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论著

# CX3CR1参与NF-κB在脊髓水平调控大鼠炎性痛的研究

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摘要：

目的：观察鞘内注射核因子-κB（nuclear factor-κB，NF-κB）抑制剂吡咯烷二硫氨基甲酸(pyrrolidine dithiocarbamate，PDTC) 对单关节炎（monoarthritis，MA）模型大鼠痛阈值和脊髓中CX3C趋化因子受体-1（CX3C chemokine receptor 1，CX3CR1)表达的影响。方法：48只成年雄性Sprague-Dawley大鼠鞘内置管成功后，随机分为4组，即sham组（假手术组）、MA组（单关节炎组）、PDTC预处理组及PDTC后处理组，每组大鼠均为12只。鞘内置管5 d后制作MA模型。Sham组：左侧踝关节腔内注射50 μL生理盐水，鞘内注射10 μL生理盐水；MA组：左侧踝关节腔内注射50 μL完全弗氏佐剂（complete Freund’s adjuvant，CFA），鞘内注射10 μL生理盐水；PDTC预处理组：鞘内注射10 μL PDTC (100 μmol/L)，30 min后左侧踝关节腔内注射50 μL CFA；PDTC后处理组：左侧踝关节腔内注射50 μL CFA，30 min后鞘内注射10 μL PDTC (100 μmol/L)。于术前及术后不同时间点测定痛阈值，用免疫组织化学法观察L5脊髓节段小胶质细胞的表达情况，并在鞘内注射后第1，3，5，7天取L4-L5脊髓膨大节段检测NF-κB mRNA和CX3CR1 mRNA的表达。结果：与MA组相比，sham组、PDTC预处理组及PDTC后处理组的大鼠同侧后肢各时间点痛阈值明显升高，差异有统计学意义(P<0.05)；与MA组相比，PDTC预处理组及PDTC后处理组大鼠的L5脊髓节段的小胶质细胞数量明显减少，脊髓中CX3CR1 mRNA和NF-κB mRNA的表达均明显减少，差异均有统计学意义(均P<0.05)。结论：鞘内注射NF-κB抑制剂PDTC可以缓解CFA所致MA模型大鼠的痛觉异常。其机制可能与NF-κB信号通路通过调节CX3CR1的表达而参与炎性痛的发生、发展有关。

关键词： 单关节模型 吡咯烷二硫氨基甲酸 核因子-&kappa B CX3C趋化因子受体1

# Regulation of inflammatory pain by NF-κB and CX3CR1 at the spinal cord of rats

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Abstract:

ObjectiveTo observe the effect of intrathecal injection of nuclear factor-κB (NF-κB) inhibitor of pyrrolidine dithiocarbamate (PDTC) on pain sensitivity thresholds and the expression of spinal cord CX3C chemokine receptor 1 (CX3CR1) in monoarthritis (MA) model in rats. MethodsForty-eight Sprague-Dawley rats were randomly divided into 4 groups (12 each) after successful intrathecal catheterization: (1) sham operation with physiological saline group (the sham group); (2) MA with normal saline group (the MA group); (3) 10 μL 100 μmol/L PDTC before MA (the PDTC pre-treatment group); (4)MA before 10 μL 100 μmol/L PDTC (the PDTC post-treatment group). Normal saline or PDTC was injected 5 d after the intrathecal catheterization. Pain sensitivity thresholds were measured in the 4 groups before and after the intrathecal injection at different time points. Rat monoarthritis model was subsequently built by injecting complete Freund’s adjuvant (CFA) into the left ankle joint of the rats. On day 3 after the intrathecal injection, expression of microglia in the L5 spinal cord segment was observed by immunohistochemical method, and the lumbar segments L4-L5 of spinal cord were taken to perform RT-PCR to examine the expression of NF-κB mRNA and CX3CR1 mRNA.ResultsCompared with the MA group, the pain sensitivity thresholds in the sham group, the PDTC pre-treatment group and the PDTC post-treatment group at each time point after the intrathecal injection increased significantly (P<0.05), while microglia in the L5 spinal cord segment decreased significantly (P<0.05) and expression of CX3CR1 mRNA and NF-κB mRNA in the lumbar segments L4-L5 of spinal cord decreased significantly (P<0.05).ConclusionThe hyperalgesic effect of the CFA-induced model of monoarthritis can be relieved by intrathecal injection of NF-κB inhibitor PDTC. Its mechanism is possibly related to NF-κB signal pathway which is involved in the formation of inflammatory pain through regulating CX3CR1 expression.

Keywords: monoarthritis model；pyrrolidine dithiocarbamate；nuclear factor-κB；CX3C chemokine receptor 1

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