In a separate experiment U 10,520 (100 μg in 0.1 ml arachis oil) was administered s.c. to immature female rats, and groups of 10 were sacrificed 8, 14, 22, 30, 46 and 66 h later. By 14 h [^{3}H]-R5020 binding increased from 1.03 ± 0.15 pmol/uterus (controls) to 5.22 ± 0.04 pmol/uterus. The administration of cycloheximide (5 μg in 0.1 ml 0.9% saline s.c. 2 hourly) for 6 h before and 16 h after U 10,520 produced a 16 h delay in the increase in [^{3}H]-R5020 binding.

Experiments were also undertaken to determine the ligand specificity of [^{3}H]-R5020 binding in 100,000 *g* supernatants derived from oestradiol or U 10,520 stimulated uteri.

Progesterone and norethindrone produced concentration-dependent (1×10^{-8}–3.3×10^{-7} M) inhibition of [^{3}H]-R5020 (1×10^{-8} M) binding, whereas testosterone, triamcinolone and cortisol were without effect up to 3.3×10^{-7} M for both cytosols.

In conclusion, nafoxidine-like antioestrogens stimulate progesterone receptor synthesis *in vivo*, demonstrating that an ability to be isomerised to a more oestrogenic configuration is not a pre-requisite for activity. However, these studies have not excluded the possibility that other metabolites of these antioestrogens may initiate the progesterone receptor synthesis.

References

HORWITZ, K.B., KOSEKI, Y. & MCGUIRE, W.L. (1978). Estrogen control of progesterone receptor in human breast cancer: role of estradiol and antiestrogen. *Endocr.*, **103**, 1742–1751.

KOSEKI, Y., ZAVA, D.T., CHAMNESS, G.C. & MCGUIRE, W.L. (1977). Progesterone interaction with estrogen and antiestrogen in the rat uterus—receptor effects. *Steroids*, **30**, 169–177.

LEGHA, S.S., SLAVIK, M. & CARTER, S.K. (1976). Nafoxidine—an antioestrogen for the treatment of breast cancer. *Cancer*, **38**, 1535–1541.

VU HAI, M.T. & MILGROM, E. (1977). Characterization and assay of the progesterone receptor in rat uterine cytosol. *J. Endocr.*, **76**, 21–31.

Interactions between chlordiazepoxide and food deprivation determining choice in a food-preference test

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Rolls & Rolls (1973) introduced a form of food-preference test in which food-deprived rats are given a choice between familiar laboratory chow and a range of palatable, *novel* foods. Bilateral lesions of the basolateral amygdala appear to overcome food neophobia, since unlike control animals, lesioned animals spend much more time eating the novel foods than the familiar chow (Box & Mogenson, 1975; Rolls & Rolls, 1973). Pharmacological treatment can mimic the amygdala lesion effect, since spiperone also increases the choice of novel foods (Cooper, Sweeney & Toates, 1979). In contrast, chlordiazepoxide and diazepam, at relatively low doses, do not exhibit an antineophobic action, as proposed by Poschel (1971); instead, they increase the time spent eating familiar food, whilst leaving the response to novel foods relatively unchanged (Cooper & Crummy, 1978; Cooper, Crummy & Skan, 1977; Cooper & Francis, 1979). The benzodiazepine action is consistent with a direct stimulation of appetite.

In the present experiment, each rat was observed for 600 s in a box which had 6 food containers equally spaced on the grid floor. The 6 foods were familiar chow pellets, and a range of novel foods: apple, chocolate, biscuit, carrot, cheese, Sugar Puffs. The rat's behaviour was monitored on a CCTV system. Each test session was recorded at 2 frames per second, and subsequently each frame was scored according to several behavioural categories. These included eating food (coded according to each food variety), contact with food (similiarly coded), locomotion, rearing, sniffing (head and vibrissae movement without locomotion), and grooming. A computer program converted the frame analysis into durations for each behavioural category. The subjects were 48 adult male Lister rats, half were tested 22 h food-deprived and half were 3 h food-deprived. At each deprivation level, the animals were assigned to 4 injection groups: chlordiazepoxide HCl at 2.5, 5.0 and 10.0 mg/kg, and saline as a control injection. All injections were given i.p., 30 min before the test period. All feeding tests were run at the start of the dark phase of the daily dark-light cycle.

In the saline-treated groups, the 22 h food-deprived rats had shorter latencies to begin feeding ($t = 3.06$, 10 d.f., $P < 0.01$), and spent considerably longer eating familiar chow ($t = 4.10$, $P < 0.002$) compared with the 3 h food-deprived rats. Chow eating times were 218.2 ± 20.1 s (mean ± s.e. mean) and 69.8 ± 15.9 s respectively. In contrast, increasing the level of food deprivation did not significantly affect the time spent eating novel foods. The more deprived animals spent less time engaged in sniffing behaviour than the less deprived animals ($t = 5.48$, $P < 0.0003$),

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,