implanted in the brains of male Sprague-Dawley rats (275–300 g) using standard stereotaxic techniques (Costall & Naylor, 1976). Locomotor activity was measured by placing rats in individual perspex cages, each fitted with one photocell unit, and measuring the number of interruptions of the light beam occurring every 10 min for a total of 4 h.

The injection of dopamine (3.13–50 μg) into the ACB of nialamide (100 mg/kg i.p. 2h) pretreated rats induced dose related hyperactivity. An established response to dopamine (50 μg) was antagonized by intra-ACB eserine (1.25–5.0 μg) and carbachol (>2.5 μg). Intra-ACB atropine (6.25–25 μg) caused a transient reduction in hyperactivity during the first hour with no subsequent enhancement. A 30 min pretreatment with atropine (5.0 mg/kg i.p.) antagonized the eserine (5.0 μg) induced reduction of dopamine hyperactivity, although peripherally administered atropine (1.0–10 mg/kg i.p.) failed to modify the dopamine hyperactivity *per se*. Intra-ACB mecamylamine (25 μg) failed to consistently modify dopamine hyperactivity or the response to eserine (5.0 μg). Haloperidol (0.1–0.8 mg/kg i.p.) antagonized an established dopamine (50 μg) hyperactivity: the antagonistic effect of 0.8 mg/kg i.p. haloperidol was not modified by a 30 min pretreatment with atropine (5.0 mg/kg i.p.).

It is concluded that whilst the hyperactivity induced by intra-ACB dopamine can be antagonized by an enhanced cholinergic muscarinic effect, the neuroleptic antagonism is not dependent on an enhanced cholinergic activity. The failure of atropine to enhance mesolimbic dopamine hyperactivity or to antagonise the neuroleptic inhibitory effects on a mesolimbic dopamine system differentiates the nature of the neuroleptic-cholinergic interaction from that in the extrapyramidal dopamine systems. This data may have implications for the understanding of the clinical effects of combined neuroleptic and anticholinergic therapy with respect to the antipsychotic (mesolimbic?) and extrapyramidal side effects associated with neuroleptic action.

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Neurotensin: electrophysiological studies of its action on the guinea-pig taenia coli

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Recently we reported that the tridecapeptide neurotensin (NT) contracted the guinea-pig taenia coli by directly interacting with this smooth muscle (Kitabgi & Freychet, 1978). This led us to study the effects of NT on the membrane potential and conductance of the guinea-pig taenia coli, using the sucrose gap method (Bülbring & Tomita, 1969). Single and double sucrose gap experiments were done at 37°C and 20°C, respectively. In double sucrose gap experiments, hyperpolarizing and depolarizing currents of constant intensity were alternately applied to the muscle preparations. Membrane potential and isometric change in tension were simultaneously recorded.

At 37°C, the guinea-pig taenia coli often exhibited spontaneous activity. Spikes (about 20mV) were accompanied by phasic contractions. NT at low concentration (0.5 nM) induced a slow depolarization (about 5 mv). The peptide reduced the size of the spikes but increased their frequency. This resulted in an increase in the frequency of phasic contractions. With NT (10 nM), the membrane depolarization (about 20 mv) was rapid. Spike frequency was initially increased and their size reduced until they were blocked by the depolarization. Initial phasic contractions were followed by a tonic contraction associated with the depolarization.

At 20°C, the guinea-pig taenia coli showed little or no spontaneous activity. Spikes were induced by depolarizing currents and accompanied by phasic contractions. NT (50 nM) rapidly depolarized the muscle. Spikes were blocked at maximal depolarization (20–25 mv). The depolarization was accompanied by a tonic contraction. Membrane conductance was increased as indicated by the reduction of electrotonic potentials induced by hyperpolarizing currents. Dose-response curves of NT-induced depolarization and contraction gave ED_{50} of 1.7 nM and 4.5 nM respectively. The maximally effective dose of peptide was the same (about 50 nM) for both dose-response curves.

When Na^+ in normal physiological solution was replaced by Li^+ or Mg^{++}, there was a marked inhibition of NT-induced depolarization (60–70%) and contraction (>50%). This was accompanied by a reduction in the NT-induced increase in membrane conductance. In Ca^{++}-free solution, the NT-induced depolarization was inhibited by 25% and in a solution containing Mn^{++} (5mM), the inhibition was 50%.

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	—	—	—	—	—	—