but did not differ in durations of locomotion, rearing or grooming. The principal effects of chlordiazepoxide treatment occurred in the less deprived groups. Thus, for example, chlordiazepoxide (5 mg/kg) given to 3 h deprived rats reduced latency to feed ($t = 5.03$, $P < 0.001$); increased the time eating chow ($t = 2.58$, $P < 0.03$), whilst leaving the time eating novel foods unchanged; reduced the time engaged in sniffing behaviour ($t = 6.11$, $P < 0.0001$); but left the durations of locomotion, rearing and grooming unchanged. In effect, 3 h deprived animals given chlordiazepoxide (5 or 10 mg/kg) behaved in ways that were statistically indistinguishable from 22 h deprived non-drugged animals. Hence, chlordiazepoxide treatment does interact with deprivation level; chlordiazepoxide affects rats with brief food deprivation so that they behave as if they are much more hungry.

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References

BOX, B.M. & MOGENSON, G.J. (1975). Alternations in ingestive behaviors after bilateral lesions of the amygdala in the rat. *Physiol. Behav.*, **15**, 679–688.

COOPER, S.J. & CRUMMY, Y.M.T. (1978). Enhanced choice of familiar food in a food preference test after chlordiazepoxide administration. *Psychopharmacology*, **59**, 51–56.

COOPER, S.J., CRUMMY, Y.M.T. & SKAN, A. (1977). Changes in food-choice towards familar and unfamiliar foods following benzodiazepine administration. *Exp. Brain Res.*, **28**, R12–13.

COOPER, S.J. & FRANCIS, R.L. (1979). Food choice in a food-preference test: Comparison of two mouse strains and the effects of chlordiazepoxide treatment. *Psychopharmacology*, (in press).

COOPER, S.J., SWEENEY, K.F. & TOATES, F.M. (1979). Effects of spiperone on feeding performance in a food-preference test. *Psychopharmacology*, (in press).

POSCHEL, B.P.H. (1971). A simple and specific screen for benzodiazepine-like drugs. *Psychopharmacologia (Berl.)*, **19**, 193–198.

ROLLS, E.T. & ROLLS, B.J. (1973). Altered food preference after lesions in the basolateral region of the amygdala in the rat. *J. comp. physiol. Psychol.*, **83**, 248–259.

Fenfluramine; continuous monitoring of its effects on feeding and drinking in rats

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An anoretic drug action should be specific to feeding, and should involve a reduced feeding motivation, not simply an impairment in the manner of eating. Our work re-examines fenfluramine's status as an anorectic drug, and extends previous findings by continuously charting the time-courses of fenfluramine's effect, not only on several parameters of feeding, but also on drinking.

Eight adult male hooded rats were each housed in a box containing a food dispenser (giving 45 mg Noyes pellets) and a water dispenser (water provided by contact with drinking spout). Every pellet delivery and every water delivery in each box was timed accurately to 0.1 s (real-time) using a Motorola M6800 microprocessor. Data were transferred to a PDP11–40 computer, and for the feeding results, the times were used to compute the times of occurrence of meals, meal size, meal frequency, and rate of eating within meals. Comparable computations were performed on the drinking data. The system collected data continuously over 23 h periods (dark period 19.00-07.00 h). Fenfluramine (2.5, 5 or 10 mg/kg) or saline control was injected i.p. at 17.30 hours. At least 72 h separated successive injections; each animal served as its own control and orders of injection were counterbalanced.

Fenfluramine (5.0 and 10.0 mg/kg) reduced total food intake ($P < 0.05$). At 5.0 mg/kg, meal size was significantly reduced over the first three bins up to the end of the dark period. Meal frequency was unchanged in the first time period (up to 23.00 h) but was significantly elevated ($P < 0.05$) throughout the remainder of the dark period and subsequent 12 h light period. Eating rate was significantly depressed in the first part of the dark period (up to 23.00 h), and then recovered to control levels by the light period (Blundell & Latham, 1978; Cooper & Francis, 1979; Cooper & Sweeney, 1979). Fenfluramine's effects on drinking were similar. Thus during the first period (up to 23.00 h), total intake, size of drinking bout and drinking rate were significantly depressed ($P < 0.05$). Interestingly, during the subsequent light period, there was a significant elevation of food intake compared with control levels as a result of the increased meal frequency.

Further analysis of the rats' behaviour was obtained from videotapes (1 frame per s), recorded from the time of injection to the end of the dark period. Fenfluramine (5 mg/kg) produced up to a 30% increase in sleep duration, at the expense of feeding,

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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References

BLUNDELL, J.E. & LATHAM, C.J. (1978). Pharmacological manipulation of feeding: possible influences of serotonin and dopamine on food intake. In: *Central Mechanisms of Anorexic Drugs.* ed. Garattini, S. & Samanin, R. pp. 83–109. Raven Press, New York.

COOPER, S.J. & FRANCIS, R.L. (1979). Feeding parameters with two food textures after chlordiazepoxide administration, alone or in combination with *d*-amphetamine or fenfluramine *Psychopharmacology*, **62**, 253–259.

COOPER, S.J. & SWEENEY, K.F. (1979). Effects of spiperone on feeding parameters in the rat and interactions with (+)-amphetamine, mazindol or (±)-fenfluramine. *Br. J. Pharmac.*, **66**, 147–148P.

SLOVITER, R.S., DRUST, E.G. & CONNOR, J.D. (1978). Specificity of a rat behavioral model for serotonin receptor activation. *J. Pharmac. exp. Ther.*, **206**, 339–347.

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.