determined spectrofluorometrically (Shore, 1959) these were the same for normal and aggressive mice.

Our results add another factor to the many already known to affect amphetamine toxicity. They also provide a new lead to the understanding of biological changes occurring during the development of the aggressive behaviour.

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A method for evaluating imipramine-like agents in rats*

SIR,—Demonstration of imipramine-like activity in animals is difficult. Stein & Seifter (1961) reported that the increase in self-stimulation rate induced by methamphetamine was enhanced by imipramine as a result of augmentation of the central adrenergic reward system. We have now investigated the behavioural effects of amphetamine and imipramine in animals trained for an automatic pole-climbing apparatus (Aceto, Kinnard & Buckley, 1963).

A group of six male albino rats (250–350 g) was trained to climb a pole in response to an auditory signal, and so avoid a shock delivered by an electrified grid floor. A successful climb depressed a microswitch which terminated the trial and permitted a longer intertrial period. The apparatus was programmed so that 100 trials could be presented during a 2 hr session. Each trial consisted of 8 sec of auditory tone (avoidance phase), 6 sec of auditory tone plus shock (escape phase) and 58 sec of intertrial time. A shock scanning device was used which energized the grid by scanning at the rate of 3 times/sec. Current was measured by ammeter, and rats were shocked with 500 V at about 3 mA.

Animals were trained to avoid shock in 95% or better of the trials. In the experiments reported here, none of the drug-treatments significantly impaired the ability of the rats to successfully avoid or escape. The avoidance response latency for each rat was recorded by means of a pen polygraph; 16 control days revealed that the rats climbed the pole in an average time of 5·4 sec, with a range of 4·9 to 6·0 sec. Salts of the drugs, imipramine (hydrochloride) and amphetamine (sulphate), were injected intraperitoneally in saline once a week

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just before the experiment, with control experiments using only saline injections at a similar time of day twice a week. All drug-treatments were replicated and the data represent the average of two experiments.

TABLE 1. ACTION OF IMIPRAMINE AND AMPHETAMINE ON AVOIDANCE LATENCIES IN AUTOMATIC POLE-CLIMB RESPONSE

	Average group avoidance (sec) for numbers of trials after injection									
	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	81–90	91–100
Controls (16 days)	5·3	5·2	5·4	5·7	5·3	5·5	5·4	5·4	5·3	5·3
Imipramine (10 mg/kg) ..	4·8	4·7	5·5	5·3	5·6	5·9	6·0	5·3	5·8	5·9
Amphetamine (0·25 mg/kg)	4·8	3·9*	4·4	5·0	5·4	5·5	5·7	5·4	5·0	5·3
Amphetamine (1 mg/kg) ..	3·3*	2·2*	2·2*	2·4*	3·0*	3·1*	3·3*	3·6*	3·8*	4·0*
Imipramine (10 mg/kg) + amphetamine (0·25 mg/kg)	3·5*	1·6*	1·8*	2·5*	2·8*	3·5*	3·5*	3·6*	3·5*	3·8*

* $P < 0.05$ from controls.

Results, as summarized in the Table, indicate that 1 mg/kg of amphetamine significantly facilitated avoidance response latency and 10 mg/kg of imipramine, a dose which was without effect in this test, potentiated the effects of 0·25 mg/kg of amphetamine into a response obtained when 1 mg/kg of amphetamine was given alone. The method seems suitable for screening imipramine-like agents.

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Non-depolarising neuromuscular blockade by 3α,17α-bis(quaternary ammonium) 5α-androstanes

SIR,—Although many molecular features are known to influence neuromuscular blocking activity and plausible alternative explanations exist (Loewe & Harvey, 1952; Cavallito & Gray, 1960; Waser, 1959, 1962), the potent neuromuscular blocking activity characteristic of certain bisquaternary salts is often envisaged in terms of a "two-point" attachment in which the cationic heads interact simultaneously with separate anionic sites of the acetylcholine receptors on the post-synaptic membrane as first proposed by Barlow & Ing (1948a, b) and Paton & Zaimis (1948, 1949).

Deductions concerning the spatial separation of these anionic sites have been made (Barlow, 1960 and refs cited) in terms of the interonium distance of the decamethonium molecule, since this compound in several species exhibits the highest potency of the homologous polymethylenebis(trimethylammonium) salts, in the belief that maximal potency is a direct reflection of ability to span exactly the gap between two of the sites which are considered to lie in a regular lattice. It was assumed that the decamethonium molecule underwent interaction