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

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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.

Whereas carbachol-depolarization was sustained over several minutes, GABA-depolarization declined rapidly after the first few seconds in spite of the continued presence of GABA. Subsequent application of GABA then had no action, but carbachol remained effective.

GABA-like depolarization was produced by the following compounds (approximate molar potencies relative to GABA in brackets): 3-amino-propanesulphonic acid (3), γ-amino-β-hydroxybutyric acid (0·3), β-guanidino-propionic acid (0·06), guanidinoacetic acid (0·06), β-alanine (0·01), γ-aminovaleric acid (0·01) and taurine (0·001). 'Cross-desensitization' occurred between GABA and these compounds. Amino acids producing no detectable potential change at 10^{-2}M included glycine, ϵ-aminocaproic acid, D- and L-α-amino-*n*-butyric acid, α-amino-*iso*-butyric acid, and glutamic acid.

The effects of antagonists on matched responses to GABA and carbachol were compared. Hexamethonium did not affect responses to GABA in concentrations which completely antagonized carbachol. In contrast, bicuculline was 20 times more effective against GABA than against carbachol, and picrotoxin 2 times more effective.

Thus rat ganglion cells possess GABA-receptors which, in terms of specificity, resemble those in the mammalian central nervous system. From a practical viewpoint isolated ganglia may be more convenient for assessing the activity of GABA-analogues and antagonists since they seem devoid of receptors for short-chain amino acids like glycine. It is not yet clear why GABA depolarizes, rather than hyperpolarizes, the ganglion cells. A reverse (outward) movement of chloride is one possibility, since E_{Cl} may be more positive than E_m in ganglion cells (Woodward, Bianchi & Erulkar, 1969). This would explain the low-amplitude response and its rapid decline.

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Reversal learning facilitated by a single injection of lysergic acid diethylamide (LSD 25) in the rat

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The results of many animal experiments are consistent with the hypothesis, originally proposed by Bradley & Elkes (1957), that LSD 25 increases sensitivity to sensory stimuli. Reports from human subjects that LSD facilitates insight in problem-solving situations are consistent with this view. It seems likely, therefore, that LSD will facilitate learning in laboratory animals and experiments were carried out to test the effects of various doses of LSD on performance in a learning situation where rats were required to reverse a previously acquired brightness discrimination.