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–

24 mg/kg I.P.), atropine (0·5–20 mg/kg I.P.), methixene (0·5–20 (80) mg/kg I.P.) and meth-atropine (20 mg/kg I.P.). Meth-atropine, lacking central action, was inactive throughout.

Both hyoscine and atropine induced a short period of stereotyped sniffing in untreated rats, as reported by Arnfred & Randrup (1968), but following methixene this effect was weak and only induced by extremely high doses (80 mg/kg). Pretreatment with H 44/68 abolished this response in the case of atropine, but not in the case of hyoscine, suggesting the involvement of different mechanisms of action for each drug.

When (+)-amphetamine (5 mg/kg S.C.) was given to rats 30 min after one of the three anticholinergic drugs, the animals became hypersensitive to noise and touch. This diminished as stereotypies developed, only to increase again as stereotyped behaviour declined. In accordance with earlier reports the stereotyped behavour itself was enhanced and prolonged (Arnfred & Randrup, 1968).

When the anticholinergics were administered 30 min after (+)-amphetamine, i.e. when stereotyped behaviour had already commenced, only slight hypersensitivity developed. Stereotyped behaviour was again prolonged, but only weakly enhanced.

The effects of the anticholinergics on the H 44/68:(+)-amphetamine catalepsy depended on the time of their administration. (+)-Amphetamine (5 mg/kg S.C.) was always given 4 h after H 44/68 (250 mg/kg I.P.), and catalepsy developed gradually during the next 3 h. When any of the three anticholinergics was added to the combination 30 min before (+)-amphetamine, hypersensitivity was very marked with increased locomotor activity and rearing. No stereotypies developed, and catalepsy was antagonized in a dose dependent manner.

When given 30 min after (+)-amphetamine, the activities of the three anticholinergic drugs were rather different. Hypersensitivity failed to develop. Atropine and hyoscine produced a weaker antagonism of the catalepsy, whereas methixene not only failed to antagonize the catalepsy, but actually hastened its onset, and in a high dose (80 mg/kg) slightly increased its intensity.

The differing effects of methixene, compared with hyoscine and atropine, when given *after* H 44/68:(+)-amphetamine, are difficult to explain. The fact that only methixene inhibits dopamine re-uptake (Farnebo, Fuxe, Hamberger & Ljungdahl, 1970), may be of relevance.

The time course of the occurrence of stereotypies and hypersensitivity in these experiments suggests that the mechanisms underlying stereotyped behaviour are antagonistic to those subserving hypersensitivity. This is supported by the potentiation of hypersensitivity during blockade of stereotypies by H 44/68, a finding which indicates that the hypersensitivity is independent of on-going catecholamine synthesis.

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