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PKCγ–positive neurons gate light tactile inputs to pain pathway through pERK1/2 neuronal network in trigeminal neuropathic pain model

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Abstract

Aims: To explore the possible relationship between protein kinase C gamma (PKCγ) and phosphorylated forms of extracellular signal-regulated kinases 1/2 (pERK1/2) in the rat medullary dorsal horn and the facial hypersensitivity indicative of dynamic mechanical allodynia (DMA) following chronic constriction of the infraorbital nerve (CCI-IoN).

Methods: A well-established rat model of trigeminal neuropathic pain involving CCI-IoN was used. Facial mechanical hypersensitivity was tested with non-noxious dynamic mechanical stimulation (air-puff), and the medullary dorsal horn was examined immunohistochemically using PKCγ and pERK1/2 as pain markers. Statistical analysis was performed using Student t test or one-way analysis of variance (ANOVA).

Results: Increased PKCγ and pERK1/2 expressions within the medullary dorsal horn were associated with DMA following CCI-IoN. A segmental network composed of PKCγ-positive cells located in medullary dorsal horn laminae II/III, contacting more superficially located pERK1/2-expressing cells, was identified. Ultrastructural analysis confirmed the presence of PKCγ to pERK1/2-positive cells. Moreover, intracisternal administration of the selective PKCγ inhibitor KIG31-I blocked both the DMA and pERK1/2 expression in a dose-dependent manner. Although the number of pERK1/2-positive cells was significantly elevated with air-puff stimulation, DMA rats not receiving air-puff stimulation showed significant pERK1/2 expression, suggesting they were experiencing spontaneous pain.

Conclusion: PKCγ cells in the medullary dorsal horn may be involved in DMA following CCI-IoN through the activation of pERK1/2-expressing cells, which then may relay non-nociceptive information to lamina I cells in the medullary dorsal horn.