Preliminary investigation of a process of desensitization on mammalian presynaptic γ-aminobutyric (GABA) receptors

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There is reason to believe that presynaptic inhibition of primary afferent terminals is mediated by a chloride-dependent effect of GABA (Barker, Nicoll & Padjen, 1975; Davidson & Simpson, 1976; Gmelin, 1976; Obata, 1976). Since this action of GABA appears to be identical to that on the neurones of the sympathetic and dorsal root ganglion (Nishi, Minota & Karczmar, 1974; Feltz & Raminsky, 1974; Adams & Brown, 1975; Deschenes, Feltz & Lamour, 1976) we have recorded the changes in membrane potential and conductance evoked by GABA on single neurones of the rat dorsal root ganglion *in situ* (pentobarbitone anaesthesia, 40 mg/kg, i.p.) with double-barrelled, intracellular microelectrodes filled with K^+ acetate or sulphate.

Typically, the response of the ganglionic neurones to GABA was a biphasic depolarization. Brief applications of GABA resulted in a transient depolarization whose peak amplitude ($\leqslant$25 mV) and time to peak (2–5 ms) was dependent on the membrane potential (reversal level –40 mV) and the magnitude of the GABA application. The response to GABA was saturable and towards the end of the application the decaying depolarization was interrupted by a hump. When GABA (10^{-5} to 10^{-3} M) was added to the superfusate or the iontophoretic pulses of GABA (20–100 nA, 1 s duration) were repeated more often than 0.1 Hz or their duration extended to 10 s, the initial depolarization decayed to a plateau level, which was maintained at about one-third of the initial level for the remainder of the GABA application. K^+-sensitive electrodes showed these changes in potential to be accompanied by an increase in the extracellular K^+ concentration. During action potentials this increase in the extracellular K^+ was also apparent from a decrease in the amplitude of the hyperpolarizing after-potentials.

When the ganglion was superfused with GABA (10^{-4} to 10^{-3} M), the depolarizing responses to brief iontophoretic pulses of GABA applied at a distance of 30–80 μm from the soma during the plateau phase of the maintained depolarization, were reduced in amplitude. Since this loss in GABA sensitivity could not be restored by hyperpolarizing the membrane and was accompanied by a reduction in the increased Cl^- conductance normally associated with the response, the desensitization was not attributable to a change in equilibrium level of the ions involved.

With financial support of the D.G.R.S.T. (73–1125) and of the C.N.R.S. (ERA 237). M.D. was a Canadian MRC-CRSQ postdoctoral fellow: present address: Département de Physiologie, Faculté de Médecine, Université Laval, Quebec C1K 7DA Canada. B. R–D holds from the D.G.R.S.T. and I.A.M.O.V. training program fellowship.

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