were poorly sustained and a transient post-tetanic facilitation of the twitch response was observed. As with other competitive neuromuscular blocking agents the blockade induced by AH 8165 was reversed by neostigmine, 0·1 mg/kg i.v. In further experiments in which the tibialis muscle was stimulated directly, AH 8165 had no effect on these responses at doses far in excess of those which caused neuromuscular blockade.

Fully effective neuromuscular blocking doses of AH 8165 did not affect the blood pressure, heart rate or the E.C.G. However, at very high doses, 2–5 mg/kg, falls in blood pressure (5–50 mmHg) occurred sometimes accompanied by slight increases in heart rate (5–25 beats/min). Further analysis of these blood pressure effects showed that they were not due to histamine release but resulted from ganglion blocking activity.

In the anaesthetized dog and monkey AH 8165, 0·05–0·4 mg/kg i.v., caused short lasting, competitive neuromuscular blockade but the duration of action in the monkey was slightly longer (1·5 ×) than that seen in the cat or dog. In all the species examined AH 8165 possessed competitive neuromuscular blocking activity, and the compound had a quicker onset and a shorter duration of action than (+)-tubocurarine, gallamine or pancuronium. AH 8165 has potential as a muscle relaxant in surgery and, perhaps, in electroconvulsive therapy; clinical trials are in progress.

The effects of procaine, amylobarbitone on drug induced changes in the surface potentials of an isolated sympathetic ganglion

O. A. DOWNING (introduced by M. D. DAY)

Pharmacological Laboratories, Department of Pharmacy, The University of Aston in Birmingham, Gosta Green, Birmingham B4 7ET

Procaine and amylobarbitone are examples of drugs which have moderately selective depressant actions on autonomic ganglia and on nerve-skeletal muscle preparations. Because of technical difficulties it has not been possible to define their mode of action on the ganglion cells as thoroughly as has been achieved for these and other compounds on the skeletal muscle receptors.

In the present study a number of drugs have been studied for their effects on dose-response curves of depolarization to carbachol on the isolated superior cervical ganglion of the rat; the method being similar to that employed for an isolated skeletal muscle preparation by Nicholls & Quilliam (1956) and Payton (1966). The drugs were also compared for their effect on the rate of recovery of the ganglion from nicotine evoked depolarization, following the removal of nicotine from the bath.

Isolated de-sheathed superior cervical ganglia were obtained from Wistar strain rats (ca.200 g) anaesthetized with 25% urethane I.P. The ganglia were suspended in Krebs solution at room temperature (19·0–24·5° C) and changes in the surface potentials were measured by means of the moving-fluid-electrode technique as described by Brown (1966).

The ganglion blocking agents hexamethonium ($4{\cdot}5\times^{-4}$M), tetra-ethylammonium ($1{\cdot}5\times10^{-3}$M), and pempidine ($5{\cdot}3\times10^{-5}$M) in concentrations which just abolished transmission, caused a parallel shift to the right of the dose response curves of depolarization for carbachol, with some variable degree of depression of the maximum depolarization.

Procaine ($1{\cdot}5\times10^{-4}$M) and amylobarbitone ($6{\cdot}4\times10^{-4}$M) in concentrations which just abolished transmission did not produce any parallel shift of the dose response curves but depressed the mean maximum values of depolarization by 41·2% (n=3) and 65·4% (n=3) respectively.

The effect of amylobarbitone and procaine on the time course of the surface potentials after washing out carbachol were different, so the effect of the drugs were studied on the time course of the potentials following the removal of nicotine ($3{\cdot}2\times10^{-5}$M) from the bath since this is slow (Brown, 1966).

All the ganglion blocking agents tested increased the rate of recovery to isopotential when added to the bath immediately following the removal of nicotine. Procaine had a similar action but amylobarbitone had no effect even with concentrations of up to $2{\cdot}6\times10^{-3}$M which had a pronounced depressant effect on pre-ganglionic action potentials.

Procaine and barbiturates are considered to have similar actions on membrane conductance changes associated with the action potential in the nerve axon (Blaustein, 1968).

It is concluded that the different effects of procaine and amylobarbitone on the rate of recovery of the ganglion from the depolarizing effects of nicotine, may indicate that procaine has a selective component of action on the nicotinic receptor at this site, which amylobarbitone lacks.

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Depolarization of isolated rat ganglia by γ-aminobutyric acid and related compounds

N. G. BOWERY* and D. A. BROWN

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

Gamma-aminobutyric acid (GABA) depolarizes cat superior cervical ganglia *in vivo* (de Groat, 1970). This probably has no functional significance, since neither GABA nor glutamic decarboxylase are normally present in the ganglia (Nagata, Yokoi & Tsukada, 1966). However, we have recently found that isolated rat ganglia can accumulate exogenous GABA and that the GABA retained can be released again by some types of stimuli normally thought to release 'transmitter' GABA from isolated brain tissue (Bowery & Brown, 1971). This raised the possibility (yet unproven) that GABA might be introduced into the ganglion as an artificial transmitter or transmission-modulator, and has led us to examine further the depolarizing action of GABA on rat ganglia.

Isolated rat superior cervical ganglia were desheathed and maintained in Krebs solution at 25°C pre-equilibrated with 95% oxygen/5% carbon dioxide. Depolarization was recorded with a moving-fluid surface electrode (Pascoe, 1956). The ganglion was depolarized by GABA at concentrations of 10^{-6}M and upwards: maximal GABA-depolarization (at 10^{-4}M) was about one-quarter of that produced by carbachol.