morphine (Kuschinsky, 1976). This suggestion is supported by the finding that the known dopamine antagonist, chlorpromazine (5 mg/kg, i.p.) given 1 h previously abolished the increased activity induced by the peptide (0.15 μg) and by morphine (0.6 μg).

The effect of the peptide (i.c.v.) on the EEG of conscious rats was studied in animals (male 300 to 350 g) chronically implanted with skull electrodes and intraventricular cannula (Goff, Miller, Smith, Smith & Wheatley, 1975). The peptide at 5 μg ($n=2$) induced EEG spiking of almost immediate onset followed by facial and forelimb clonus 6 min later. Spiking continued for at least 45 min but the clonus was of shorter duration (9 and 30 min respectively for each rat). Morphine is known to induce EEG spiking when injected directly into the brain of rats (Teitelbaum, Blosser & Catravas, 1976).

Our studies on BW 180C provide further evidence that synthetic opioid pentapeptides which are less labile than endogenous enkephalins possess an anti-nociceptive action similar to that of morphine (Pert, 1976). Additionally, our studies have revealed that these peptides may also possess a similar behavioural profile to morphine.

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Reversal of morphine-induced suppression of active avoidance behaviour by the tetracyclic antidepressant mianserin

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The antidepressant drug mianserin (Org GB 94) has been shown to effectively antagonize in rats the catatonia (both muscle rigidity and akinesia) produced by morphine (Preston, unpublished observations). The present study was undertaken to examine if mianserin would also antagonize other behavioural effects of morphine. It has been reported that morphine depresses avoidance responses in rats (Verhave, Owen & Robbins, 1959). We have therefore tested whether mianserin and some other antidepressants or 5-hydroxytryptamine (5-HT)-receptor blocking agents antagonize the incapacitating effect of morphine on the performance of a two-way active avoidance response.

For each experiment 50 or 60 male Wistar rats (weighing 200–250 g) received avoidance training in automated shuttleboxes. During a trial a light in the lid of the box signalled impending electric shock to the feet through the grid floor. A rat could prevent onset of the shock by moving to the opposite side of the box within the first 6 s of illumination (avoidance). Shuttling after the onset of shock caused the current to shut off (escape); failure to escape led to 25 s of shock. Trials took place once a minute. In addition to the number of avoidances and escapes, the number of intertrial responses was also recorded.

The training schedule was as follows: days 1, 2 and 3: 50 trials per day; day 4: 25 trials. On day 5, rats were randomly allotted to groups (9–10 rats per group) which received either placebo s.c. + placebo i.p., 10 mg/kg morphine s.c. + placebo i.p., or 10 mg/kg morphine s.c. + test drug i.p. All injections were given 40 min before the start of the test session of 25

trials. The compounds studied were mianserin (4 and 16 mg/kg), amitriptyline (1, 4 and 16 mg/kg), imipramine (1, 4 and 16 mg/kg), methysergide (2.5 and 5 mg/kg) and cinanserin (4 and 16 mg/kg). The two-tailed permutation test was used for the statistical evaluation of the results.

Rats rapidly acquired the avoidance response. Treatment with morphine not only eliminated avoidance responses but also strongly suppressed escape and intertrial responses. Mianserin only slightly reversed the effect of morphine on avoidance behaviour. However, rats given morphine + mianserin showed a significantly larger number of escapes and intertrial responses than morphine + placebo-treated animals. Methysergide and cinanserin also restored the ability of morphine-treated rats to score escape and intertrial responses, although to a lesser degree than mianserin. Amitriptyline and imipramine were ineffective.

Methysergide and cinanserin have been shown to antagonize the antinociceptive action of intracerebrally administered morphine (Yaksh, DuChateau & Rudy, 1976). Like methysergide and cinanserin, mianserin possesses 5-HT receptor blocking properties (Vargaftig, Coignet, de Vos, Grijsen & Bonta, 1971). The ability of these compounds to antagonize the incapacitating effect of morphine on the performance of rats in a shuttlebox supports the idea that 5-HT mechanisms are involved in some of the effects of morphine. The restoration of intertrial responses by mianserin, methysergide and cinanserin suggests that these drugs reversed the morphine-induced akinesia. Restoration of escape responses indicates that antagonism of analgesia may also be involved.

Mianserin, though a clinically effective antidepressant (Murphy, 1975; Wheatley, 1975), was a negative in conventional animal screening tests for antidepressants (Van Riezen, 1972). The finding that amitriptyline and imipramine failed to act like mianserin in the present experiments adds to the notion that the latter compound may be pharmacologically different from tricyclic antidepressants.

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The effect of ethanol on a passive avoidance task in rats

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It has previously been shown (Chesher, 1974) that ethanol (1.5 g/kg, i.p.) enhances the learning of an active conditioned avoidance task in rats. This effect was abolished if the animals had been pre-treated with the catecholamine synthesis inhibitor α-methyl-*p*-tyrosine. The task made use of a two-compartment shuttle box; to escape an electric shock, the animals had to learn to change compartments within 5 s of the sounding of a buzzer.

In the experiments to be described the effect of ethanol was tested on a passive avoidance task: instead of running to another compartment, the animals had to refrain from doing so to avoid a shock.

The apparatus, similar to that described by Jarvik & Kopp (1967), consisted of a two-compartment box with an interconnecting opening. The rat was placed into one compartment which was lit by a 25 W incandescent light, and the time before it entered the adjacent, dark compartment was determined. Rats usually prefer the dark when given a choice. A shutter prevented the rat from retracing its steps, and it was given a footshock of 1 mA for 5 seconds. Animals were re-tested in the same apparatus 1 or 7 days later. Male Sprague-Dawley rats (200–390 g) were used.

When tested 30 min after ethanol (1.5 g/kg, i.p.) rats ($n=45$ per group) entered the dark compartment on both trial 1 and trial 2 with a significantly shorter