Reduced inflammatory hyperalgesia with preservation of acute thermal nociception in mice lacking cGMP-dependent protein kinase I.

cGMP-dependent protein kinase I (PKG-I) has been suggested to contribute to the facilitation of nociceptive transmission in the spinal cord presumably by acting as a downstream target of nitric oxide. However, PKG-I activators caused conflicting effects on nociceptive behavior. In the present study we used PKG-I(-/-) mice to further assess the role of PKG-I in nociception. PKG-I deficiency was associated with reduced nociceptive behavior in the formalin assay and zymosan-induced paw inflammation. However, acute thermal nociception in the hot-plate test was unaltered. After spinal delivery of the PKG inhibitor, Rp-8-Br-cGMPS, nociceptive behavior of PKG-I(+/+) mice was indistinguishable from that of PKG-I(-/-) mice. On the other hand, the PKG activator, 8-Br-cGMP (250 nmol intrathecally) caused mechanical allodynia only in PKG-I(+/-) mice, indicating that the presence of PKG-I was essential for this effect.

Immunofluorescence studies of the spinal cord revealed additional morphological differences. In the dorsal horn of 3- to 4-week-old PKG-I(-/-) mice laminae I-III were smaller and contained fewer neurons than controls. Furthermore, the density of substance P-positive neurons and fibers was significantly reduced. The paucity of substance P in laminae I-III may contribute to the reduction of nociception in PKG-I(-/-)
mice and suggests a role of PKG-I in substance P synthesis.

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