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.

References

BLUNDELL, J.E., LATHAM, C.J. & LESHAM, M.B. (1976). Differences between the anorexic actions of amphetamine and fenfluramine—possible effects on hunger and satiety. *J. Pharm. Pharmac.*, **28**, 471–477.

BROWN, R.F., HOUPT, K.A. & SCHRYVER, H.F. (1976). Stimulation of food intake in horses by diazepam and promazine. *Pharmac. Biochem. Behav.*, **5**, 495–497.

COOPER, S.J. (in press). Behavioural studies of drug interactions. *Chemical Influences on Behaviour*, ed. Brown, K. & Cooper, S.J. London: Academic Press.

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

FRATTA, W., MEREU, G., CHESSA, P., PAGLIETTI, E. & GESSA, G. (1976). Benzodiazepine-induced voraciousness in cats and inhibition of amphetamine-anorexia. *Life Sci.*, **18**, 1157–1166.

STEPHENS, R.J. (1973). The influence of mild stress on food consumption in untrained mice and the effect of drugs. *Br. J. Pharmac.*, **47**, 146P.

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).

Table 1 Significant changes in GABA and NA concentrations*

	GABA		NA
	Striatum	*Amygdala*	*Amygdala*
SOC-CON	1206 ± 19	1000 ± 18	0.35 ± 0.02
SOC-FPD	1167 ± 30	987 ± 19	0.43 ± 0.03
ISOL-CON	1177 ± 25	994 ± 21	0.35 ± 0.02
ISOL-FPD	1262 ± 27	921 ± 23	0.37 ± 0.02

Values are the means (μg/g wet weight of tissue) ± s.e. mean of 8 determinations.
* Data analyzed 2 × 2 Analysis of Variance: Fixed Effects followed by Student's *t*-test.
SOC-CON = grouped animals—control.
SOC-FPD = grouped animals—injected with α-flupenthixol decanoate (5 mg/kg once weekly).
ISOL-CON = isolated animals.
ISOL-FPD = isolated animals injected once weekly with α-flupenthixol decanoate.

Neuroleptics are known to inhibit the action of amphetamine, although this is generally thought to be associated with the ability of these compounds to inhibit DA receptors (van Rossum, 1966). From this study it appears that α-FPD exerts its antagonistic action on GABA and NA in the amygdala without affecting the concentrations of striatal DA. However, it must be emphasised that only steady state concentrations were determined and that the possibility remains that α-FPD alters DA turnover in these animals. Despite this reservation, it would be anticipated that chronically administered α-FPD would increase the steady state concentrations of DA in the striatum as a consequence of prolonged DA receptor blockade. The fact that this change was not observed may suggest that social isolation alters DA receptor sensitivity to α-FPD.

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References

MORINAN, A. (1978). Social isolation in the young rat: neurochemical correlates of chronic amphetamine treatment. *Ir. J. Med. Sci. in press.*

MORINAN, A. & LEONARD, B.E. (1976). The effects of social isolation in the young rat on concentrations of some neurotransmitters in the brain. *Ir. J. Med. Sci.* **145,** 310–1.

NYMARK, M., FRANCK, K.F., PEDERSEN, V., BOECK, V. & MØLLER-NIELSEN, I. (1973). Prolonged neuroleptic effect of α-flupenthixol decanoate in oil. *Acta Pharmac. Toxicol.* **33,** 363–76.

SAHAKIAN, B.J., ROBBINS, T.W., MORGAN, M.J. & IVERSEN, S.D. (1975). The effects of psychomotor stimulation on stereotypy and locomotor activity in socially-deprived and control rats. *Brain Res.* **84,** 195–205.

VAN ROSSUM, J.M. (1966). The significance of dopamine receptor blockade for the mechanism of action of neuroleptic drugs. *Arch. Int. Pharmacodyn.* **106,** 492–4.

VON DEN DRIESSCHE, J. (1977). Beitrag zur Pharmakologie eines Neuroleptikums: Flupenthixol. *Arzneimittel. Forsch.* **27,** 2121–25.

Drug effects in a GABA-dependent rotational behaviour model and on [^{3}H]-GABA receptor binding: studies with the enantiomers of baclofen HCl

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Baclofen is β-(p-chlorphenyl) derivative of γ-aminobutyric acid (GABA) whose status as a GABA-like drug is unclear; for example, there is conflicting evidence as to whether the electrophysiological effects of baclofen can or cannot be antagonised by the GABA antagonist bicuculline (see Waddington, 1977a, for refs). (−) But not (+) baclofen has been shown to produce a depression of activity in nigral neurons following intracerebral and iontophoretic application into the substantia nigra, but the insensitivity of these responses to antagonism by picrotoxin or bicuculline suggests that there stereospecific effects are not mediated by a mechanism involving GABA. (Kelly & Moore, 1978; Olpe, Koella, Wolf & Haas, 1977). They may therefore represent general neuronal