A technique allowing e.e.g. and activity recording together with intraventricular administration of drugs in the conscious rabbit

R. G. HILL and A. A. MILLER

Pharmacology Laboratory, The Wellcome Research Laboratories, Beckenham, Kent BR3 3BS

This technique allows simultaneous e.e.g. and behavioural activity recording in the conscious rabbit and facilitates intraventricular administration of drugs.

1. The e.e.g. potentials are picked up by stainless steel screws inserted in the skull and are led via a multi-channel miniature electrical connector (ITT Cannon, Basingstoke) to the recorder.

2. The intraventricular cannula described by Hayden, Johnson & Maickel (1966) for use in the rat proved equally suitable for the rabbit. Constructed of Perspex, its lighter weight compared with that of commercially available cannulae is advantageous. Confirmation of the implantation site (lateral ventricle) and the patency of the cannula after implantation was readily determined by withdrawing cerebrospinal fluid into a sterile Hamilton syringe (10 μl, 701 RN).

3. Behavioural activity was recorded simultaneously with the e.e.g. recordings on a polygraph by means of an ultrasonic Activity Monitor (C. F. Palmer, High Wycombe, Bucks.). The ultrasonic transducers were mounted vertically above the box in which the animal was placed.

The screws, connector and cannula were attached during halothane anaesthesia using standard aseptic techniques. After recovery animals prepared in this way have shown no overt deviation from normal behaviour and have remained healthy giving good e.e.g. records for up to a year.

REFERENCE

HAYDEN, J. F., JOHNSON, L. R. & MAICKEL, R. P. (1966). Construction and implantation of a permanent cannula for making injections into the lateral ventricle of the rat brain. *Life Sciences*, **5**, 1509–1515.

Microiontophoretic study of depressant amino acids and the specificity of their antagonists

R. G. HILL, M. A. SIMMONDS and D. W. STRAUGHAN

Department of Pharmacology, The School of Pharmacy, 29/39 Brunswick Square, London WC1N 1AX

Attempts to examine the specificity of convulsants, applied microiontophoretically, as GABA antagonists in the cerebral cortex have been limited by the absence of an effective control agonist (see Hill, Simmonds & Straughan, 1972). It seemed worthwhile, therefore, to find an alternative brain area in which to continue our investigations. The cuneate nucleus would seem to be the area of choice since cuneate neurones are readily sensitive to both GABA and glycine (Galindo, Krnjević & Schwartz, 1967). Further, this nucleus is easily accessible, no surgical removal of the cerebellum being required (cf. other brain stem sites) and no special supports are needed for the animal (cf. spinal cord sites).

All cats are anaesthetized with halothane in N_2O/O_2 for the duration of the experiment. A midline incision down to the nape of the neck is continued through the cervical musculature, which is then reflected to reveal the atlanto-occipital membrane. The membrane is removed and the bone overlying the cerebellum chipped back until the cerebellar vermis is revealed. A specially designed pressor foot is inserted through this opening and serves to prevent respiratory pulsations, which can be a great problem when working in brain stem areas.

Conventional seven-barrelled micro-pipettes are inserted through holes in the pressor foot 2 to 3 mm caudal to the obex, and escape of C.S.F. through these holes helps to keep the brain moist and warm. Extracellular action potentials are recorded whilst GABA, glycine and various antagonists are applied to single neurones (see Hill, Simmonds & Straughan, 1972), and stable recording conditions are maintained for two or three hours without difficulty.

Only spontaneously firing neurones are used, in order to avoid the type of over excitation produced by a combination of picrotoxin and glutamate described by Galindo (1969). As neurones are not physiologically identified it is possible that they are not exclusively in the cuneate nucleus. However, the pharmacological picture of sensitivity to GABA, glycine and the various antagonists is consistent throughout the population studied.

The preparation and on-line analysis of action potential data will be demonstrated.

This work is supported by the M.R.C. and by the Wellcome Trust via grants to D. W. S. R. G. H. is a Wellcome Research Student.

REFERENCES

GALINDO, A. (1969). Gaba-picrotoxin interaction in the mammalian central nervous system. *Brain Res.* **14**, 763–767.

GALINDO, A., KRNJEVIĆ, K. & SCHWARTZ, S. (1967). Microiontophoretic studies on neurones in the cuneate nucleus. *J. Physiol., Lond.*, **192**, 359–378.

HILL, R. G., SIMMONDS, M. A. & STRAUGHAN, D. W. (1972). Antagonism of GABA by picrotoxin in the feline cerebral cortex. *Br. J. Pharmac.*, **44**, 807–809.

Pharmacology of the neuronal excitation and inhibition induced by an acute seizure focus in feline cortex

G. CLARKE, R. G. HILL and D. W. STRAUGHAN

Department of Pharmacology, The School of Pharmacy, 29/39 Brunswick Square, London WC1N 1AX

When sodium benzyl penicillin is applied topically to the cerebral cortex, it produces an acute seizure focus characterized by large amplitude spikes and waves in the electrocorticogram (E.Co.G.) and accompanied by paroxysmal activity of single neurones (Matsumoto & Ajmone-Marsan, 1964; Clarke & Hill, 1972). Microinjection of a concentrated penicillin solution into the grey matter produces a more discrete focus so unit activity in and around the area can be mapped with precision (Clarke, Hill & Straughan, 1972). Some features of this preparation are demonstrated.

A sharp E.Co.G. spike with a total duration of 20 to 50 ms is recorded from the focus via the microinjection cannula. This spike is used to trigger a small computer and also the sweep of a storage oscilloscope, so that unit activity time-locked to paroxysmal events in the focus can be studied. Neurones in the immediate vicinity of the focus and also in homotopic areas of the opposite hemisphere have been examined using standard microelectrophoretic techniques and extracellular recording. A typical response shows a burst of action potentials (about 20 ms in duration) synchronous with the E.Co.G. spike, followed by a period of inhibition (lasting about 200 ms) before the firing pattern returns to normal. Thus, in addition to providing a model of epileptiform events, this preparation provides an effective endogenous excitatory and inhibitory input to cortical neurones.

Although the focally evoked burst of action potentials looks similar in all areas, there are pharmacological differences. Thus, within a radius of about 2 mm of the microinjection, the firing is resistant to GABA, whereas evoked firing in more distant areas is readily depressed by GABA in characteristic fashion. The inhibitory pause, best seen relatively distant to the microinjection, looks similar to the inhibition induced by electrical stimulation of the cortex. However, only the latter inhibition is reduced