relationship between the disappearance of the receptor and the loss of synaptic contacts.

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Some morphine-like properties of a potent antinociceptive synthetic pentapeptide in relation to physical dependence in rodents

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A pentapeptide analogue of leucine-enkephalin, BW 180C (Tyr.D-Ala.Gly.Phe.D-Leu), has been shown to possess a similar profile to that of morphine in antinociceptive tests in mice and in behavioural tests in mice and rats (Baxter, Goff, Miller & Saunders, 1977). It was therefore of interest to determine the extent to which the peptide also resembled morphine in tests designed to predict abuse liability. It has already been reported that the peptides, methionine-enkephalin and β-endorphin, are capable of inducing tolerance and dependence in rats when given directly into the brain (quoted by Iversen & Dingledine, 1976).

Comparative data will be provided for the effects of the peptide and morphine in the following tests in mice and rats.

The drugs were administered intracerebroventricularly (i.c.v.) to mice by direct brain injection and to rats through a chronically implanted cannula in a lateral ventricle.

Anti-nociceptive studies undertaken in rats using standard tail flick (radiant heat) and tail pressure methods revealed that the peptide and morphine had a significant anti-nociceptive action at doses (i.c.v.) of $\geqslant$1.25 μg and $\geqslant$0.3 μg/rat respectively.

The ability of the drugs to substitute for morphine was investigated in rats which were made tolerant to and dependent on morphine using the method of Buckett (1964). Rats maintained on morphine (400 mg/kg i.p. twice daily) were withdrawn by withholding morphine for 40 hours. Both BW 180C and morphine (i.c.v.) were able to suppress the characteristic withdrawal signs (shaking and writhing).

In studies in mice using the naloxone precipitated jumping test it was found that the characteristic compulsive jumping was precipitated by naloxone (80 mg/kg s.c.) in mice injected 1 h previously with BW 180C (i.c.v.) and morphine (i.c.v. or s.c.). Higher doses of BW 180C were required to elicit naloxone-precipitated jumping following s.c. injection. In contrast a variety of non-opioid centrally acting substances failed to give a jumping response in this test.

We conclude that BW 180C resembles morphine in the two simple tests reported and thus synthetic opioid pentapeptides may present a potential for abuse liability in man. However, it remains to be determined whether such compounds may initiate and sustain self-administration.

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