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## Kappa 3 receptors and levorphanol-induced analgesia.

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#### Abstract

Levorphanol is a widely used opiate analgesic. Although structurally related to morphine, levorphanol has high affinity for a number of receptor subtypes, including both kappa 1 and kappa 3. Prior reports had implicated a kappa component of levorphanol-induced antinociception. Evidence is now presented suggesting that levorphanol-induced analgesia is produced by a mixture of mu and kappa 3 mechanisms. Levorphanol was a potent analgesic in the tail-flick assay, when given systemically, spinally or supraspinally. Isobolographic analysis of the combined administration of levorphanol, spinally and supraspinally implied synergistic interactions. Naloxonazine reduced levorphanol-induced analgesia, implicating a role for mu1 receptors. The kappa 1 antagonist nor-binaltorphimine at a dose which reversed analgesia induced by U50,488H did not antagonize levorphanol-induced analgesia. Additional studies revealed no cross tolerance in either direction, between levorphanol with the kappa 1 analgesic U50,488H. Together, these results strongly argue against a role for kappa 1 receptors in levorphanol-induced analgesia. However, mice tolerant to the kappa 3 analgesic, naloxone benzoylhydrazone (NalBzoH), showed cross tolerance to levorphanol, implying a role of kappa 3 mechanisms in levorphanol-induced analgesia.

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