drinking, grooming and activity duration, during the first 4 h period in the dark. Fenfluramine (10.0 mg/kg) induced marked signs of stereotypy associated with strong central 5-HT receptor stimulation (lateral head movements, body circling, splayed hindlimbs) (Sloviter, Drust & Connor, 1978). We conclude that fenfluramine does not function specifically as a true anorectic agent in rats not deprived of food and water; its effect may involve a nonspecific sedative action which depresses both feeding and drinking.

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Behavioural and EEG studies on an anaesthetic enkephalin peptide

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Interest in opioid peptides has mainly concentrated on their anti-nociceptive effects. However, β-endorphin and the synthetic pentapeptide, [D-Met^2.Pro^5]-enkephalinamide, given by intraventricular (i.v.c.) administration induce loss of the righting reflex (LRR) in rats (Browne & Segal, 1978). We have found that the synthetic peptide, Tyr.D-Ala.Gly.Phe.D-Leu.NHEt HCl (BW831C) induced LRR both by i.v.c. and intravenous (i.v.) injection in mice and rats and intravenously in rabbits.

To induce LRR the ED_{50} values for BW831C were 2.8 (1.8–4.4) μg i.v.c. and 125.3 (102.5–159.7) mg/kg in mice (albino, female, 18 to 25 g) and 37.5 (32.4–43.7) mg/kg i.v. in rats (Wistar, male, 100 to 150 g). LRR also occurred after 20 μg, but not at 10 μg, i.v.c. in rats and after 40 mg/kg, but not at 20 mg/kg, i.v. in rabbits (Dutch, male, 2.0–2.5 kg). In comparative studies morphine did not induce LRR at up to 320 μg/mouse i.v.c. in mice and it is known that morphine i.v.c. does not cause LRR in rats (Bloom, Segal, Ling & Guillemin, 1976). LRR was produced by etorphine (Immobilon), the comparative ED_{50} value being 2.2 (2.0–2.4) μg/kg i.v. in rats. The onset of LRR was slower after i.v. anaesthetic dosages of BW831C or etorphine than after pentobarbitone sodium (PBS): the latencies for BW831C (80 mg/kg, $n = 10$), etorphine (3.7 μg/kg, $n = 10$) and PBS (40 mg/kg, $n = 10$) were 90 s, 75 s and 6 s respectively in rats and for BW831C (160 mg/kg, $n = 8$) and PBS (50 mg/kg, $n = 20$) were 150 s and 28.5 s respectively in mice.

The overt effects of BW831C at sub-anaesthetic dosages in mice resembled those of morphine and synthetic pentapeptides (Baxter, Goff, Miller & Saunders, 1977): at 1.25 μg i.v.c. the compound induced hyperactivity and Straub tail. However, when the dosage of BW831C was increased to anaesthetic levels in mice, the behavioural symptoms progressed through ataxia, immobility and catalepsy to a flaccid paralysis. In rats, BW831C and etorphine, induced rigidity and gross salivation. Rigidity in rats was reported following β-endorphin (Browne & Segal, 1978). In rabbits, and some rats, forelimb and facial clonus occurred after BW831C. In all species high doses of BW831 caused deaths due to respiratory arrest. All the above behavioural effects of BW831C and etorphine were rapidly abolished by naloxone (1.5 mg/kg i.v. or s.c.).

EEG studies with BW831C in conscious rats with chronically implanted skull electrodes (Goff, Miller, Smith, Smith & Wheatley, 1975), and in halothane anaesthetized rats revealed high amplitude spiking at 40 mg/kg i.v. ($n = 3$ per preparation) and 10 μg i.v.c. ($n = 3$ per preparation). Burst suppression was observed after 20 μg i.v.c. ($n = 3$). Similar effects were reported after β-endorphin i.v.c. (Havlicek, La Bella, Pinsky, Childiaeva & Friessen, 1978) and after injections of morphine, met-enkephalin and other synthetic pentapeptides into brain tissue (Tietelbaum, Blosser & Catravas, 1976; Urca, Frenk, Liebeskind & Taylor, 1978; Baxter *et al.*, 1977).

It is concluded that some synthetic anti-nociceptive peptides, like some examples in earlier series of synthetic analgesics, display anaesthetic properties.

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Evidence for dopamine receptors on GABA-releasing nerve terminals in rat nucleus accumbens

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The rat nucleus accumbens is considered to be intimately involved in motor function (Kelly & Moore, 1976) and in the action of neuroleptic drugs (Bartholini, 1976), and is densely innervated by ascending axons of the mesolimbic dopamine (DA) pathway (Lindvall & Björklund, 1974). Turnover studies have suggested that neurones utilizing DA and γ-aminobutyric acid (GABA) may be closely interrelated within the nucleus accumbens (Marco, Mao, Cheney, Reveulta & Costa, 1976). The present study investigates the DA-GABA interrelationship in rat nucleus accumbens.

The nucleus accumbens was dissected from male Sprague–Dawley rats (150–200 g) and was found to contain a high GABA concentration: 6.3 ± 0.5 μmole/g (s.e. mean, $n = 6$). Slices of nucleus accumbens (0.2 × 0.2 mm) were incubated with [^{3}H]-GABA (9 nM) for 10 min at 37°C and accumulated [^{3}H]-GABA to a tissue: medium ratio of 65 ± 4 ($n = 7$). Nipecotic acid (25 μM), an inhibitor of the neuronal high affinity uptake of [^{3}H]-GABA (Johnston, Krogsgaard-Larsen, Stephanson & Twitchin, 1976), caused $63 \pm 6\%$ ($n = 4$) inhibition of control uptake ($P < 0.001$). The release of newly accumulated [^{3}H]-GABA was examined by superfusion of slices of nucleus accumbens with Krebs bicarbonate and collection of serial fractions. The resting release of [^{3}H]-GABA rapidly reached a steady baseline and protoveratrine A (100 μM), one of a group of veratrine alkaloids acting on neuronal release processes, increased the rate of efflux of [^{3}H]-GABA.

DA (500 μM) alone had no effect on the resting efflux of [^{3}H]-GABA, but during the exposure of slices of nucleus accumbens to protoveratrine A inhibited the release of [^{3}H]-GABA. This effect could also be mimicked by a range of dopamine agonists. The rank order of potency determined in these experiments was apomorphine > N-n-propylnorapomorphine > 1-phenyl-7,8-dihydroxy-2,3,4,5-tetrahydro-1H-3-benzazepine (SKF 38393A) > 2-amino-5,6-dihydroxy-1,2,3,4-tetrahydronapthalene (isoADTN) > 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronapthalene (ADTN) > epinine > dopamine. Clozapine, sulpiride and thioridazine, a group of neuroleptic drugs considered to act in limbic regions (Bartholini, 1976), attenuated the inhibitory action of apomorphine, while fluphenazine and *cis*-flupenthixol were ineffective.

The results provide evidence for a transmitter role for GABA in the rat nucleus accumbens and indicate that a population of DA receptors may modulate the activity of GABA-releasing nerve terminals.

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