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.

The work was financed by a grant from Organon B.V. (Netherlands). Flupenthixol Decanoate and Viscoleo(R) were gifts from Dr. I. Møller-Nielsen, H. Lundbeck and Co., Copenhagen (Denmark).

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

depressant effects. We have compared the enantiomers of baclofen in a GABA-dependant behaviour model where unilateral intranigral injection of GABA-like drugs in rats produces contralateral rotational behaviour and in which racemic baclofen has been shown to be active (Waddington, 1977a,b, 1978). We have also studied the effects of the enantiomers on [^{3}H]-GABA receptor binding following the demonstration that racemic baclofen can displace specifically-bound [^{3}H]-GABA (Olsen, Ticku, Van Ness & Greenlee, 1978; Waddington & Cross, unpublished observations). The effects of (+) and (−) baclofen in these test systems have been compared with those of muscimol, the most potent and specific GABA agonist presently available.

Male Sprague-Dawley rats, 150–200g, were given unilateral stereotaxic injections of drugs into the nigra in 1μl saline, as previously described (Waddington, 1977a, b, 1978), and resulting rotational behaviour quantified using an automated rotometer system (Waddington & Crow, 1978).

High affinity, Na^+-independant [^{3}H]-GABA receptor binding studies were performed on crude synaptic membrane preparations of whole rat brain using a method similar to that of Enna & Snyder (1975), with [^{3}H]-GABA at a concentration of 10 nM.

(+), (−) and (±) baclofen (500 ng) induced contralateral rotational responses, and these responses were of similar magnitude, though baclofen is over 100 × less potent than muscimol.

(+), (−) and (±) baclofen displaced specifically-bound [^{3}H]-GABA with IC_{50}'s of 38 μM, through baclofen was 1000 × less potent than muscimol (IC_{50}, 40 nM) and 100 × less potent than GABA itself (IC_{50}, 400 nM).

The enantiomers of baclofen were equally active in a GABA-dependant rotational model and in displacing [^{3}H]-GABA binding, and these properties are thus distinct from stereospecific GABA-independant neuronal depressant effects. However, they must be considered only weakly active in comparison with the specific GABA-agonist muscimol.

A.J.C. & J.L.W. and MRC Scholars. We are grateful to Ciba-Geigy, Basel, Switzerland, for gifts of drugs.

References

ENNA, S.J. & SNYDER, S.H. (1975). Properties of γ-aminobutyric acid (GABA) receptor binding in rat brain synaptic membrane fractions. *Brain Res.*, **100**, 81–97.

KELLY, P.H. & MOORE, K.E. (1978). Dopamine concentrations in the rat brain following injections into the substantia nigra of baclofen, γ-aminobutyric acid, γ-hydroxybutyric acid, apomorphine and amphetamine. *Neuropharmacol.*, **17**, 169–174.

OLPE, H.-R., KOELLA, W.P., WOLF, P. & HAAS, H.L. (1977). The action of baclofen on neurons of the substantia nigra and of the ventral tegmental area. *Brain Res.*, **134**, 577–580.

OLSEN, R.W., TICKU, M.K., VAN NESS, P.C. & GREENLEE, D. (1978). Effects of drugs on γ-aminobutyric acid receptors, uptake, release and synthesis *in vitro*. *Brain Res.*, **139**, 277–294.

WADDINGTON, J.L. (1977a). Induction of rotational behaviour by intranigral baclofen suggests possible GABA-agonist activity. *Experientia*, **33**, 1345–1346.

WADDINGTON, J.L. (1977b). GABA-like properties of flurazepam and baclofen suggested by rotational behaviour following unilateral intranigral injection: a comparison with the GABA-agonist muscimol. *Br. J. Pharmac.*, **60**, 263P–264P.

WADDINGTON, J.L. (1978). Rotational behaviour and striatal dopamine metabolism following unilateral activation of nigral GABA mechanisms: GABAergic modulation of dopaminergic and non-dopaminergic neurons in rat substantia nigra. *Br. J. Pharmac.*, (in press).

WADDINGTON, J.L. & CROW, T.J. (1978). Methodological problems in the measurement of drug-induced rotational behaviour. *Psychopharmacol.*, (in press).

Effects of intrapallidal administration of convulsant drugs on head-turning evoked by striatal stimulation in rats

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In a previous study Crossman, Lee & Slater (1977a) showed that electrical stimulation of the rat neostriatum produces head-turning which is readily modified by manipulating γ-aminobutyric acid (GABA) function in the globus pallidus (GP). Picrotoxin, an established GABA antagonist, facilitates head-turning when injected into GP. This is consistent with the view that pallidal GABA is involved in striatally-mediated movements. We have extended this work and propose that striatal stimulation combined with drug injection into GP provides a model for studying GABA neurotransmission *in vivo*.

A number of other convulsants have been reported to be GABA antagonists, for example, bicuculline, (+)-tubocurarine, penicillin G and leptazol (Hill, Simmonds & Straughan, 1973; MacDonald & Barker, 1977) although it is uncertain whether GABA antagonism is the sole mechanism by which these substances cause convulsions. If these convulsants are