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baclofen can displace specifically-bound [^{3}H]-GABA (Olsen, Ticku, Van Ness & Greenlee, 1978; Waddington & Cross, unpublished observations).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.

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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

GABA antagonists then they might be expected to mimic picrotoxin in GP. We have investigated this possibility.

Female Sprague-Dawley rats (170–190 g) were fitted with a bipolar stimulating electrode in one neostriatum and a cannula in the ipsilateral GP as previously described (Crossman, Lee & Slater, 1977b). Biphasic pulses (0.1 – 0.3 mA; 25 Hz) caused contralateral head-turning. The duration of threshold stimulation needed for a 90° head-turn was recorded 10 times at 2 min intervals. Drugs were dissolved in 1 μl of saline and injected into GP following which the testing procedure was repeated.

When picrotoxin was injected into GP every animal produced an immediate decrease in the latency of the head-turn response (e.g. 2 μg: latency decrease −55%; $P < 0.001$; $n = 45$). This was a dose-dependent effect within the range 0.25 – 2.0 μg. No statistically significant effects were recorded following saline (1 μl) in GP. In contrast, the potent GABA agonist muscimol slowed the head-turn (e.g. 10 ng: +106%; $P < 0.001$; $n = 12$). A dose-related effect was obtained (1–25 ng). Slowing of the head-turn was also recorded following injection into GP of either 50 μg of GABA (+38%; $P < 0.05$; $n = 5$) or 10 μg of the GABA uptake inhibitor (−)-2,4-diaminobutyric acid (+31%; $P < 0.01$; $n = 19$).

Of the convulsants tested only (+)-tubocurarine (1 – 2 μg) appeared to mimic picrotoxin in facilitating the head-turn (e.g. 1 μg: −24%; $P < 0.001$; $n = 7$). Bicuculline slowed the head-turn response (e.g. 4 μg: +63%; $P < 0.001$; $n = 7$). A similar effect was observed with penicillin G (e.g. 4 μg: +54%; $P < 0.01$; $n = 5$). Leptazol (10 – 50 μg) had no effect on head-turning.

This animal model reveals a clear difference in the effects of convulsants in GP. (+)-Tubocurarine mimics the action of the GABA antagonist picrotoxin while bicuculline and penicillin G behave more like GABA agonists. Some analogous findings with these compounds have been reported by others using iontophoresis (Hill, Simmonds & Straughan, 1971, 1973; Krnjević, Puil & Werman, 1977). This disparity in the actions in GP of supposed GABA antagonists might be resolved by further studies on the morphology of inhibitory synapses and the nature of the GABA receptors in GP.

L.A.L. is an SRC student.

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Glial cell function and the GABA-feedback hypothesis

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An impressive body of evidence now suggests that glial cells of the CNS have far more important functions than a simply 'supportive' role.

Kuffler & Nicholls (1966) suggested that glia may play a significant role in neurotransmission by taking up potassium ions released during prolonged depolarisation of neurones. Increased glial cell potassium stimulates production of GABA which may be translocated back to nerve endings to modulate neurotransmitter release by interaction with presynaptic receptors (Tower & Young, 1973).

We have attempted to separate neurones and glial cells from mammalian CNS with a view to determining differences in specificity of drug action. In the course of the study we have detected differences in the two general cell types which may support the GABA hypothesis mentioned above.

Slices of rat cerebral cortex were incubated for 30 min at 37°C in an imidazole/HCl buffer (50 mM, pH 7.4) containing sucrose (0.5 M) and glucose (10 mM) and then forced through nylon bolting cloth (130 μm pore size) to dissociate the cells. The resulting suspension was layered on to a discontinuous sucrose gradient of 0.9, 1.45 and 2.0 M sucrose and centrifuged at