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Glucocorticoid receptor inhibit the activity of NF-κB through p38 signaling pathway in spinal cord in the spared nerve injury rats

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Abstract:

Aims: The glucocorticoid receptors (GRs) are an active regulator in inflammatory responses. The inflammatory reaction plays an important role in neuropathic pain, but the underlying mechanisms that GR regulates the inflammatory responses in neuropathic pain are still unknown. The activation of GRs has been shown to participate in the p38MAPK-mediated suppression of transcription activation. An unanswered question is whether GRs take part in inflammatory responses in neuropathic pain through p38MAPK signaling pathway.

Main methods: The spared nerve injury (SNI) in rats was used as a model of neuropathic pain. Pain sensitivity was tested by von Frey filaments. The expression of GR, p-p38 and NF-κB were detected by Western blot and immunofluorescence. Elisa was used to examine the expression of IL-6 and TNF-α.

Key findings: Nerve injury led to p38 activation and GR expression decline in spinal cord of SNI rats. Intrathecal injection of the p38MAPK antagonist SB203580 activated GR and decreased NF-κB, resulting in pain relief since three days post-operation in SNI rats. Moreover, Intrathecal injection of the GR antagonist RU38486 counteracted the effect of SB203580 on NF-κB expression along with the release of IL-6 and TNF-α. On the contrary, activation of the GR by intrathecal administration of dexamethasone, a GR agonist, inhibited the expression of NF-κB and the release of IL-6 and TNF-α, resulting in pain relief.

Significance: Activation of p38MAPK in spinal cord could downregulate the GR expression and thereby activate NF-κB, thus promoting the release of IL-6 and TNF-α and participating in the development of neuropathic pain.