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Comparison of <latex>μ, κ</latex> and <latex>σ</latex> Opioids on Spinal Nociceptive Responses

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Whereas μ receptor activation reduces spinal responses to most peripheral nociceptive stimuli, κ and σ receptor activation can have differential effects between various types of nociceptive stimulus. This has led us to start a comparative study of μ (fentanyl), κ (U-50, 488H) and σ (ketamine) preferring agonists on spinal nociceptive and other responses.

We perform experiments on spinalized anaesthetized (α-chloralose and/or pentobarbitone) rats and on spinalized decerebrated cats. Electronically controlled devices administer reproducible sensory stimuli of various nociceptive and non-nociceptive kinds. Extracellular recordings are made from dorsal horn cells (laminae III–VI) and from motoneurons. Firing frequency and counts of evoked action potentials per response are displayed on a pen recorder. In this series of experiments two or all three of the compounds have been compared on most cells by intravenous administration.

In these spinalized preparations all three agents reduce mechanical nociceptive responses and, although the ranges of doses overlap, are usually effective at lower doses on motoneuronal as compared with dorsal horn nociceptive responses; this is particularly true for ketamine. The effective doses are often as low as, or lower than, those reported to be analgesic in behavioural tests; thus fentanyl 2 μg kg^{-1}, U-50, 488H 2 mg kg^{-1} and ketamine 4 mg kg^{-1} generally attenuate motoneuronal nociceptive responses by 50–100 %. Nociceptive responses are usually reduced more than non-nociceptive responses although the selectivity is not always great.

Since ketamine, at sub-anaesthetic doses, is a selective antagonist of the actions of the *N*-methyl aspartate group of excitatory amino acids (Anis *et al.* 1983) our experiments indicate that *N*-methyl aspartate receptors are important in mediating nociceptive responses onto ventral but not onto dorsal horn neurons.

Thus in rats μ-, κ- and σ-preferring agonists all have potent spinal actions which are more readily detectable on motoneurons than on dorsal horn cells and which are preferential for but not limited to nociceptive responses.

Reference

Anis, N. A., Berry, S. C., Burton, N. R. & Lodge, D. 1983 *Br. J. Pharmac.* **79**, 565–575.