Depolarizing actions of γ-aminobutyric acid (GABA) on mammalian brain slices

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(introduced by D.A. BROWN)

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γ-Aminobutyric acid (GABA) depresses neuronal firing in the mammalian olfactory cortex (Legge, Randić & Straughan, 1966). In the present experiments, we have examined the action of GABA on prepyriform neurones in the guinea pig isolated olfactory cortex using intracellular and extracellular recording techniques.

Surface slices of olfactory cortex including the lateral olfactory tract (LOT) were cut at ~600 μm thickness. Intracellular recordings from single prepyriform neurones were made using a single resistance- and capacitance-balanced microelectrode filled with 4M K^+ acetate, as described by Scholfield (1976). For extracellular recording, slices were mounted at 45° to the vertical (cut surface downwards) on the agar base of a large Ag/AgCl reference electrode and continuously superfused on both sides with Krebs solution. A fine Ag/AgCl electrode was placed on the distal end of the LOT to record drug-evoked d.c. potential changes. Drugs were added to the superfusate in fixed concentrations and applied to the pial surface of the slice. All experiments were performed at ambient temperature.

Intracellular Recording. Neurones in the prepyriform cortex gave resting potentials of about 75 mV and resting input resistances of 20–200 MΩ. Addition of GABA (0.05–5mM) always produced a small, reversible depolarization. The amplitude of the depolarization (⩽20 mV) increased with GABA concentration but showed no clear maximum up to 5 mM. The depolarization was accompanied by a dose-related increase in membrane conductance. Responses appear to be mainly mediated by an increase in Cl^- conductance, since the depolarization was increased in low Cl^- solution. In spite of the depolarizing nature of GABA action, the increased membrane conductance inhibited direct spike generation.

Extracellular Recording. Superfusion with GABA (0.1–10 mM) produced a transient surface-negative potential change (surface depolarization). This response was dose dependent, approaching maximum at 10 mM (0.59 ± 0.03 mV; mean ± s.e. mean, $n = 54$). Depolarizations were quick in onset (< 1 min) and showed rapid fade during continued application. Receptors responsible for depolarization accorded with conventional GABA receptors as judged from agonist specificities and from the antagonist effects of picrotoxin and bicucilline.

Although the depolarization we observe in this preparation is contrary to the usual hyperpolarization reported in the central nervous system (see Krnjević, 1974), it does accord with studies on several other mammalian systems, (e.g. neurones in tissue culture: Obata, 1974; sensory ganglia: Deschenes, Feltz & Lamour, 1976; and sympathetic ganglia: Adams & Brown, 1975). Moreover, it should be emphasized that in our experiments, GABA still exerted an effective inhibitory action.

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