Though BRL 1288 may have some central anticholinergic properties these are particularly weak on cortical neurones and are probably of little significance. Its main action appears to be a depressant one which is probably related to its local anaesthetic properties.

G.C. is an M.R.C. Scholar.

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Effect of imipramine on unit activity in the midbrain raphé of rats

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Intravenously administered lysergic acid diethylamide and other psychotomimetics reduce the firing rate of cells in the dorsal and median raphé nuclei of anaesthetized rats (Aghajanian, Foote & Sheard, 1968; 1970; Foote, Sheard & Aghajanian, 1969). This effect has been attributed to stimulation of central 5-hydroxytryptamine receptors. In the present experiments the action of a drug which affects 5-hydroxytryptamine transmission in another way, *viz.* by blocking the membrane pump for reuptake, has been investigated. Unit activity in the raphé nuclei was recorded in male albino rats (215–275 g) under light anaesthesia (chloral hydrate 350–400 mg/kg i.p.) using tungsten microelectrodes.

All raphé units tested responded to imipramine with a slowing or cessation of firing, though the sensitivity of units varied widely. In preliminary experiments a single dose of 1·25 mg imipramine (approx. 5·0 mg/kg i.v.) caused complete inhibition of firing of raphé units without decreasing the firing rate of control units in the pedunculus cerebellaris superior. The onset of effect was comparable to that of intravenously administered lysergic acid diethylamide; that is maximum effect achieved within 30 s and more rapid than the effect of intravenous pargyline (18·5 mg/kg) which took more than 60 s to reach maximum effect.

In other experiments, imipramine was injected in 0·25 mg doses at intervals of 2 min until an effect was noted, approximately 2 mg/kg producing threshold inhibition and approximately 4 mg/kg giving 100% inhibition. In some cases it was possible to construct cumulative dose-response curves, but in other cases the curve was too steep.

Recovery from imipramine did not occur within 30 min of onset; thus, compared with lysergic acid diethylamide, the effect is persistent and similar to that of monoamine oxidase inhibitors.

The inhibitory effect of imipramine on raphé unit firing appears likely to be related to an increase of 5-hydroxytryptamine, since the inhibitory effect of imipramine given intraperitoneally was seen with a similar dose to that needed to block the reuptake of 5-hydroxytryptamine *in vivo* (Ross & Renyi, 1969). An effect on cate-

cholaminergic neurones seems unlikely since amphetamine (0·5–2·0 mg/kg, i.v.) does not inhibit raphé units under these conditions.

I am grateful for the help and encouragement of Professor D. W. Straughan. This work was supported by a Medical Research Council grant to Professor D. W. Straughan.

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Effects of chronic and acute cannabis treatment upon thiopentone anaesthesia in rabbits

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Four groups of rabbits were used. Each of the first group, 'acute cannabis', received 50 mg/kg crude cannabis (100 mg/ml in saline, stabilized with 40 mg/ml of Tween 80) intravenously 45 min before anaesthesia. Each of the 'chronic cannabis' group received 50 mg/kg crude cannabis subcutaneously daily for 63 days until 5 days before thiopentone administration. The 'chronic Tween' group received the same daily doses of Tween 80 as the chronic cannabis group. The control animals were untreated. The cannabis used was obtained by removal of ethanol from Tincture of Cannabis (Gill, Paton & Pertwee, 1970).

Sodium thiopentone (5%) was injected intravenously into the rabbit ear vein over approximately 2 min, until both corneal reflex and reaction to a standard ear-pinch had just ceased. Recovery was followed by recording, for each animal, the time from the midpoint of the injection to the appearance of each of the following signs: (1) slight reaction to ear-pinch and corneal touch; (2) pronounced reactions

TABLE 1.

Group	No. of rabbits	Dose of thiopentone (mg/kg)	Duration of injection (min)	Time (mean value in min ± S.E.) to reach recovery stage (see text): 1	2	3	4	5	6
Control	3	30	1·9	3·8	6·1	—	8·8	11·1	20·6
			±0·2	±0·4	1·0		2·7	0·9	2·7
Acute cannabis	3	22·3	2·1	7·3	11·2	—	6·2	16·7	24·8
		±2·6	±0·2	±0·9	1·9		0·6	1·8	3·5
	1	30·0*	2·5	20·0	35·0	—	44·0	58·0	66·0
Chronic cannabis	3	23·7	1·8	5·1	6·7	9·4	7·0	12·3	19·2
		±0·3	±0·1	±0·5	0·3	2·1	1·0	4·0	3·1
	6†	23·9	1·8	4·6	5·9	7·6	7·9	10·2	15·8
		±0·9	±0·2	±0·5	0·4	1·7	1·0	2·0	2·3
Chronic Tween	3	31·7	2·3	5·1	7·5	9·8	—	12·3	15·7
		±1·2	±0·2	±0·6	0·5	0·7		0·8	1·6
	4†	31·8	2·2	4·9	6·9	8·0	5·5	11·7	16·8
		±0·8	±0·2	±0·5	0·7	1·8		1·4	1·6

* This dose passed the normal end-point. † Individual rabbits received a second treatment with thiopentone 3 or more days after the first.