

论文

吗啡依赖小鼠脑组织cGMP水平、鸟苷酸环化酶及磷酸二酯酶活性的调节

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摘要:

以递增剂量吗啡sc,使小鼠产生对吗啡的躯体依赖,观察脑组织cGMP水平、PDE和sGC的活性变化及PKA对其磷酸化调节。结果表明,(1)小脑、纹状体、海马及大脑皮质cGMP含量显著降低;(2)在小脑、海马中sGC活性明显降低,PDE活性无明显变化,在纹状体及大脑皮质中均明显升高,且体外磷酸化水平也均明显下降,PKA抑制剂可抑制此变化;(3)纳洛酮拮抗组未见上述变化。结果提示,吗啡依赖小鼠脑组织cGMP水平普遍降低,在小脑和海马可能因sGC活性下降引起,在纹状体及大脑皮质可能因PDE活性升高所致。

关键词: 吗啡 依赖 鸟苷酸环化酶 磷酸二酯酶 环磷酸鸟嘌呤

MODULATION OF cGMP LEVELS, SOLUBLE GUANYLATE CYCLASE AND PHOSPHODIESTERASE ACTIVITIES IN BRAIN OF MORPHINE DEPENDENT MICE

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Abstract:

By inducing morphine dependence in mice, the changes of cGMP contents, phosphodiesterase (PDE) and soluble guanylate cyclase (sGC) activities and their phosphorylation regulated by protein kinase A(PKA) were observed. It was found that: (1) cGMP contents in cerebellum, striatum, hippocampus and cerebral cortex were significantly lower. (2) The sGC activities were apparently decreased in cerebellum and striatum. In the striatum and cerebral cortex the sGC activities and phosphorylation levels *in vitro* were significantly increased and were inhibited by PKA inhibitor. (3) The PDE activities showed no change in cerebellum and hippocampus, but in striatum and cerebral cortex PDE activities and phosphorylation levels *in vitro* were significantly increased and were inhibited by PKA inhibitor. (4) These changes described above were not observed in mice treated with naloxone 30 min prior to daily morphine injection. Our data indicate that the decrease of cGMP contents occurred generally in brain regions of morphine dependent mice. The decrease of cGMP contents in cerebellum and hippocampus may be due to the decrease of sGC activities, but the decrease of cGMP contents in striatum and cerebral cortex may be mainly due to the increase of PDE activity. Both sGC and PDE activities were regulated by PKA.

Keywords: Dependence Soluble guanylate cyclase Phosphodiesterase cGMP Phosphorylation Morphine

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