It is concluded that the increased excitability of amphibian cord following bicuculline may be dissociated from antagonism of the depressant effects of the inhibitory transmitters GABA and glycine.

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Action of γ-aminobutyric acid (GABA) on rat sympathetic ganglion cells

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Contrary to its usual hyperpolarizing action on central neurones, GABA depolarizes sympathetic ganglia (de Groat, 1970; Bowery & Brown, 1972). We have studied the mechanism of this action in isolated rat superior cervical ganglia using at room temperature conventional intracellular recording techniques.

All cells impaled responded to 100 μM GABA. This concentration produced a near maximal response. Higher concentrations produced rapid desensitization. Cells with recorded resting membrane potentials (E_m)>42 mV responded with depolarization, which could be reversed to hyperpolarization by passing steady depolarizing current. Cells with E_m<45 mV were usually hyperpolarized, which in turn could be reversed by hyperpolarizing currents. Cells hyperpolarized by GABA were depolarized by carbachol.

Both depolarization and hyperpolarization were accompanied (Fig. 1) by (i) failure of direct or orthodromic action potentials or a reduction of their positive overshoots, (ii) depression of the synaptic potential, and (iii) a large fall in the input resistance to hyperpolarizing current pulses.

The variation of potential change with E_m suggests a reversal potential for GABA action (E_{GABA}) of about −42 mV. A similar value was obtained from the intersection of extrapolated current-voltage curves for hyperpolarizing pulses measured at rest and

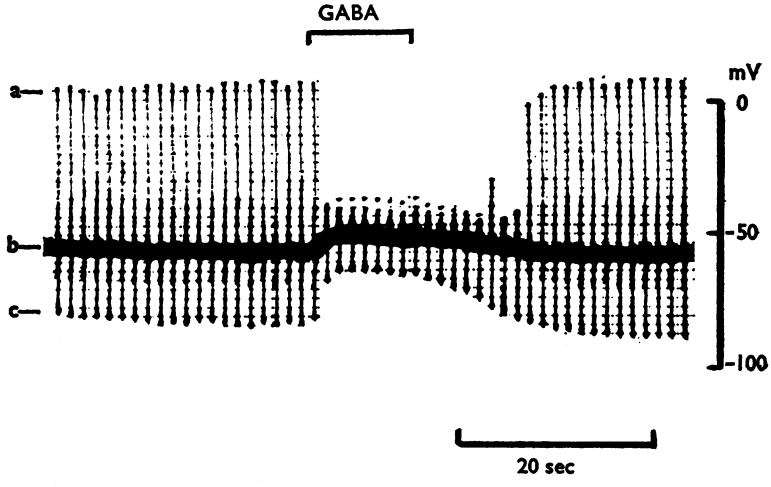

FIG. 1. Intracellular record from a neurone in an isolated rat superior cervical ganglion showing the effect of a 10 s application of GABA (100 μM) on (a) action potentials recorded in response to preganglionic nerve stimuli, (b) membrane potential, and (c) potential deflexions produced by applying hyperpolarizing current pulses (70 ms duration, 0·33 nA) 175 ms after each preganglionic nerve shock. During the exposure to GABA the orthodromic spike failed, leaving a synaptic potential; the membrane potential was reduced from −55 to −48 mV and the apparent input resistance reduced from 85 MΩ to 36 MΩ.

during GABA action. Thus, E_{GABA} seems close to the value for E_{Cl} (−42 mV) for ganglion cells calculated by Woodward, Bianchi & Erulkar (1969).

When external Cl^- was replaced with the impermeant anion isethionate, GABA depolarization was greatly enhanced (up to 50 mV) or hyperpolarization reversed to depolarization. Successive responses to GABA in isethionate solution waned rapidly, and were progressively restored on replacing Cl^-. This suggests that a brief application of GABA could produce a substantial net change in $[Cl^-]_i$ under these conditions.

We conclude that GABA increases Cl^- permeability in ganglion cells as in central neurones, and that ganglion depolarization occurs because $E_{Cl}<E_m$.

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Uptake of γ-aminobutyric acid (GABA) by sensory root ganglia

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Brain slices (Iversen & Neal, 1968), sympathetic ganglia (Bowery & Brown, 1972) and retinae (Neal & Iversen, 1972) accumulate GABA by a high affinity uptake system, and autoradiographic studies suggest that this uptake occurs into both neurones and glial cells. Despite the lack of nerve terminals, a similar uptake of GABA has now been found in rat and cat sensory root ganglia.

Cat and rat ganglia were desheathed and incubated in oxygenated Krebs solution containing ^{3}H-GABA (0·1 μM). The Km value for GABA uptake of approximately 25 μm was similar to that in brain slices. As in the superior cervical ganglion the uptake of ^{3}H-GABA continued over a 4 h period. Amino-oxyacetic acid (AOAA) (10^{-5}M) added to the incubation media appeared to facilitate this uptake and tissue:medium ratios of 95:1 were achieved. Enhanced uptake also occurred in ganglia from animals pretreated with AOAA (40 mg/kg). Sensitive assay procedures showed the tissue of the ganglia to contain 0·26 μ moles/g tissue of GABA and a glutamic acid decarbovylase activity of (0·45 μ moles/g tissue)/hour. Similar levels were found in the ventral and dorsal roots by us in rats and by others in the cat.

Light microscopic autoradiography was carried out on glutaraldehyde fixed cat and rat ganglia following incubation in 80 μCi/ml ^{3}H-GABA (40 μM). Autoradiographs developed after a 7-day exposure period showed an intense uptake localized exclusively over satellite glial cells. The neuronal cell bodies, the remnants of the connective tissue sheath and the myelinated fibres were devoid of labelling.

When ganglia were incubated with 80 μCi/ml of ^{3}H-alanine or ^{3}H-glycine (80 μM) a 5-week exposure was necessary to obtain a similar silver grain density to that seen with ^{3}H-GABA after a one-week exposure. In contrast to GABA, both these amino acids were localized in neurones as well as in satellite glial cells. The active uptake of GABA in the sensory root ganglion is thus specific to this amino acid and exclusively localized in satellite glial cells.

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