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论文

阿片类药物对NG108-15细胞Ca^{2+}/钙调蛋白依赖的蛋白激酶II信息通路的作用

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摘要:

目的 观察阿片类依赖时Ca^{2+} 钙调蛋白依赖的蛋白激酶II信息通路的变化。方法 以NG108-15细胞作为体外的细胞模型,分别用竞争性蛋白结合法及放射免疫法、PDE法、γ-^{32} P参入法测定cAMP水平、钙调蛋白(CaM)活性和钙调蛋白依赖的蛋白激酶II(CaMKII)活性。结果 DPDPE作用NG108-15细胞48h可使细胞浆和细胞核CaM和CaMKII活性升高,该变化可被CaM特异性拮抗剂W-7所抑制;CaMKII特异性抑制剂KN-62可抑制CaMKII活性的增高,而对CaM活性无明显影响。DPDPE作用NG108-15细胞48h后,加入纳洛酮,CaM活性、CaMKII活性进一步增高。结论 Ca^{2+} CaMKII信息通路参与了阿片依赖的机制。

关键词: 阿片类药物 钙调蛋白 钙调蛋白依赖的蛋白激酶II

EFFECTS OF OPIOIDS ON Ca^{2+}/CALMODULIN DEPENDENT PROTEIN KINASE SIGNAL PATHWAY IN NG108-15 CELLS

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Abstract:

AIM To observe the change of Ca^{2+}/calmodulin dependent protein kinase II (CaMK II) signal pathway in opioid dependent NG108-15 cells. METHODS NG108-15 cells were used as an *in vitro* model system. Competitive protein binding assay and radioimmunoassay were used to examine the intracellular cAMP accumulation. Calmodulin activity was assayed by PDE method. CaMK II activity was assayed by γ-^{32} P incorporation of syntide-2. RESULTS DPDPE long-term treatment increased calmodulin activity and CaMK II activity in both cytoplasm and nucleus of NG108-15 cells. Specific calmodulin antagonist W-7 was found to significantly inhibit the elevation of calmodulin and CaMK II activity which resulted from DPDPE long-term treatment, and CaMK II inhibitor KN-62 also inhibited elevation of CaMK II activity by DPDPE long-term treatment. When naloxone was added to NG108-15 cells which were long-term treated by DPDPE, calmodulin and CaMK II activity increased, indicating that naloxone withdrawal can increase Ca^{2+}/CaMK II pathway activity. CONCLUSION The results indicate that Ca^{2+}/CaMK II pathway was involved in the mechanisms of opioids dependence when DPDPE was long-term administered to NG108-15 cells.

Keywords: calmodulin calmodulin dependent protein kinase II opioids

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