of spontaneous contractions. On the other hand beta-adrenoceptor blockade (propranolol), after alpha-adrenoceptor blockade (phentolamine) also reduced the size of contractions (5/5 rats). Phentolamine given after propranolol slightly increased contraction size but did not return it to normal (3/5 occasions).

In rats given progesterone (100 mg i.m.) 24 h before observation the responses to the antagonists were reversed, that is, phentolamine reduced the size of the contractions (8/9 rats). Propranolol given after phentolamine (8 observations) increased the amplitude of spontaneous contractions on one occasion; on 4/8 occasions there was only slight increase and in the other 3 rats no change or a further reduction in the size of the contractions. In rats pretreated with progesterone (100 mg i.m.) together with stilboestrol (5 mg i.m.) the results were similar to those obtained when progesterone alone was given.

Tetraethylammonium (2 mg) or hexamethonium (4 mg) given intravenously were previously reported, like alpha-adrenoceptor blockage, to increase the size of the contractions (Deis & Pickford, 1964). In the present series, (15 observations) combined alpha- and beta-adrenoceptor blockade generally decreased the size of contractions. When a ganglion blocking agent was given after phentolamine and propranolol, there was a tendency to an increase in the size of spontaneous contractions.

The effects of combined alpha- and beta-adrenoceptor blockade on the amplitude of spontaneous uterine contractions are not the same as those of ganglion blockade. The reason for the difference remains to be determined.

Reference

DEIS, R.P. & PICKFORD, MARY (1964). The effect of autonomic blocking agents on uterine contractions of the rat and the guinea-pig. *J. Physiol.* (*Lond.*), **173**, 215–225.

Characterisation of acid secretory responses of the rat isolated gastric mucosa to electrical field stimulation

A.W. BAIRD & I.H.M. MAIN

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

The rat isolated gastric mucosa (Main & Pearce, 1978a) has been used to study the effects of drugs on acid secretion in the absence of circulating hormones or extrinsic nerves. The present objective was to investigate the effect of electrical field stimulation on this preparation.

Paired mucosal preparations from rats weighing 80–100 g were mounted in organ baths containing buffered serosal solution (Main & Pearce, 1978a). Unbuffered solution superfused the mucosal surface at 0.5 ml/min then passed to a vessel in which it was titrated continuously to pH 7. Field stimulation was applied via platinum ring electrodes (ring diameter 7.5 mm) placed above and below the mucosa (diameter 11.2 mm). Voltage was monitored on an oscilloscope. In six experiments on unpaired preparations, stimulation at 2 V, 10 Hz, 1 ms for 10 min caused an increase in acid output of 0.94 ± 0.21 μmol (mean ± s.e. mean, results expressed as increase over extrapolated basal output). The second and third responses, obtained at 90 min intervals, were 1.03 ± 0.23 and 0.64 ± 0.18 μmol respectively. Subsequent stimuli gave progressively smaller responses. Secretion increased within 5 min and reached a peak at approximately 15 minutes. During prolonged periods of stimulation, responses were poorly maintained. Voltages greater than 5 V caused changes in acid output which were partly dependent on the polarity of the electrodes. Stimulus frequencies of between 1 and 10 Hz gave graded responses.

The secretory response to electrical stimulation was abolished by tetrodotoxin (10^{-6} M) which did not block histamine (5×10^{-5} M) and by atropine (3×10^{-6} M) which blocked methacholine (5×10^{-7} M) but not histamine. It was potentiated by eserine (3×10^{-5} M). The response was abolished by Ca^{2+}-free solutions and recovered on restoring Ca^{2+} to 0.9 or 3.6 mM, whereas the effects of pentagastrin and histamine are not inhibited by Ca^{2+}-free solutions (Main & Pearce, 1978b). In contrast to its inhibitory effect on the field-stimulated mouse isolated whole stomach (Angus & Black, 1978), hexamethonium (2.6×10^{-4} M) had no effect on the rat mucosa. When added to one mucosal preparation from each pair 60 min prior to the second period of stimulation, the second response expressed as a percentage of the first, was $52.7 \pm 10.1\%$ and $55.5 \pm 21.8\%$ ($n = 6$) for control and hexamethonium-treated groups respectively. Metiamide (10^{-5} M), which partly inhibits gastrin but not methacholine in this preparation (Main & Pearce, 1978c), had no significant effect on electrical stimulation (control $89.5 \pm 7.2\%$, metiamide $83.4 \pm 11.7\%$, $n = 6$).

These results demonstrate that the rat isolated gastric mucosa secretes acid in response to electrical field stimulation. The effect is mediated by postganglionic cholinergic nerves which do not require mucosal histamine for their action.

This work was supported in part by an MRC grant to IHMM. We are grateful to Dr M.E. Parsons of Smith, Kline and French Ltd. for the metiamide.

References

ANGUS, J.A. & BLACK, J.W. (1978). Production of acid secretion in the mouse isolated stomach by electrical field stimulation. *Br. J. Pharmac.*, **62**, 460P.

MAIN, I.H.M. & PEARCE, J.B. (1978a). A rat isolated gastric mucosal preparation for studying the pharmacology of gastric secretion and the synthesis of release of endogenous substances. *J. Pharmacological Methods*, **1**, 27–38.

MAIN, I.H.M. & PEARCE, J.B. (1978b). Effect of calcium on acid secretion from the isolated rat gastric mucosa during stimulation with histamine, pentagastrin, methacholine and dibutyryl cyclic adenosine-3′,5′-monophosphate. *Br. J. Pharmac.* (in press).

MAIN, I.H.M. & PEARCE, J.B. (1978c). Gastrin, histamine, dibutyryl cyclic AMP and calcium on acid secretion from the rat isolated gastric mucosa. Abstract submitted to the Seventh Int. Congr. of Pharmacology, Paris (July, 1978).

Motor output to flight muscles and inhibition of acetylcholinesterase after injection of dimethoate into locusts

G.A. BUCKLEY, D.H. GODDEN & S.K. PARRISH

Department of Life Sciences, Trent Polytechnic, Nottingham

Smallman & Fisher (1958) showed that inhibition of acetylcholinesterase (AChE) by organophosphorous insecticides increases the acetylcholine content of the insect central nervous system, the rate of increase depending on the degree and duration of AChE inhibition. In this study we have attempted to correlate inhibition of AChE with an example of stereotyped behaviour, the motor output to the flight muscles in the locust (*Schistocerca gregaria*).

Adult locusts were tethered and 50 μm diameter copper wire electrodes inserted into the flight muscles. The locusts were flown in a heated (28°C) airstream and the motor output to the flight muscles monitored (Wilson & Weis-Fogh, 1962) through a transient recorder onto a chart recorder. After an initial five minute control period the animal was injected with a dose of dimethoate, in 20 μl of locust saline, into the terminal abdomen and flown for a further twenty-five minutes. After this time the thoracic ganglia were removed for homogenisation in 0.2 M phosphate buffer (pH 7.4) followed by assay of AChE by the method of Ellman, Courtney, Andres & Featherstone (1961). The interburst intervals (and therefore the wingbeat period) were measured for one second each minute for the control period and one second in each two minutes after injection of the drug or locust saline. The time course of inhibition of AChE was also determined in flying locusts injected with the largest dose of dimethoate (250 μg).

The results (Figure 1) suggest that there is a relationship between inhibition of AChE and change in interburst interval with a threshold for effect at approximately 40% inhibition. This same relationship is found whether the different levels of AChE activity are produced by different doses of dimethoate or by taking locusts at different times after injection of dimethoate (250 μg). These observations are similar to the effects of malathion on levels of cyclic GMP in the central nervous system of the flesh fly (Bodnaryk, 1977).

References

BODNARYK, R.P. (1977). Correlation between organophosphate poisoning, acetylcholinesterase inhibition, and increased cyclic GMP levels in malathion-treated insects. *Can. J. Bioch. Physiol.*, **55**, 534–542.

ELLMAN, G., COURTNEY, K.L., ANDRES, V. & FEATHERSTONE, R.M. (1961). A new and rapid colorimetric determination of acetylcholinesterase activity. *Biochem. Pharmacol.*, **1**, 88–95.

SMALLMAN, B.N. & FISHER, R.W. (1958). Effect of anticholinesterases on acetylcholine levels in insects. *Can. J. Bioch. Physiol.*, **36**, 575–586.

WILSON, D.M. & WEIS-FOGH, T. (1962). Patterned activity of co-ordinated motor units, studied in flying locusts. *J. Exp. Biol.*, **39**, 643–667.