, was also measured by the method of electrochemical luminescence immunoassay. The mRNA expressions of $ErbB_2$, PKB and Bcl-xl were detected in the left ventricular free walls by RT-PCR method. The expressions of phospho-PKB and Bcl-xl on protein level were also detected by Western blotting. The contractibility of cardiac muscle decreased significantly, which consisted with the increase of BNP. Compared with control group, the mRNA expressions of $ErbB_2$, PKB and Bcl-xl were depressed, and similar results were also found in the protein expression analysis of phospho-PKB and Bcl-xl. The expressions of $ErbB_2$, PKB and Bcl-xl were down-regulated during heart failure in rhesus monkey which suggested the important roles of $ErbB_2$ receptor and PKB in the mechanism of heart failure.

Keywords: apoptosis $ErbB_2$ receptor protein kinase B heart failure

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