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论著

特麦角脲对海洛因自身给药大鼠部分脑区多巴胺D2受体及强啡肽蛋白与基因表达的影响

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摘要 目的 探讨特麦角脲治疗海洛因依赖的作用机制。方法 成年雄性SD大鼠，随机分为正常对照组、海洛因依赖形成期生理盐水干预组、海洛因依赖形成期特麦角脲干预组、复发期生理盐水干预组和复发期特麦角脲干预组；除正常对照组外，其余4组分别建立海洛因静脉自身给药和线索诱发复发模型，干预后灌注固定，留取各脑区切片，采用免疫组化和原位杂交技术，分别检测各脑区多巴胺D2受体蛋白和mRNA、强啡肽原蛋白、前强啡肽原mRNA表达水平。结果 伏核多巴胺D2受体蛋白在海洛因依赖形成期表达下调，在复发期表达上升，多巴胺D2受体基因表达与蛋白表达基本一致，特麦角脲可使复发期受体蛋白表达回降。杏仁核中央核多巴胺D2受体蛋白和基因表达在复发期上调，特麦角脲可使基因表达回降。前额叶多巴胺D2受体蛋白和基因表达在形成期上调，蛋白表达在复发期下调，特麦角脲使复发期基因表达下调。伏核强啡肽蛋白和基因在复发期表达上调，特麦角脲使之回降。杏仁核中央核强啡肽蛋白在复发期表达上调，特麦角脲使之回降。结论 海洛因依赖形成期中脑边缘系统多巴胺活动升高，复发期活动降低，特麦角脲对此有双向调节作用。复发期强啡肽活动上升，特麦角脲可使之降低，有治疗海洛因滥用的潜力。

关键词 特麦角脲 海洛因依赖 受体, 多巴胺D

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Effects of terguride on protein and mRNA expressions of dopamine D2 receptor and dynorphin in different brain regions of rats after heroin self administration

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Abstract

OBJECTIVE To study mechanisms of terguride on the treatment of herion dependence. **METHODS** Adult male SD rats were randomly assigned into 5 groups: normal control group, saline treatment during heroin use period group, terguride treatment during heroin use period group, saline treatment during heroin reinstatement period group, terguride treatment during heroin reinstatement period group, the last 4 groups established heroin intravenous self administration and cue induced reinstatement models, and after interfernce and perfusion to get the following five brain regions 〔including ventral tegmental area (VTA)〕sections. The expression of dopamine D2 receptor protein and mRNA, prodynorphin protein and preprodynorphin mRNA was detected by immunohistochemistry and hybridization *in situ*. **RESULTS** The expression of dopamine D2 receptor was downregulated during heroin use period and upregulated during heroin reinstatement period in nucleus accumbens shell (AcbSH) region, the expression of dopamine D2 receptor mRNA was parallelled with the protein expression approximately, terguride could downregulate the high expression of receptor protein during reinstatement. The expression of dopamine D2 receptor protein and mRNA was upregulated during heroin reinstatement period in central nucleus amygdalae (CeA) region, and terguride could downregulate this high expression. The expression of dopamine D2 receptor protein and mRNA was upregulated during heroin use period and downregulated during heroin reinstatement period in CA1 region of hippocampus and prefrontal cortex (PFC), terguride could downregulate the high expression of mRNA during heroin reinstatement period. The expression of dynorphin protein and mRNA was upregulated during heroin reinstatement period, terguride could downregulate this high expression. The expression of dynorphin protein was upregulated during heroin reinstatement period, and terguride could downregulate this high expression. **CONCLUSION** The activity of mesolimbic dopamine is boosted up during heroin use period and depressed during reinstatement period, terguride can regulate this dysregulation. The activity of dynorphin is boosted up during cue induced reinstatement, and terguride has the downregulation effect. So the preclinic study demonstrated that terguride has the potential benefit in heroin dependence.

Key words terguride heroin dependence receptors,dopamine D2

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