JNK activation contributes to DP5 induction and apoptosis following traumatic spinal cord injury.

許重義
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Abstract

Growing evidence suggests that cells undergo apoptosis after spinal cord injury (SCI). However, little is known about the early events that trigger apoptosis in the contused cord. The BH3-only subfamily of proapoptotic regulators (e.g., bim, bad, and dp5) is recognized as initiators of the apoptotic cascade, and is subject to stringent control, both at the transcriptional and post-translational level. In the current study, we studied upstream events regulating trauma-induced apoptosis in the spinal cord. Within 1 h after SCI in rats, DP5 was induced, while Bim and Bad levels remained unchanged. In parallel, SCI also activated the stress-induced c-Jun N-terminal kinase (JNK), leading to the phosphorylation of c-Jun, with a similar temporal profile. Immunohistochemical analysis revealed that p-JNK and DP5 colocalized to neurons and oligodendrocytes undergoing apoptosis in the injured cord, but were absent in uninjured spinal cord. Furthermore, inhibition of JNK activity with in vivo delivery of SP600125 or a jnk1 antisense oligodeoxynucleotide (ODN) attenuated DP5 induction and caspase-3 activation. These results suggest that JNK activation contributes to trauma-induced DP5 expression and subsequent apoptosis in SCI.

Keywords: Apoptosis; BH3-only family; Caspase 3; DP5; JNK; Spinal cord injury