dence that this inhibition also occurs *in vivo*, and these compounds are particularly interesting since they are used to treat obesity and hyperlipidaemia respectively.

Chronic treatment of rats with benfluorex before feeding with glucose decreased the relative rate of hepatic triacylglycerol synthesis. This effect was more marked if the rats were fed with ethanol which increases the activity of phosphatidate phosphohydrolase in the liver by about 5-fold. Benfluorex partly prevents the ethanol-induced increase in the synthesis and accumulation of triacylglycerols in the liver which appears to be caused by the increased flux of phosphatidate to diacylglycerol. Benfluorex could decrease this flux by interacting with phosphatidate, but it also partly prevents the ethanol-induced increase in the concentration of active phosphohydrolase (Brindley, 1978).

If triacylglycerol synthesis can be inhibited by restricting the conversion of phosphatidate to diacylglycerol, then phosphatidate ought to accumulate. This occurs to a limited extent and some of the phosphatidate can be used for acidic phospholipid synthesis (Brindley, 1978). It appears likely that most of the excess phosphatidate in the liver is converted back to glycerol phosphate. Toxic doses of amphiphilic amines inhibit phospholipase A activities and produce a phospholipidoses (Brindley, 1978), but lower concentrations could favour the deacylation of phosphatidate relative to its dephosphorylation. Norfenfluramine (2 mM) and chlorpromazine (0.8 mM) inhibited phosphatidate phosphohydrolase activity by 13 and 81% respectively. The simultaneous deacylation was increased by 24% with norfenfluramine and it was only decreased by 26% with chlorpromazine. These results were obtained with a microsomal plus supernatant fraction of rat liver that was labelled with [^{3}H]-phosphatidate in the membranes.

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Feeding parameters in the rat: interactions of chlordiazepoxide with (+)-amphetamine or fenfluramine

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Benzodiazepines can antagonize amphetamine-induced anorexia (Cooper, in press; Fratta, Mereu, Chessa, Paglietti & Gessa, 1976), but interactions with fenfluramine have not been investigated. Typically food intake data is restricted to the amount of food consumed; in the present study, the amount of food intake was subdivided into two feeding parameters, feeding duration and rate of eating. Here we report on interactions between chlordiazepoxide with either (+)-amphetamine or fenfluramine on feeding parameters in the rat.

Male, adult Sprague-Dawley rats (240–280g) were handled daily for 8 days prior to testing. On the day before testing, food (Diet 41B pellets) were removed at 17.00 h, and feeding tests were run the following morning. Each rat was tested for 10 min in a test-cage, similar to the home-cage, with familiar food pellets available (to avoid neophobic responses). The measures taken were latency to begin feeding (s); total duration of feeding (s); amount consumed (g); eating rate (g per 100s feeding). 120 rats were allocated to 15 injection conditions (n = 8 per group). Injections of chlordiazepoxide (0, 5.0 or 10.0 mg/kg) were given alone or in conjunction with either (+)-amphetamine (0.5 or 1.0 mg/kg) or fenfluramine (2.0 or 4.0 mg/kg). All injections were given i.p., 30 min before the feeding test, and isotonic saline served as the control injection.

By itself chlordiazepoxide did not affect the amount of food intake, compared with the control level of intake (2.2 $\pm$ 0.24 g; mean $\pm$ s.e. mean). Both (+)-amphetamine and fenfluramine, however, significantly reduced food intake ($F = 21.75$, d.f. 2,63, $P < 0.001$ and $F = 51.69$, d.f. 2,63, $P < 0.001$) respectively. The anorexic effects were matched, e.g. intakes after (+)-amphetamine (0.5 mg/kg) and fenfluramine (2.0 mg/kg) were 1.3 $\pm$ 0.18 and 1.3 $\pm$ 0.19 respectively. Chlordiazepoxide (5.0 mg/kg) effectively blocked the anorexic effect of (+)-amphetamine, reflected in the significant drug-interaction term ($F = 2.78$, d.f. 4,63, $P < 0.03$), but failed to block the effect of fenfluramine. Chlordiazepoxide reliably prolonged the duration of feeding ($F = 19.2$, d.f. 2,63, $P < 0.001$), whilst both (+)-amphetamine and fenfluramine attenuated feeding duration ($F = 15.9$, d.f. 2,63, $P < 0.001$ and $F = 29.29$ d.f. 2,63, $P < 0.001$, respectively). The effects of chlordiazepoxide and (+)-amphetamine on feeding duration were additive (i.e. a non-significant drug interaction, $F < 1.0$). However, there was a significant interaction between chlordiazepoxide and fenfluramine ($F = 5.03$, d.f. 4,63, $P < 0.002$), and the higher dose of chlordiazepoxide increased the effect of fenfluramine to shorten the eat-

ing duration. Chlordiazepoxide significantly reduced the rate of eating ($F = 25.0$, d.f. 2,63, $P < 0.001$), which in effect counteracted the prolonged feeding duration to produce no change in the amount of food consumed. Whilst (+)-amphetamine exerted no overall effect on eating rate ($F < 1.0$), fenfluramine significantly reduced eating rate ($F = 28.7$, d.f. 2,63, $P < 0.001$). Both chlordiazepoxide and fenfluramine therefore reduced eating rate, and their effects were essentially additive (non-significant interaction term, $F < 1.0$). Chlordiazepoxide markedly reduced the latency to begin feeding ($F = 9.48$, d.f. 2,63, $P < 0.001$). In contrast both (+)-amphetamine and fenfluramine significantly increased the latency to begin feeding ($F = 4.14$, d.f. 2,63, $P < 0.02$ and $F = 12.6$, d.f. 2,63, $P < 0.001$, respectively). Chlordiazepoxide strongly antagonised the effect of (+)-amphetamine on latency to eat (drug-interaction term, $F = 2.02$, d.f. 4,63, $P = 0.10$), but did not counteract the lengthened latencies to eat observed in fenfluramine-treated animals.

These data support suggestions that (+)-amphetamine and fenfluramine differ in the detailed mechanisms of action which mediate their anorexic effects (Blundell, Latham & Lesham, 1976). They also indicate important differences in the interactions of these anorectic drugs with chlordiazepoxide, a compound which generally facilitates feeding responses in a range of mammalian species (Brown, Houpt & Schrvver, 1976; Cooper & Crummy, in press; Fratta *et al.*, 1976; Stephens, 1973).

Servier Laboratories generously supplied fenfluramine.

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Social isolation in the young rat: neurochemical effects of treatment with a long-acting neuroleptic, α-flupenthixol decanoate

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Social isolation of young weanling rats for a period of three weeks has produced changes in biogenic amine concentrations associated with certain brain regions (Morinan & Leonard, 1976). In addition, isolated rats have been shown to be more sensitive to such psychotropic drugs as (+)-amphetamine (Sahakian, Robbins, Morgan & Iversen, 1975, Morinan, 1978).

The action of the thioxanthene neuroleptic α-flupenthixol, whose pharmacological properties properties have been described by von den Driessche (1977), are prolonged by using the depot preparation of the decanoate dissolved in a low-density vegetable oil (Viscoleo(R); Nymark, Franck, Pedersen, Boeck & Møller-Nielsen, 1973). The present study was carried out to investigate the neurochemical changes caused by chronic treatment with α-flupenthixol decanoate (α-FPD).

Male Wistar rats (60–70g) were housed as described previously (Morinan, 1978). Sub-cutaneous injections of α-FPD (Fluxanol(R) 5 mg/kg) or vegetable oil (Viscoleo(R) 0.1 ml/kg) were given on a weekly basis. At the end of the isolation period, the concentration of γ-aminobutyric acid (GABA), dopamine (DA) and noradrenaline (NA) were estimated in the midbrain, corpus striatum, hippocampus and amygdala.

Table 1 shows the only significant changes in the steady state concentrations of the areas examined. (All data were subjected to a 2 × 2 Analysis of Variance: Fixed Effects, followed by a Student's t test where relevant). In the amygdala, α-FPD caused a decrease in GABA ($F(1,28) = 4.35$, $P < 0.05$), and an increase in NA ($F = 6.40$, $P < 0.025$). In the striatum there was a significant drug environment interaction effect for GABA ($F = 5.93$, $P < 0.025$), due to an increased concentration in isolates after α-FPD treatment ($t(14) = 2.30$, $P < 0.025$). No change in DA concentration was found in any of the brain regions.

In the amygdala, the concentrations of GABA and NA were decreased and increased respectively. Administration of (+)-amphetamine causes the opposite effects to those found with α-FPD (Morinan, 1978).