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).

REFERENCES

JANSSEN, P. A. J. (1964). In *Animal Behaviour and Drug Action*, ed. Steinberg, H., p. 425. Ciba Foundation Symposium. London: J. & A. Churchill.

MARRIOTT, A. S. (1968). The effects of amphetamine, caffeine and methylphenidate on the locomotor activity of rats in an unfamiliar environment. *Int. J. Neuropharmac.*, **7**, 487–491.

RUSHTON, R. & STEINBERG, H. (1963). Dose-response relations of amphetamine-barbiturate mixtures. *Nature, Lond.*, **197**, 1017–1018.

RUSHTON, R. & STEINBERG, H. (1964). Modification of behavioural effects of drugs by past experience. In *Animal Behaviour and Drug Action*, ed. Steinberg, H., pp. 207–219, Ciba Foundation Symposium. London: J. & A. Churchill.

STEINBERG, H., RUSHTON, R. & TINSON, C. (1961). Modification of the effects of an amphetamine barbiturate mixture by the past experience of rats. *Nature, Lond.*, **192**, 533–535.

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.

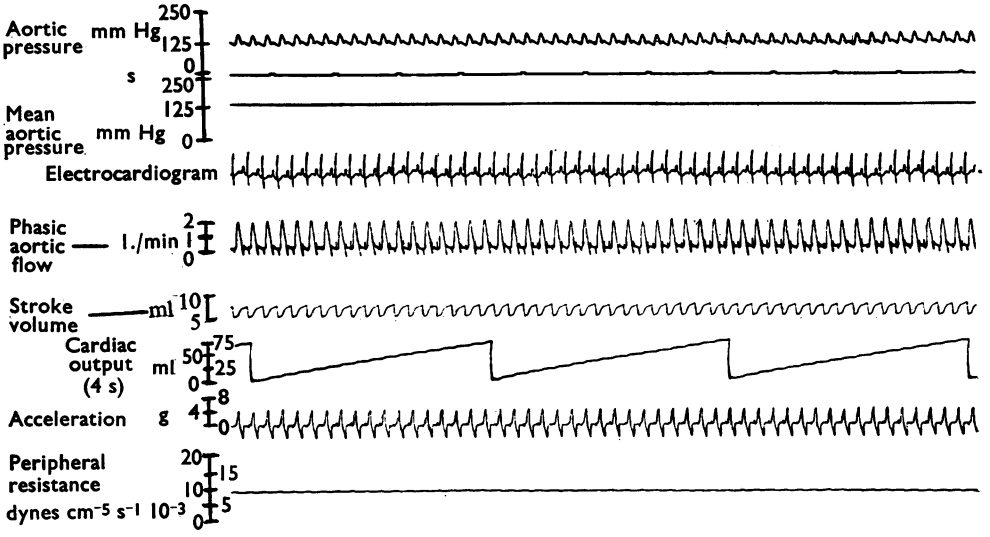

FIG. 1. Recording from a dog anaesthetized with chloralose.

Peripheral vascular resistance (excluding coronary circulation). Mean aortic pressure and mean aortic flow were derived by passing the respective pulsatile signals through a " leaky " integrating operational amplifier. Resistance was computed by dividing pressure by flow using a " multiplier-divider " (Philbrick/Nexus Research). The system was calibrated by calculating peripheral resistance for various values of pressure and flow (Kaneko, Page & McCubbin, 1964); the relationship between resistance and pen deflection (V/cm) was linear.

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REFERENCES

HUGHES, R. (1967). Continuous recording of aortic pressure and coronary flow in unanaesthetized dogs. *J. Physiol., Lond.*, **188**, 16–17*P*.

KANEKO, Y., PAGE, I. H. & MCCUBBIN, J. W. (1964). Haemodynamic studies in normotensive and renal hypertensive chronic spinal dogs. *Am. J. Physiol.*, **206**, 562–566.

KOLIN, A. & KADO, R. T. (1959). Miniaturization of the electromagnetic blood flowmeter and its use for the recording of circulatory responses of conscious animals to sensory stimuli. *Proc. natn. Acad. Sci. U.S.A.*, **45**, 1312–1321

NOBLE, M. I. M., TRENCHARD, D. & GUZ, A. (1966). Left ventricular ejection in conscious dogs: 1. Measurement and significance of the maximum acceleration of blood from the left ventricle. *Circulation Res.*, **19**, 139–147.

The response of stimulated and quiescent phrenic nerve diaphragm preparations to digoxin and ouabain

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The action of cardiac glycosides on the heart appears to involve inhibition of an adenosine triphosphatase and of active sodium transport. However, these effects are widespread and are not confined to cardiac muscle; the membrane adenosine triphosphatase of the heart is not particularly sensitive to the glycosides, and the glycosides are not particularly concentrated in heart muscle. The question arises,