there is no rete and the carotid supply to the brain is through the internal carotid artery. The cat experiments previously reported (Stephens & Corne, 1966) were repeated on baboons to determine whether these anatomical differences affected the response of intracranial pressure (ICP) to drugs and might invalidate correlations between responses in cats and responses in primates and man.

Nine baboons of either sex were anaesthetized with pentothal (10 mg/kg, I.V.) and chloralose (50 mg/kg, I.V.) after sedation with phencyclidine (1.0 mg/kg, I.M.). The ICP transducer (Corne & Stephens, 1966) was slightly modified, the sensing area being protected in a box covered with a thin rubber membrane. This was placed in contact with the dura through a trephine hole and cemented in place with acrylic cement. Blood pressure, end tidal CO_2 concentration and ICP were monitored continuously and arterial pCO_2 periodically. The animals were artifically ventilated so that the resting arterial pCO_2 was 35–45 mm Hg. Drugs were injected I.V. (saphenous) or I.A. (lingual).

The ICP response to noradrenaline (0.05–1.0 μg/kg) was similar in form and duration to the systemic arterial pressor response. Adrenaline (0.1–1.0 μg/kg) also induced simple ICP responses, but these were often associated with biphasic arterial responses. Both histamine (0.5–10 μg/kg) and bradykinin (0.1–4.0 μg/kg) induced an increase in ICP associated with arterial depressor responses at low doses and depressor/pressor responses at higher doses. Bradykinin I.A. was ten times more effective than I.V. upon ICP and was the only drug used that showed a marked route difference in effectiveness. An I.V. infusion of histamine caused a long progressive rise in ICP, whereas the blood pressure returned to control level rapidly. Addition of 3% CO_2 to the inspired gases induced a considerable increase in ICP and pulse amplitude. Blood pressure was unaffected.

As the skull forms a rigid, largely closed container it seems likely that rapid increases in ICP reflect increases in cerebral blood volume (vasodilatation?) and decreases reflect reductions of blood volume (vasoconstriction?). The increase in ICP after histamine, bradykinin and CO_2 probably indicated active vasodilatation, whereas the ICP response to noradrenaline may have been a passive following of the blood pressure response. The ICP and blood pressure responses to adrenaline were dissimilar in form, so a direct action upon the cerebral vasculature cannot be discounted.

Some minor differences were observed. The ICP responses of cats to catecholamines showed more variation than those of baboons, and the primates were relatively insensitive to histamine. Qualitatively, however, the activity of the cerebral vasculature that we measured in cats is comparable with that in baboons.

This work was carried out while S. J. C. and R. J. S. were members of the Department of Pharmacological Research, Parke, Davis & Co., Hounslow, Middlesex.

REFERENCES

CORNE, S. J. & STEPHENS, R. J. (1966). Peri-arterial and extradural devices for measuring changes of blood pressure and intracranial pressure in conscious animals. *J. Physiol., Lond.*, **188**, 9–10*P*.

STEPHENS, R. J. & CORNE, S. J. (1966). The measurement of changes of blood pressure and intracranial pressure in conscious laboratory animals. *Br. J. Pharmac. Chemother.*, **27**, 443 (title only).

Nitrazepam delays onset and shortens duration of visual after-images

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The effects of nitrazepam (5 and 10 mg), amylobarbitone sodium (100 and 200 mg) and placebo were compared in ten healthy male medical students. Dark-adapted subjects

reported on the after-image following exposure for 15 sec at 6 feet distance to a cross in circle pattern illuminated from behind by a 150 W light source; this is a technique for obtaining a stabilized retinal image, and hence after-image, which avoids using contact lenses (Bennet-Clark & Evans, 1963; Evans, 1965). The after-image obtained in this way undergoes changes similar to those described using other methods. Nitrazepam, particularly in the larger dose, was found in comparison with placebo at 90 min and 150 min after treatment to increase the latency (the time between the end of the flash and the first appearance of the image) and shorten the duration (total time over which the image was reported) of the after-image (Table 1). These differences are unlikely to have been due simply to inability or unwillingness to report the subjective experience: the rate of verbal output under the three experimental conditions did not differ significantly and the results from those subjects who actually slept and had to be awoken for the test were indistinguishable from those who did not sleep, whereas the performances on other motor tasks by these two sub-groups were similarly slowed. The possible effect of nitrazepam on dark adaptation is at present being investigated.

TABLE 1. (A) *Latency and* (B) *duration of after-image reports* (in sec)

			Amylobarbitone sodium				Nitrazepam			
	Control		100 mg		200 mg		5 mg		10 mg	
Time after drug (min)	90	150	90	150	90	150	90	150	90	150
(A) Mean	7·1	5·9	6·8	7·8	8·0	4·9	9·3	10·0	10·2	9·5
S.E.	0·9	0·8	1·1	1·6	0·9	0·6	0·4	0·5	0·7	0·4
(B) Mean	82·0	81·7	81·2	71·8	74·5	77·4	65·2	71·6	48·4	57·9
S.E.	2·9	3·2	10·1	9·9	5·4	8·0	9·4	6·4	10·3	9·5

$n=10$.

REFERENCES

BENNET-CLARK, H. C. & EVANS, C. R. (1963). Fragmentation of patterned targets when viewed as prolonged after-images. *Nature, Lond.*, **199**, 1215–1216.

EVANS, C. R. (1965). Some studies of pattern perception using a stabilized retinal image. *Br. J. Psychol.*, **56**, 121–133.

Analytic methods for the study of drug effects on avoidance-conditioning in the rat

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Unlike most learning tasks, the measurement of conditioned avoidance (CAR) learning is dependent on time restrictions imposed by the situation used. Thus, any factor delaying or hastening responses in this type of learning has a greater influence on performance than in other learning situations. Three major determinants of CAR behaviour are perceptual ability, motivational level and locomotor capacity. To evaluate a drug action on CAR acquisition it is crucial therefore to differentiate which of these variables are affected. Most studies of drug effects on avoidance conditioning have been concerned with motivational effects (anxiety) alone. In this study an attempt was made to provide independent measures of these three variables.

The apparatus consisted of a straight alley 56 in long × 4 in wide with a start box 11 in × 9 in at one end and a goal box of similar dimensions at the other. Raising the start box door operated a warning buzzer (CS). After 3 sec, a shock was delivered through the grid floor of the start box and alley but not of the goal box. Starting latencies and running