in mean pressure of rapid onset (90 min after methyldopa treatment mean systolic pressure reduced from 190·4 ± 2·5 to 147·5 ± 2·00 mmHg (2 mg/kg) and from 191·2 ± 2·2 to 138·4 ± 2·9 mmHg (4 mg/kg)). The mechanism of the central hypotensive action of α-methyldopa appeared to be similar to that when given peripherally since it was abolished by the higher doses of Ro4-4602 but not by the lower doses. Disulfiram and sodium diethyldithiocarbamate (DDC) are potent inhibitors of dopamine-β-hydroxylase (Goldstein, Anagnoste, Lauber & McKereghan, 1964) and when administered to hypertensive rats at a dose of 100 mg/kg caused falls in mean systolic blood pressure (190·7 ± 1·8 to 159·4 ± 2·3 and 183·5 ± 1·9 to 151·8 ± 2·4 mmHg respectively). In hypertensive rats pre-treated with either disulfiram or DDC (100 mg/kg) the antihypertensive effect of α-methyldopa administered either centrally or peripherally was completely abolished. These observations strongly suggest that α-methyldopa exerts its antihypertensive effect by a central mechanism as suggested by Henning (1969). However, the abolition of the antihypertensive action of α-methyldopa by disulfiram and DDC is inconsistent with the postulate of Farmer (1965), that the antihypertensive effect is due to accumulation of α-methyldopamine, but is consistent with the false neurohumoral transmitter theory to explain the central action of α-methyldopa in relieving hypertension.

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The effects of different anaesthetics on responses of brain stem neurones to iontophoretically applied transmitter substances

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Anaesthesia is known to alter the responsiveness of neurones in the c.n.s. to substances applied microiontophoretically (Bloom, Costa & Salmoiraghi, 1965; Johnson, Roberts & Straughan, 1969; Crawford, 1970).

The effects of tribromoethanol, urethane and pentobarbitone anaesthesia on the responses of spontaneously active single neurones in the brain stem of cerebellectomized rats to microiontophoretic applications of acetylcholine (ACh), L-noradrenaline (NA) and 5-hydroxytryptamine (5-HT) were examined. The results were compared with those from decerebrate unanaesthetized control preparations.

The types of responses of brain stem neurones to ACh, (−)-NA and 5-HT in anaesthetized animals resembled those from the unanaesthetized control preparations.

The proportions of responses in animals anaesthetized with tribromoethanol (200 mg/kg) and urethane (1·8 g/kg) were not significantly different from controls. However, in animals anaesthetized with pentobarbitone (50 mg/kg) the proportion of neurones excited by ACh was significantly reduced, although responsiveness to NA and 5-HT was unaltered (Table 1). Similar results were obtained in anaesthetized animals which were artificially ventilated to avoid hypoxia.

Statistical analysis of the spontaneous firing rates of the neurones showed that there was no significant difference between neuronal firing rates in urethane or tribromoethanol-anaesthetized animals compared with controls. However, there was a significantly greater ($P<0·01$) proportion of neurones studied in pentobarbitone-anaesthetized rats with firing rates below 10 impulses/sec.

Further studies have shown that although a non-specific depression in neuronal firing rate often occurred after intravenous or microiontophoretic administration of barbiturates, specific antagonism to ACh excitation could still be demonstrated.

Thus, neither tribromoethanol, urethane nor pentobarbitone anaesthesia affected the types of responses to microiontophoretically applied ACh, NA or 5-HT in the brain stem of the rat. Pentobarbitone, however reduced the number of ACh excitations observed. This action appears to be specific.

TABLE 1. *The proportions of brain stem neurones (%) in anaesthetized and unanaesthetized rats responding to microiontophoretic applications of ACh, 5-HT or NA. The total number of neurones studies is given in parentheses. +=excitation; 0=no effect; —=inhibition.*

	Acetylcholine				Noradrenaline				5-Hydroxytryptamine			
	+	0	—		+	0	—		+	0	—	
Tribromoethanol	79	19	2	(169)	41	32	27	(187)	71	18	11	(195)
Urethane	85	11	4	(311)	44	20	36	(201)	69	13	18	(211)
Pentobarbitone	41	50	9	(219)	51	25	24	(209)	79	12	9	(212)
Unanaesthetized	81	16	3	(229)	42	32	26	(198)	81	16	3	(203)

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Interaction of anticholinergic agents with α-methyl-p-tyrosine and (+)-amphetamine

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Catalepsy is induced by (+)-amphetamine in rats pretreated with H 44/68 ((±)-α-methyl-p-tyrosine methylester HCl), an inhibitor of tyrosine hydroxylase (Sayers & Spencer, 1971). Since anticholinergic drugs can antagonize both cholinergic- and neuroleptic-induced catalepsy (Zetler, 1968), their effect on the H 44/68: (+)-amphetamine catalepsy was investigated to determine whether a cholinergic component is involved here. The anticholinergic agents employed were hyoscine (0·6–