1 to 2 h during which time it usually developed spontaneous activity. In some experiments it was stimulated orthodromically with a bipolar electrode inserted into the intraventricular musculature using pulses of 0.5 ms duration and up to 5 V amplitude at source, delivered from a Grass S8 stimulator.

The Purkinjé fibres were impaled with glass floating microelectrodes containing 3 M KCl (resistances between 10 and 30 megohms) and the electrical activity amplified with either a W.P.M. 4 electrometer probe or a Mentor N950 intracellular probe system. The action potentials were displayed on an oscilloscope and recorded simultaneously on a Grass Model 7 Polygraph, a Mingograph spray pen galvanometer and a tape recorder.

Ketamine hydrochloride altered the transmembrane potentials in a dose-related and reversible manner. Concentrations of 1×10^{-5} M were subthreshold whereas 5×10^{-5} M and 1×10^{-4} M slowed the frequency and increased the action potential duration of spontaneous preparations, actions consistent with an antiarrhythmic effect. Higher concentrations of 5×10^{-4} M ketamine initially led to a shortening of the action potential duration then failure of the original spontaneous activity. During recovery pacemaker-like activity developed associated with a loss of resting membrane potential. In electrically-driven preparations 5×10^{-4} M ketamine significantly shortened the duration of the action potentials, allowed the appearance of spontaneous potentials between evoked potentials and markedly augmented the response to adrenaline, actions consistent with an arrhythmogenic effect. These findings suggest a basis for isolated reports of cardiac side effects and interactions (e.g. Koplan & Cooperman, 1971) and as the concentrations administered in clinical practice are higher than those employed in the present experiments, cardiac side effects should not be unexpected.

This study was supported by grants-in-aid to J.T.H. from the Medical Research Council of Canada (Term Grant MT1216) and from the Ontario Heart Foundation.

References

DOWDY, E.G. & KAYA, D. (1968). Studies of the mechanism of cardiovascular responses to C1581. *Anesthesiology*, 29, 931-943.

GOLDBERG, A.H., KEANE, P.W. & PHEAR, W.P.C. (1970). Effects of ketamine on contractile performance and excitability of isolated heart muscle. *J. Pharmacol. Exp. Ther.*, 175, 388-394.

KOPLAN, J.A. & COOPERMAN, L.H. (1971). Alarming reactions to ketamine in patients taking thyroid medication–treatment with propranolol. *Anethesiology*, 35, 229-230.

HAMILTON, J.T., JONES, T.R., KIRALY, S.J. & PARKER, J.M. (1972). Some observations of the action of ketamine (C1581) on the neuromuscular junction *in vitro*. *Arch. Anaes. and Resusc.*, 2, 75-84.

TRABER, D.L., WILSON, R.D. & PRIANO, L.L. (1968). Differentiation of the cardiovascular effects of C1581. *Anesth. and Analg.*, 47, 769-777.

Some observations on electrically-inexcitable cells (neuroglia?) in rat sympathetic ganglia

P.R. ADAMS & D. A. BROWN*

Department of Pharmacology, St Bartholomew's Hospital Medical College, Charterhouse Square, London, E.C.1 & Department of Pharmacology, The School of Pharmacy, University of London, 29/39 Brunswick Square, London, WC1N 1AX

During the course of some recent experiments using intracellular recording methods in isolated rat superior cervical ganglia (Adams & Brown, 1973) we frequently impaled cells which had high initial membrane potentials (80-90 mV) but low input resistances (<5 MΩ) and which responded passively to depolarizing current pulses. These resemble the 'inexcitable' cells in guinea-pig sympathetic chain ganglia described by Blackman, Crowcroft, Devine, Holman & Yonemura (1969) and by Blackman & Purves (1969), and tentatively identified by them as capsular (oligodendroglial) cells. In our experiments the frequency with which these cells were impaled was quite high (several times in each experiment), but their resting potential usually discharged rather rapidly. However, on a few occasions the membrane potential was sustained at a reasonably elevated level (50-75 mV) for sufficient time to note some of their properties. The experimental methods used have been described previously (Adams & Brown, 1973).

No action potential could be elicited in these cells either by (i) direct stimulation using depolarizing current passed through the recording microelectrode or (ii) orthodromic stimulation of the preganglionic trunk using parameters sufficient to elicit a synaptically-mediated response of normal ganglion neurones. However, single orthodromic

stimuli regularly produced small (<1 mV) depolarizations of the cells lasting much longer than a synaptic potential (1-5 s). With repetitive orthodromic stimulation at quite low frequencies (2-8 Hz) these depolarizations summed to give a steady depolarization of 3-10 mV, declining slowly after cessation of stimulation with a half-time of 5-20 s. Such responses were not seen after withdrawing the electrode.

The membrane potential was reduced in a repeatable manner by raising the K^+ concentration of the perfusing solution. Within the range 6-24 mM $[K^+]$ the membrane potential appeared to be a linear function of log $[K^+]_{out}$, with a slope of 47 mV per log unit.

Neither GABA (100 μM) nor carbachol (180 μM) altered the membrane potential: both depolarize ganglion neurones (Adams & Brown, 1973).

The properties of these cells appear to resemble those previously described for glial cells (see Kuffler & Nicholls, 1966; Lasansky, 1971), but differ from the 'unresponsive cells' of the cerebral cortex described by Krnjevic & Schwarz (1967) in their lower input resistance and failure to respond to cholinomimetic stimulation or to GABA.

Glial cells in sympathetic ganglia can accumulate exogenous γ-amino-butyric acid (GABA) (Young, Brown, Kelly & Schon, 1973); this may be released again by raising $[K^+]$ or by electrical stimulation (Bowery & Brown, 1972). The present observations might be relevant to the mechanism of this release and to possible interactions of neurones and glia.

This work was supported by a grant from the Medical Research Council.

References

ADAMS, P.R. & BROWN, D.A. (1973). Actions of γ-aminobutyric acid (GABA) on rat sympathetic ganglion cells. *Br. J. Pharmac.*, 47, 639-640P.

BLACKMAN, J.G., CROWCROFT, P.J., DEVINE, C.E., HOLMAN, M.E. & YONEMURA, K. (1969). Transmission from preganglionic fibres in the hypogastric nerve to peripheral ganglia of male guinea-pigs. *J. Physiol.*, **201**, 723-743.

BLACKMAN, J.G. & PURVES, R.D. (1969). Intracellular recordings from ganglia of the thoracic sympathetic chain of the guinea-pig. *J. Physiol.*, **203**, 723-743.

BOWERY, N.G. & BROWN, D.A. (1972). γ-aminobutyric acid uptake by sympathetic ganglia. *Nature, New Biol.*, **238**, 89-91.

KRNJEVIC, K. & SCHWARZ, S. (1967). Some properties of unresponsive cells in the cerebral cortex. *Exper. Brain Res.*, 3, 306-319.

KUFFLER, S.W. & NICHOLLS, J.G. (1966). The physiology of neuroglial cells. *Ergebn. Physiol.*, 57, 1-90.

LASANSKY, A. (1971). Nervous function at the cellular level: glia. *Ann. Rev. Physiol.*, 33, 241-256.

YOUNG, J.A.C., BROWN, D.A., KELLY, J.S. & SCHON, F. (1973). Autoradiographic localization of sites of ^{3}H-γ-aminobutyric acid accumulation in peripheral autonomic ganglia. *Brain Res.*, 63, 479-486.

A comparison of the rate of onset of excitation and inhibition by decamethonium acting at frog endplate receptors

P.R. ADAMS
(introduced by D.A. BROWN)

Department of Pharmacology, St Bartholomew's Hospital Medical College, Charterhouse Square, London, E.C.1

del Castillo & Katz (1957) found that pulses of decamethonium (DECA) produced slower depolarizations when applied iontophoretically to endplate receptors than did acetylcholine or carbachol (CARB). They suggested that as DECA appeared to reach the receptors quickly (as judged by the slowing in rate of rise of a simultaneously elicited CARB response) this slow onset of depolarization might reflect slow activation of the DECA-receptor complex. Since these observations might have general implications for receptor theory, this problem has been re-examined, with particular attention to the rate of onset of antagonism by DECA of CARB responses.

The methods were similar to del Castillo & Katz (1957) except that triple-barrelled micropipettes were sometimes used, a saline-filled barrel then being available for control of electrical artefacts. The pipette was manipulated in the vicinity of an endplate region, during intracellular recording, until rapid CARB responses (<20 ms rise-time) were obtained. A short pulse to the DECA barrel then gave a slow depolarization (Figure 1). A long pulse (0.5-1.0 s) to the CARB barrel was then applied and DECA reapplied during the CARB depolarization (Figure 1). Since DECA is a partial agonist, it inhibited CARB, and the membrane hyperpolarized (del Castillo & Katz, 1957).

In 12 experiments the time to peak of the DECA excitation was 88 ± 9.6 ms (mean ± s.e.)