μ- AND κ-OPIOID ANTINOCICEPTION ENHANCED IN THE PRESENCE OF D-2 BUT NOT D-1 DOPAMINE ANTAGONISTS IN THE MOUSE

K.F.Rooney, R.D.E.Sewell and P.S.J.Spencer, Division of Pharmacology, The Welsh School of Pharmacy, UWIST, PO Box 13, Cardiff CF1 3XF

Considerable controversy surrounds the enhancement of opioid analgesia by the butyrophenone antipsychotic haloperidol in post-operative and terminal pain (Judkins et al.,1982). The involvement of dopaminergic pathways in opioid analgesia is generally accepted (Lal,1975) and studies have previously shown an enhancement of morphine analgesia in the presence of haloperidol in laboratory animals (Kamata et al.,1985). Recently, reportedly selective dopamine (DA) D-1 antagonists such as SCH 23390 (R(+)-8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-1H-3-benzazepine-7-ol) and its 7-bromo derivative SKF 83566 have been introduced (Kaiser and Jain,1985).

The present study sets out to determine the effects of these newer agents and accepted D-2 antagonists (haloperidol and (-)-sulpiride) upon μ, κ and δ-opioid induced antinociception. In these experiments, nociceptive response latencies (secs) were determined using the mouse tail immersion test at 48°C (Sewell and Spencer, 1976). Dopamine antagonists were administered intraperitoneally (i.p.) 30 minutes prior to a sub-maximal dose of opioid agonist. Sufentanil (μ) and U50,488H (κ) (trans-3,4-dichloro-N-methyl-N-(2-(1-pyrrolidinyl)-cyclohexyl)-benzeneacetamine) were administered i.p. and D-Ala^2-D-Leu^5-enkephalin (DADL) (δ) was administered intracerebroventricularly. Nociceptive sensitivity was subsequently monitored for 100 minutes.

Table 1 Percentage change in integral antinociceptive effect of opioid analgesics following co-administration of DA receptor antagonists.

	HALOPERIDOL (0.1mg/kg)	(-)-SULPIRIDE (10mg/kg)	SCH 23390 (0.1mg/kg)	SKF 83566 (0.1mg/kg)
SUFENTANIL (10μg/kg)	19.9 ± 7.8*	23.4 ± 8.0*	-1.2 ± 7.3	0.1 ± 6.8
U50,488H (10mg/kg)	22.9 ± 6.0*	25.4 ± 5.7*	-3.9 ± 6.5	-11.4 ± 8.5
DADL (1μg/animal)	39.6 ± 6.6*	1.3 ± 6.4	-0.1 ± 7.1	2.5 ± 6.4

* = $p<0.05$

The results indicate that DA D-2 antagonists at doses which cause no inherent central sedation enhance μ- and κ-opioid antinociception, whilst the effect on δ-agonist activity was equivocal. Conversely, in the presence of reportedly selective D-1 antagonists, μ-, κ- and δ-opioid induced antinociception remained unmodified.

Hence the possible use of D-1 antagonists as adjuncts to opioid analgesia would appear to be limited.

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