A simple and cheap method of screening glass microelectrodes

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The recording of fast intracellular potential changes during micro-iontophoretic studies is complicated by the attenuation of high frequency responses by the distributed capacitance between the recording electrode and the multibarrelled iontophoretic electrode assembly. This attenuation is particularly troublesome in coaxial electrodes of the type described by Sonnhof (1973). The problem can be overcome by the use of screened recording electrodes—the screen being driven from the input amplifier at unitary gain. Provided that the input amplifier has good HF characteristics, this method will also allow accurate measurement of cell membrane resistance by current pulses through the recording electrode (cf. Eide, 1968). An efficient method to screen electrodes was developed by Eide, Engberg & Sonnhof (see Sonnhof, 1973), but this necessitates access to expensive high vacuum equipment for 'sputtering' a thin layer of gold onto the micropipettes. Further the electrodes must be filled with electrolyte *after* this goldplating when their interior is no longer visible. To avoid these complications we have used the following procedure.

Single, *filled,* electrodes were coated to within 1 mm of the tip with graphite from an aerosol can (Graphit 33, Kontakt Chemie, Rastatt, W. Germany). The electrode was held in a clamp so that the tip dipped into 99% ethanol and then sprayed so that an even layer of graphite was deposited on the glass. The coated electrode was then inserted into the central canal of the iontophoretic assembly, where it was surrounded with a small amount of saline. The graphite screen *or* the saline was connected to a unitary gain output of the amplifier output via a 100 nF capacitor.

The present technique has proved to be quite comparable to the gold screening in conjunction with coaxial multibarrel electrodes (for illustration see Figure 1 of the communication by Engberg, Flatman & Lambert, 1975, this meeting). Graphite screening can also be used to neutralize the capacitance of single electrodes in other types of recording, if the screen is insulated by a thin layer of lacquer covering the part that enters the tissue or conducting fluid.

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Combined EEG recording and intraventricular administration of drugs in the conscious rat

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This technique, a modification of that described previously by Hill & Miller (1973) for use in the rabbit, allows the combination of EEG recording and intraventricular administration of drugs in the conscious rat.

EEG activity is recorded from a 4-pin miniature electrical connector (ITT Cannon, Basingstoke) linked to stainless steel screws inserted in the skull. The small dimensions of the connector (1.5 mm x 6 mm x 9 mm high) and especially the narrow width are of considerable advantage for use on the rat skull.

The intraventricular cannula was modified from that described by Hayden, Johnson & Maickel (1966). It was prepared from 3 mm diameter Perspex rod, the small diameter being of advantage for combination with the electrical connector.

The technique may also be combined with behavioural activity recording using ultrasonic transducers as described by Hill & Miller (1973).

The implantation of the connector, cannula and screws was performed under halothane anaesthesia. Rats prepared by this method have shown no abnormal behaviour and have provided satisfactory EEG recordings over several months.

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A centrally-acting antihypertensive agent R28935, a pimozide analogue, not acting via α-adrenergic neurones

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Clonidine and α-methyldopa (Schmitt, Schmitt & Fenard, 1973; Finch, 1974; Finch & Haeusler, 1973a; Van Zwieten, 1975) are known to exert their antihypertensive action via stimulation of central α-adrenoceptors. However, the role of dopaminergic neurones in the central regulation of blood pressure remains unclear, since the potent dopamine agonist apomorphine lowers blood pressure with an accompanying bradycardia in both the anaesthetized cat and rat (Barnett & Fiore, 1971; Finch & Haeusler, 1973b), whilst dopamine administered intraventricularly in the conscious cat has been reported to exert a hypertensive action (Day & Roach, 1974).

Erythro-1-{1-[2-(1,4-benzodioxan-2-yl)-2-OH-ET]-4-piperidyl}-2-benzimidazolinone (R.28935), structurally related to the neuroleptic pimozide (Wellens, Van Neuten & Janssen, 1975) when administered intraventricularly (i.c.v.) lowered blood pressure in conscious renal hypertensive cats for a period of 5 h without altering the resting heart rate. Pretreatment with α-adrenoceptor blocking agents phentolamine (200 μg, i.c.v.) or tolazoline (200 μg, i.c.v.) failed to modify the hypotensive action of R.28935 (25 μg, i.c.v.). Similar pretreatments with tolazoline and phentolamine completely abolished the hypotensive effects of α-methyldopa (1 mg, i.c.v.) or clonidine (20 μg, i.c.v.) respectively.

Peripheral administration of haloperidol (1-5 mg/kg i.p.) and pimozide (1-2 mg/kg i.p. or 100-200 μg, i.c.v.) produced a dose-dependent fall in blood pressure and associated bradycardia which was also accompanied by stereotyped behaviour. However, administration of R.28935 (0.05-0.1 mg/kg i.p.) produced a dose-dependent fall in blood pressure without any accompanying bradycardia and no behavioural changes were detected.

In the Krebs-perfused mesenteric artery preparation, R.28935, in doses of 0.1-5 mg, did not exert any vasoconstrictor action whilst clonidine (0.1-1 mg) exhibited a dose-dependent vasoconstrictor effect. Infusions of R.28935 (0.1-10 mg) exhibited a dose-dependent vasoconstrictor actions of noradrenaline, 5-hydroxytryptamine or ATP. The vasoconstrictor action of clonidine was completely abolished by infusions of phentolamine (0.5 mg/l).

From the results it is concluded that R.28935 is a novel centrally-acting antihypertensive agent not acting via central α-adrenoceptors and is devoid of peripheral sympathomimetic properties. Similar observations have been reported in studies using the anaesthetized cat, dog and rabbit ear artery preparations (Van Zwieten, 1975; Wellens, Van Neuten & Janssen, 1975).

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