of AOAA or GAG resulted only in a potentiation of haloperidol catalepsy (AOAA: 0.3 to 12.5 mg/kg: 98% to 150%* of haloperidol treated rat; GAG: 1.0 to 50 mg/kg: 94% to 138%* of haloperidol treated animals (*$P < 0.05$ versus haloperidol alone). These data indicate that the direct GABA mimetic drugs SL 76002 (DiChiara, Porceddu, Morelli, Mulas & Gessa, 1979; Lloyd, Worms, Depoortere & Bartholini, 1979) and muscimol exert a biphasic action on neuroleptic-induced catalepsy, with an inverse dose-response curve as compared with the direct GABA antagonists, bicuculline and picrotoxinin (Worms *et al*, 1978). At least three mechanisms may play a role in these interactions: low doses of directly acting GABA drugs (i) may selectively affect GABA 'autoreceptors' within the substantia nigra (Mitchell & Martin, 1978) thus decreasing GABA release and increasing DA neuron activity, (ii) may exert a preferential inhibitory effect on a nigral non-dopaminergic out-put pathway which may be an inhibitor for DA-mediated events (DiChiara *et al*, 1979), and/or (iii) may act selectively at the level of striatal GABAergic interneurons thus inhibiting cholinergic neurons.

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Leptazol antagonises the post-synaptic actions of γ-aminobutyric acid

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Neurones in the olfactory cortex show sensitivity towards γ-aminobutyric acid (GABA) and GABA might mediate post-synaptic inhibition on to these neurones (Brown & Scholfield, 1979). This report demonstrates that leptazol can antagonise post-synaptic GABA action in a similar manner to the antagonism of the presynaptic actions which occur in the cuneate nucleus (Simmonds, 1978).

Neurones in the guinea-pig olfactory cortex *in vivo* slice preparation were impaled with single barrelled microelectrodes (Scholfield, 1978*a*). Such slices were maintained in Krebs solution at 25°C and various concentrations of GABA added to the perfusate for 1–3 min alone and in the presence of leptazol. GABA action was measured from the voltage deflections produced by constant current pulses injected into the neurones and calculated as the change in input conductance of that neurone.

GABA alone increased the membrane conductance by up to 20-fold or more at bath concentrations of 0.01–0.5 mM. The maximum GABA conductance was beyond the resolution of the measurement. GABA sensitivity was reduced with leptazol and the amount of GABA antagonism was dependent on the leptazol concentration 0.1–30 mM (6 slices). Thus in leptazol (1 mM) the GABA dose-conductance curve was shifted by 2.00 ± 0.18 to the right and by 5.4 ± 0.04 in leptazol (10 mM, mean ± s.e. mean).

When the lateral ofactory tract is stimulated an inhibitory post-synaptic conductance (i.p.s.c.) is generated (Scholfield, 1978b). During this inhibitory phase the conductance is normally immeasurably high. In the presence of leptazol (10 mM) the conductance at the same latency was reduced to a value between 2-fold and 20-fold of the resting (unstimulated) conductance. Leptazol (0.1–30 mM) increased the duration of the excitatory post-synaptic potential resulting in the generation of a train of action potentials (a seizure-like discharge) compared to the single action potential normal solution.

These experiments show that leptazol antagonises GABA action post-synaptically and probably blocks GABA mediated inhibition in the same way. This consequently releases excitatory activity normally shunted out by the i.p.s.c. and together with the antagonism of the presynaptic actions of GABA contributes to the convulsant action of leptazol.

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Baclofen: a selective agonist for a novel type of GABA receptor

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Recent findings have demonstrated GABA receptors on sympathetic neuroterminals which depress transmitter outflow (Bowery & Hudson, 1979). These receptors are atypical in that they are insensitive to the GABA antagonist bicuculline and to several classical GABA agonists such as 3-aminopropane sulphonic acid (3-APS). Similar findings have been reported on transmitter outflow in sympathetic ganglia (Brown & Higgins, 1979). We now report that baclofen (β(p-chlorophenyl)GABA) is a potent agonist for this receptor.

A range of putative GABA agonists was tested for their ability to depress the evoked release of [^{3}H]-noradrenaline from rat atria as previously described (Bowery & Hudson, 1979) and the contractile response of the field stimulated mouse vas deferens preparation (stimulus parameters after Shaw & Turnbull, 1978).

In both tissues, GABA produced a dose-dependent inhibition of the response (ED_{50} 3–4 μM). Most drugs tested were less potent than on classical GABA receptors such as those mediating depolarisation in the spinal cord or autonomic ganglion.

(±)-Baclofen, however, was equipotent with GABA at inhibiting the response in both tissues (see Table 1). Cross desensitisation occurred in the atrium between GABA and baclofen, but not between GABA and carbachol. Furthermore, contraction of the vas deferens in the presence of a supramaximal concentration of GABA (10^{-4} M) was not further depressed by baclofen, although it could be further inhibited

Table 1 Molar potency ratios of GABA agonists (GABA = 1)

Tissue	*Rat atrium Inhibition of [^{3}H]-noradrenaline release*		*Mouse vas deferens Inhibition of contraction*		*Guinea-pig ileum Inhibition of contraction*		*Rat sympathetic ganglion Depolarisation*	
Drug	ED_{50} (μM)	*Potency Ratio*	ED_{50} (μM)	*Potency Ratio*	ED_{50} (μM)	*Potency Ratio*	ED_{50} (μM)	*Potency Ratio*
GABA	4.2 ± 1.4 ($n = 6$)	1	3.0 ± 0.4 ($n = 12$)	1	7.1 ± 0.5 ($n = 5$)	1	12.5*	1
Muscimol		0.015 ± 0.003 ($n = 3$)		0.13 ± 0.03 ($n = 6$)		0.04 ± 0.005 ($n = 5$)		5.1 ± 0.7**
(±)-Baclofen		0.93 ± 0.02 ($n = 3$)		1.03 ± 0.27 ($n = 6$)		0.97 ± 0.1 ($n = 5$)		≪0.0004*
3-Aminopropane sulphonic acid		≪0.0003 ($n = 3$)		≪0.003 ($n = 3$)				3.4 ± 0.33*
Maximum inhibition (% of control)	54.1 ± 2.34		32 ± 4.9		18 ± 4.2			

* Bowery & Brown (1974).
** Bowery, Collins, Hudson & Neal (1978).
* See also Ault & Evans (1978).