In the present study, the order of potency of isoprenaline, adrenaline, phenylephrine and salbutamol relative to noradrenaline (1·00) was determined. The method of tissue preparation and recording was that of Coupar & Turner (1969), with the exception that thymoxamine (2 μg/ml.) was substituted for propranolol in the Krebs solution to block the α-adrenoceptive receptors.

The results are shown in Table 1. In all tissues studied the response to β-receptor stimulation was relaxation. This included oesophagus, in which α-receptor activity is excitatory (Coupar & Turner, 1969). In ileum, colon and rectum, the orders of potency in longitudinal compared with circular muscle strips suggest a difference in the number of β-receptors in these tissues. The concentrations of adrenaline required to stimulate β-receptors were greater than those to activate α-receptors. The potency of salbutamol relative to isoprenaline was markedly greater on bronchus than on the other tissues studied.

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A technique for the continuous micro-infusion of chemicals into discrete parts of the brain in unrestrained rats

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The effects of potential transmitter substances on brain function have been studied by their direct application in solution to individual neuro-structures (Miller, 1965). To obtain selective effects the volume of chemical so introduced must be small in relation to the target area. Single micro-injections have been used for this purpose, but the quantity of chemical injected may be reduced rapidly by diffusion or enzymic destruction. To obviate this, a technique has been developed whereby micro-volumes of sterile chemicals may be continuously infused into discrete parts of the brain in unrestrained rats.

A flow-rate of less than 1 μl./hr can be achieved using a Delta micro-metering pump (Drive assembly type D/K48H; Watson-Marlow Ltd., Marlow, Bucks). The chemical solution is pumped through a Swinney Adaptor (Millipore) fitted with a " Millipore " filter (pore size 0·45 μ) and via narrow bore polythene tubing (PP10; Portex Plastics Ltd., Hythe, Kent) to a specially designed unilateral cannula (Fig. 1).

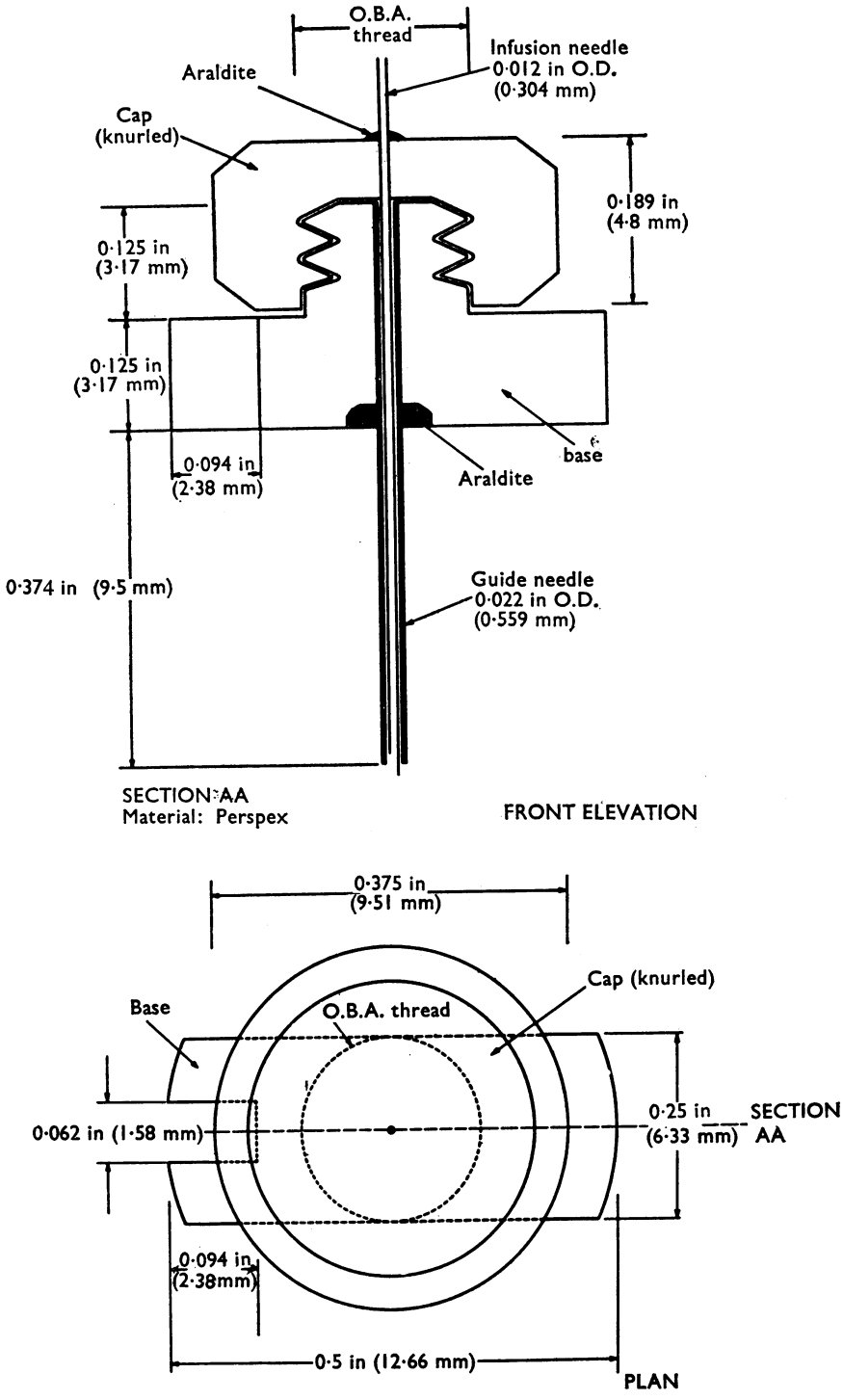

FIG. 1. A unilateral cannula for the continuous micro-infusion of solutions into the lateral hypothalamus of the rat. (Stainless steel cannulae needles were obtained from Cooper's Needle Works (Redditch) Ltd., Birmingham 20.) Experience has shown that it is better if the guide needle has an outside diameter of 0·026 in (0·660 mm).

Before each experiment, the infusion needle is sprayed with a thin coating of polytetrafluoroethylene dry lubricant (No. 889 RB; DCMC Industrial Aerosols Ltd., London, W.2) to hinder seepage of solution along the inside of the guide needle.

The technique is demonstrated by the continuous micro-infusion of noradrenaline (infusion rate 2·5 μg/μl. per hr) into the lateral hypothalamus of rat (A 5·4; L 1·8; H −2·7, De Groot, 1963) which elicits hyperphagia. It is hoped that this technique for continuous micro-infusion will be applicable bilaterally in a variety of animal species.

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Polarographic assay of monoamine oxidase

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Manometric (Davison, 1958), spectrophotometric (Weissbach, Smith, Daly, Witkop & Udenfriend, 1960), fluorimetric (Lovenberg, Levine & Sjoerdsma, 1962) and radioactive tracer techniques (Wurtman & Axelrod, 1963) have all been applied to the determination of monoamine oxidase activity. During oxidative deamination of substrates by the enzyme the oxygen consumption may be determined polarographically, using an oxygen electrode. The principle of the method is to allow oxygen to diffuse across a Teflon membrane and oxidize a platinum electrode, which results in a change in potential between this and a silver : silver chloride reference electrode. In our experiments the electrode was situated in the bottom of a perspex reaction vessel and the potential developed was monitored on a suitable pen recorder.

Monoamine oxidase activity was measured at 30° C in rat liver homogenates and mitochondrial suspensions, buffered at pH 7·4 in the presence of EDTA. In some experiments KCN was added to reduce endogenous oxygen consumption.

The following order of activity was found using different substrates: tyramine$>$ 5-hydroxytryptamine$\geqslant$dopamine$>$noradrenaline. No increase in oxygen consumption was observed in the presence of dexamphetamine or histamine. Tranylcypromine blocked tyramine oxidation at low concentrations.

The advantages of this simple technique are that it provides a rapid assay of monoamine oxidase from a wide variety of tissues, and that initial velocities for kinetic studies may be easily determined over the first 2–3 min of the reaction. The equipment is readily assembled from apparatus normally available in the laboratory and the cost of the electrode is in the region of £30.

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