Our results demonstrate that NT has two types of action on the electrical and mechanical activities of the guinea-pig taenia coli: (1) the peptide increases spike frequency; this results in an increase of the size and frequency of phasic contractions; (2) NT depolarizes the smooth muscle membrane; this results in a tonic contraction; the depolarization is probably due to an increase in Na^+ and Ca^{++} conductances.

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Determination of *in vivo* activity of putative GABA-like compounds

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The current interest in the γ-aminobutyric acid (GABA) system prompted us to investigate the activity of several putative GABA agonist and antagonist compounds in a range of *in vivo* tests. This poster communication presents data obtained with standard drugs in three simple assay procedures.

The three test procedures that we have used are haloperidol-induced catalepsy, harmaline-induced tremor and 3-mercaptopropionic acid-induced seizures.

In agreement with literature reports (Haefely, Kulsár, Möhler, Pieri, Polc & Schaffner, 1975), we find that GABA-like agonists potentiate haloperidol-induced catalepsy and that GABA antagonists antagonise the catalepsy. Potential agonists are tested in groups of 5 female mice of the Alderley Park Strain (18–20 g) against a sub-cataleptic dose of haloperidol (1 mg/kg; i.p.) and antagonists against a full cataleptic dose (10 mg/kg; i.p.). Catalepsy is assessed by means of a vertical string-wrapped rod (Zetler, 1968; Doggett, 1973), catalepsy being considered to be present if no movement up or down the rod occurs within 30 s of placing the animal on the rod. The minimal effective dose (M.E.D.) was calculated at the time of maximum drug effect using the Fisher 'exact' test for statistical significance.

Harmaline is thought to produce tremor by an effect on GABA neurones in the cerebellum (Biggio, Brodie, Costa & Guidotti, 1977; Costa, Guidotti & Mao, 1975). Putative GABA antagonists are tested using groups of 5 female rats of the Alderley Park Strain (140–160 g) against a low dose of harmaline (2.5 mg/kg; i.p.) and agonists against a high dose (10 mg/kg; i.p.) of the tremorogen (Mao, Guiddotti &

Table 1 Results obtained with a range of putative GABA agonists and antagonists in 3 simple *in vivo* assay procedures

	Haloperidol Catalepsy						*Harmaline Tremor*						*3-MPA Seizures*		
	Potentiation			*Antagonism*			*Potentiation*			*Antagonism*					
Drug	*Route*	*Pre-treatment Time (min)*	*M.E.D. (mg/kg)*	*Route*	*Pre-treatment Time (min)*	*M.E.D. (mg/kg)*	*Route*	*Pre-treatment Time (min)*	*M.E.D. (mg/kg)*	*Route*	*Pre-treatment Time (min)*	*M.E.D. (mg/kg)*	*Route*	*Pre-treatment Time (min)*	AC_{50} *(mg/kg)*
Muscimol	s.c.	30	1.5	—	—	—	s.c.	30	1.5	s.c.	30	>2.5	s.c.	30	0.7
Imidazole Acetic Acid	s.c.	30	50	—	—	—	—	—	—	s.c.	30	100	s.c.	30	>200
Baclofen	s.c.	30	5	—	—	—	—	—	—	s.c.	30	20	s.c.	30	20
Diazepam	s.c.	30	5	—	—	—	—	—	—	s.c.	30	10	s.c.	30	0.3
Amino-oxy Acetic Acid	i.p.	240	50	—	—	—	—	—	—	i.p.	240	10	i.p.	240	44
Sodium Valproate	s.c.	60	600	—	—	—	—	—	—	s.c.	30	400	p.o.	60	154
Bicuculline	—	—	—	s.c.	10	1.0	s.c.	10	1.0	—	—	—	—	—	—
Picrotoxin	—	—	—	s.c.	10	2.5	s.c.	10	0.5	—	—	—	—	—	—
3-Mercaptopropionic Acid	—	—	—	s.c.	10	25	s.c.	10	10	—	—	—	—	—	—
Allylglycine	—	—	—	s.c.	240	100	s.c.	240	40	—	—	—	—	—	—

Costa, 1975). The M.E.D. was calculated at the time of maximum activity.

The anticonvulsant dose (AC_{50}) of GABA-like agonist compounds was determined against 3-mercaptopropionic acid-induced seizures (50 mg/kg; i.p.) using groups of 6 female mice of the CBA strain (18–20 g). Mice were considered to be protected if no tonic seizure was seen within 10 min of injection of the convulsant agent.

Our results are summarised in Table 1 which also gives the routes of injection and pretreatment times for the standard drugs which we have examined. These data provide a useful profile of the *in vivo* activity of potential GABA-like drugs. Of considerable interest was the finding that muscimol, in contrast to the other putative GABA agonists and in common with GABA antagonists, potentiated harmaline tremor.

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The effect of neurotoxic lesions on neuronal systems in rat striatum

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Neurotoxic lesions have been extensively used to study the localization of neuronal systems in the rat striatum as well as providing animal models of Parkinsonism and Huntington's chorea (DuVoisin, 1976; Coyle & Schwarcz, 1977).

In the present study, 6-hydroxydopamine (6-OHDA) lesions of rat striatal dopaminergic afferents and kainic acid (KA) lesions of striatal cell bodies have been used to study the location of dopamine (DA), acetylcholine (ACh), α-aminobutyric acid (GABA) and glutamate containing neurones in rat striatum.

Male Sprague-Dawley rats (150-200 g) were injected unilaterally with either KA (2.5 μg/1 μl saline) into the striatum (Waddington & Cross, 1978) or with 6-OHDA (8 μg/4 μl saline ascorbate) into the lateral hypothalamus (Waddington & Crow, 1978). At 3 or 7 weeks after the lesion rats were decapitated and striata dissected out. Lesioned and unlesioned striata were compared for (a) the activities of the neurotransmitter synthesizing enzymes, choline acetyltransferase (CAT), tyrosine hydroxylase (TOH), glutamate decarboxylase (GAD) in striatal homogenates and (b) assessment of neurotransmitter receptors by specific binding of tritiated quinuclidinyl benzylate ([^{3}H]-QNB), [^{3}H]-KA and [^{3}H]-GABA to striatal membrane preparations. Results expressed as percentage changes were all statistically significant.

The effectiveness of 6-OHDA lesions was confirmed by a 90% reduction in TOH activity in lesioned striata. GAD activity was increased by 25% with no change in CAT activity. Specific [^{3}H]-GABA and [^{3}H]-QNB binding were reduced by 18% and 15% respectively with no change in [^{3}H]-KA binding. It has previously been demonstrated that specific binding of [^{3}H]-spiperone to the dopamine receptor is elevated by 44% in rat striatum after 6-OHDA lesions (Cross, Longden, Owen, Poulter & Waddington, 1978).

The effective destruction of striatal cell bodies by KA was confirmed by reductions of 52% and 30% in GAD and CAT activities, respectively. This lesion resulted in a 23% increase in TOH in lesioned striata. Specific [^{3}H]-QNB and [^{3}H]-KA were reduced by 61% and 40% respectively whereas [^{3}H]-GABA binding was increased by 78%. Analysis of saturation data indicated that the increase in [^{3}H]-GABA binding was characterized by a decrease in the dissociation constant for high affinity [^{3}H]-GABA binding with no change in receptor numbers. This contrasts with the effects of striatal KA lesions on nigral [^{3}H]-GABA binding where increased binding (Cross & Waddington, 1978) is characterised by an 81% increase in high affinity receptor numbers with no change in dissociation constant. In both studies the characteristics of low affinity GABA binding were unchanged.

These results suggest that (i) a proportion of [^{3}H]-GABA binding sites may be located on non-dopaminergic striatal afferents and (ii) [^{3}H]-KA