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Role of preprotachykinin A (TAC1) gene-derived peptides and the neurokinin 1 (NK1) receptor in acute nocifensive behaviours and hyperalgesia

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Substance P (SP) and neurokinin A (NKA) encoded by the preprotachykinin A (TAC1) gene are involved in neurogenic inflammation and pain via neurokinin 1 and 2 (NK1 and NK2) receptors, respectively, localized in the sensory cortex, spinal cord and primary sensory neurones. Therefore, we investigated the role of SP, NKA and the NK1 receptor in acute somatic and visceral nociception and inflammatory hypersensitivity using gene-deleted mice (TAC1-/- and NK1-/-). Formalin-evoked paw liftings and lickings in the early phase (0-5 min) induced by direct activation of sensory nerves was not altered by deleting either the TAC1 or the NK1 receptor genes. This nocifensive behaviour in the later phase (20-45 min) mediated by inflammatory mechanisms was significantly reduced in the TAC1-/- group. Abdominal contractions evoked by i.p. acetic acid were markedly decreased in TAC1-/- and NK1-/- mice. Attenuation of i.pl. resiniferatoxin-induced thermal allodynia mediated by peripheral mechanisms was greater in TAC1-/- than in NK1-/- mice, while mechanical hyperalgesia involving central sensitization was similarly decreased in both groups. It can be concluded that SP and NKA are responsible for acute visceral chemonociception and inflammatory mechanical hyperalgesia via NK1 receptor activation. However, in the role of these tachykinins in somatic nocifensive behaviours the NK2 receptor is likely to be involved, while inflammatory thermal allodynia is presumably mediated by both receptors.