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Involvement of spinal PKA/CREB signaling pathway in the development of bone cancer pain

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Abstract:
Background: It has been shown that spinal PKA/CREB signaling pathway is involved in neuropathic and inflammatory pain, but its effects on bone cancer pain have not previously been investigated. The aim of this study was to examine the potential role of the spinal PKA/CREB signaling pathway in the development of bone cancer pain.
Methods: A bone cancer pain model was made by inoculation of Walker 256 cells into the intramedullary space of rat tibia. Western blot analysis examined the expression of PKAca (PKA catalytic subunit) and phospho-CREB (p-CREB) protein levels. The authors further investigated effects of intrathecal treatment with H-89 (a PKA inhibitor, 8 nmol) or forskolin (a PKA agonist, 10 nmol) on nociceptive behavior and the expression of PKAca and p-CREB.
Results: On days 6, 9, and 15 after inoculation, the expression of PKAca and p-CREB protein levels were higher in the bone cancer pain rats compared to the sham rats. On day 9, intrathecal administration of H-89 significantly attenuated bone cancer-induced mechanical allodynia as well as upregulation of PKAca and p-CREB protein levels. These effects were completely abolished by intrathecal pretreatment with the PKA agonist forskolin.
Conclusion: The results suggest that the spinal PKA/CREB signaling pathway may participate in the development of bone cancer pain. The findings of this study may provide an evidence for developing novel analgesics to block bone cancer pain.

Key words:
bone cancer pain, PKA, CREB, signaling pathway