

**Injury-Induced Janus Kinase/Protein
C-Dependent Phosphorylation of
Growth-Associated Protein 43 and Signal
Transducer and Activator of Transcription 3 for
Neurite Growth in Dorsal Root Ganglion**

蔡世音

**Tsai SY;Yang LY;Wu CH;Chang SF;Hsu CY;Wei CP;Leu
SJ;Liaw J;Lee YH;Tsai MD**

摘要

Abstract

Elevation of corticosteroids and excessive glutamate release are the two major stress responses that occur sequentially during traumatic CNS injury. We have previously reported that sequential application of corticosterone and kainic acid (CORT + KA) mimicking the nerve injury condition results in synergistic enhancement of neurite outgrowth and expression of growth-associated protein 43 (GAP-43) in cultured dorsal root ganglion (DRG). GAP-43 is known to promote neurite extension when phosphorylated by protein kinase C (PKC). In addition, PKC can phosphorylate the signal transducer and activator of transcription 3 (STAT3) at Ser727, which is phosphorylated primarily by Janus kinase (JAK) at Tyr705. In this study, we further examine the role of PKC in this stress-induced growth-promoting effect. In the cultured DRG neurons, the JAK inhibitor AG-490 and the PKC inhibitor Ro-318220 reduced the CORT + KA-enhanced neurite growth effect when applied prior to CORT and KA treatment, respectively. Both AG-490 and Ro-318220 diminished the CORT + KA-enhanced GAP-43 expression, phosphorylation, and axonal localization. Furthermore, CORT + KA treatment synergistically phosphorylated STAT3 at Ser727 but not at Tyr705. Similar phenomena were observed in an animal model of acute spinal cord injury (SCI), in which phosphorylation of GAP-43 and phospho-Ser727-STAT3 was elevated in the injured DRG 4 hr after the impact injury. Further treatment with the therapeutic glucocorticoid methylprednisolone enhanced the phosphorylation of GAP-43 in both the DRG and the

spinal cord of SCI rats. These results suggest that elevated glucocorticoids and overexcitation following CNS injury contribute to nerve regeneration via induction of JAK/PKC-mediated GAP-43 and STAT3 activities.