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The effects of protein phosphatase inhibitors on the duration of central sensitization of rat dorsal horn neurons following injection of capsaicin

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Abstract

Protein kinases and phosphatases catalyze opposing reactions of phosphorylation and dephosphorylation, which may modulate the function of crucial signaling proteins in central nervous system. This is an important mechanism in the regulation of intracellular signal transduction pathways in nociceptive neurons. To explore the role of protein phosphatase in central sensitization of spinal nociceptive neurons following peripheral noxious stimulation, using electrophysiological recording techniques, we investigated the role of two inhibitors of protein phosphatase type 2A (PP2A), fostriecin and okadaic acid (OA), on the responses of dorsal horn neurons to mechanical stimuli in anesthetized rats following intradermal injection of capsaicin. Central sensitization was initiated by injection of capsaicin into the plantar surface of the left paw. A microdialysis fiber was implanted in the spinal cord dorsal horn for perfusion of ACSF and inhibitors of PP2A, fostriecin and okadaic acid. We found that in ACSF pretreated animals, the responses to innocuous and noxious stimuli following capsaicin injection increased over a period of 15 min after injection and had mostly recovered by 60 min later. However, pre- or post-treatment with the phosphatase inhibitors, fostriecin or OA, significantly enhanced the effects of capsaicin injection by prolonging the responses to more than 3 hours. These results confirm that blockade of protein phosphatase activity may potentiate central sensitization of nociceptive transmission in the spinal cord following capsaicin injection and indicate that protein phosphatase type 2A may be involved in determining the duration of capsaicin-induced central sensitization.

Background

Intradermal injection of capsaicin provides a useful and reversible experimental model for the study of an inflammatory pain state, characterized by hyperalgesia and allodynia [1-5]. Intradermal injection of capsaicin in human and primate subjects produces an acute inflammation, mechanical allodynia, primary heat and mechanical hyperalgesia, and secondary mechanical allodynia and hyperalgesia by activation of C- fibers and some Aδ fibers [3,4,6-8]. Capsaicin injection can cause changes in behavioral responses of rats to cutaneous stimuli and increase responses of nociceptive projection neurons in the dorsal horn of the spinal cord [8]. Presumably, changes in central processing of nociceptive information are responsible for the secondary mechanical hyperalgesia and allodynia that is induced by capsaicin [8-10].