

cutaneously in 0.25% Celacol suspension. The procedure was repeated on each of four successive days.

(i) *Studies using food hoppers with grouped rats (n=4)*. In each of five experiments with rats of either sex (mean body weight range 114–200 g) food and water consumption and body weight were recorded every 2 h. Food consumption in the cyproheptadine treated groups (6.2–50 mg/kg) was consistently higher than in controls during the first 2 h but the total daily food consumption only exceeded control values on days 3 and 4.

(ii) *Continuous recording of food consumption in individually housed rats*. A mechanical device (to be published) was used for recordings from six female rats in two experimental sessions spaced a fortnight apart when their mean body weights were 122 g and 206 g respectively. Discrete meals were recorded. Commencing almost immediately following food presentation, control animals ate their first meal over a period of about 1 h and they usually had a further two, and occasionally three or four meals.

TABLE 1. *Effect of cyproheptadine on the consumption of meals by fasted rats*

Treatment	Meal 1			Meal 2	
	Amount (g)	Duration (min)	Mean eating rate (g/min)	Amount (g)	Duration (min)
Controls (0.25% Celacol s.c.)	7.0	62	0.11	3.5	38
Cyproheptadine 12.5 mg/kg s.c.	9.8*	125*	0.08	4.2	63
Cyproheptadine 25 mg/kg s.c.	9.4	118*	0.08	2.8	44

Means for four rats on days 1–4. * Different from control value at 1% level of significance.

Cyproheptadine (12.5 and 25 mg/kg) significantly prolonged the duration of the first meal and the lower dose significantly increased food consumption (Table 1). Eating rate and the number of meals taken were decreased: on only a few occasions were more than two meals eaten. The appetite stimulant effect persisted for the same duration (2 h) as the increased electrical activity observed with the same drug in the “feeding centre” in the lateral hypothalamus of cats (Chakrabarty *et al.*, 1967).

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Initial suppression of the locomotor stimulant response to dexamphetamine in rats exposed to a novel environment

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The effect of dexamphetamine on the activity in rats is dependent upon their previous experience: in Y-maze studies, amphetamine either increased (Rushton & Steinberg, 1963) or had little effect (Marriott, 1968) upon the activity of “inexperi-

enced" rats, whereas the activity of "experienced" rats was decreased (Steinberg, Rushton & Tinson, 1961). In contrast to the maze studies, our experimental cages, which provided a continuous activity record, enabled us to study the response to dexamphetamine of "inexperienced" rats put in a novel environment for several hours.

A battery of twelve individual activity cages (each 21.5 cm × 11.5 cm × 18 cm high internal dimensions) was used. The sides were of brown plastic and the lid of clear Perspex. Movements of the rats on metal floor rods originated electrical impulses

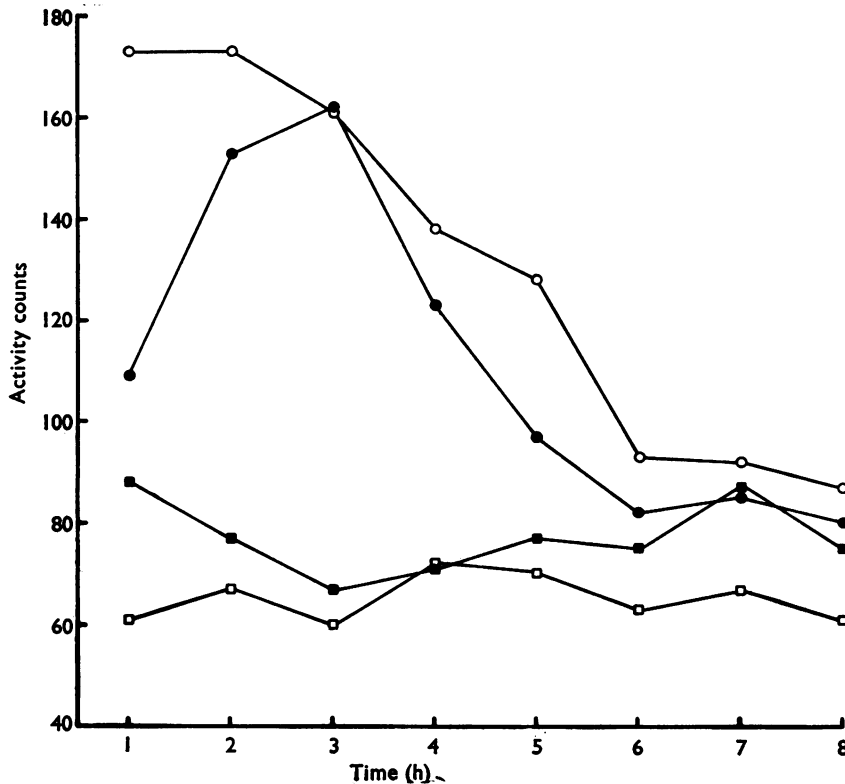


FIG. 1. Effect of dexamphetamine sulphate (1.25 mg/kg by stomach tube) on the locomotor activity of "experienced" and "inexperienced" rats in activity cages. Response of "experienced" rats to dexamphetamine (O) and to saline (□). Response of "inexperienced" rats to dexamphetamine (●) and to saline (■).

which were recorded automatically as activity counts. Male albino rats (weight range 150 to 250 g) were given dexamphetamine sulphate (1.25 mg/kg) or saline by stomach tube at approximately 16.45 h and placed in the cages for activity recording. Food and water were available. The room was artificially illuminated (tungsten lighting) from 05.00 to 17.00 h and in darkness from 17.00 to 05.00 h.

Studies were made both with rats which had been used previously in the activity boxes ("experienced") and with naive rats ("inexperienced").

Whereas the locomotor stimulant response to dexamphetamine in "experienced" rats was evident within the first hour the response of the "inexperienced" rats was suppressed for the first two hours (Fig. 1).

Steinberg has suggested that a rat placed in a novel environment experiences an initial phase of maximum curiosity and fear (Rushton & Steinberg, 1964) and from our studies it appears that the locomotor stimulant response to dexamphetamine is suppressed during this initial phase and only becomes apparent later. The results may also be explained in relation to type of activity. Increased rearing in the "inexperienced" rats during the initial phase would not be detected by our apparatus, which is specifically designed to measure sustained locomotor activity. Amphetamine increases rearing in some rat strains (Janssen, 1964).

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Integration and differentiation of phasic aortic flow and continuous recording of peripheral vascular resistance

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The following technique was devised for haemodynamic studies in dogs. These may be unanaesthetized if a cuffed flow sensor (10-18 mm) is implanted around the root of the ascending aorta and an aortic pressure cannula is inserted using procedures analogous to those described by Hughes (1967).

Integration and differentiation were carried out using a 6-channel operational amplifier manifold (Philbrick/Nexus Research) and the following were recorded on an 8-channel Beckman Dynograph (Fig. 1):

Phasic aortic flow. The velocity of blood at the root of the aorta was measured with a "Medicon K-2000A" gated 400 Hz sine-wave electromagnetic flowmeter (Kolin & Kado, 1959).

Stroke volume. Left ventricular stroke volume was recorded by integrating the flow velocity signal and discharging the capacitor of the operational amplifier through a relay switching unit by each R wave of the electrocardiogram.

Cardiac output (less coronary flow). The flow signal was integrated with an operational amplifier and the capacitor discharged by a reed relay energized every 4 s so that cardiac output was computed 15 times per min.

Acceleration. A beat-by-beat recording of maximum acceleration of blood from the left ventricle was obtained by differentiating the filtered velocity signal; this parameter is a sensitive index of myocardial contractile function (Noble, Trenchard & Guz, 1966). The 400 Hz gating frequency was removed by an operational amplifier used as a low pass filter with a cut-off frequency of 30 Hz; harmonics above 30 Hz contribute no more than 1% to the fundamental signal.