Evidence for an exclusive antinociceptive effect of nociceptin/orphanin FQ, an endogenous ligand for the ORL1 receptor, in two animal models of neuropathic pain

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Nociceptin/orphanin FQ (noci/OFQ), the endogenous ligand for the orphan ORL1 (opioid receptor-like1), has been shown to be anti- or pronociceptive and modify morphine analgesia in rats after central administration. We comparatively examined the effect of noci/OFQ on hyperalgesia and morphine analgesia in two experimental models of neuropathic pain: diabetic (D) and mononeuropathic (MN) rats. Noci/OFQ, when intrathecally (i.t.) injected (0.1, 0.3, or 1, to 10 μg/rat) was ineffective in normal rats, but reduced and suppressed mechanical hyperalgesia (paw-pressure test) in D and MN rats, respectively. This spinal inhibitory effect was suppressed by naloxone (10 μg/rat, i.t.) in both models. Combinations of systemic morphine with spinal noci/OFQ resulted in a strong potentiation of analgesia in D rats. In MN rats, an isobolographic analysis showed that the morphine+noci/OFQ association (i.t.) suppressed mechanical hyperalgesia in a superadditive manner. In summary, the present findings rev