Mechanism of action of angiotensin II on the membrane potential of rat myometrium

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Angiotensin II (Ang II) produces a contraction of visceral and vascular smooth muscle of different species (Worcel, Papadimitriou & Meyer, 1971). Since this spasmogenic action might be initiated by a change in cell membrane excitability we have attempted to study the effects of the peptide on rat myometrium membrane potential. Contraction and transmembrane potential were measured simultaneously by the double sucrose-gap method (Burnstock & Straub, 1958). Uterine strips were obtained from 220–250 g Wistar rats pretreated with diethylstilboestrol dipropionate (0.5 mg/kg) the day before the experiment. Smooth muscle strips of the longitudinal layer 3 cm long and 1 mm width were used. The solutions used were: (1) physiological solution (mmol): NaCl 120.8, KCl 5.9, $CaCl_2$ 2.5, $MgCl_2$ 1.2, $NaHCO_3$ 15.5, NaH_2PO_4 1.2, glucose 11.5, gassed with 95% O_2 and 5% CO_2 or with the same solution in which $NaHCO_3$ and NaH_2PO_4 are replaced by Tris Cl^- and gassed with 100% O_2. (2) KCl isotonic solution and (3) isotonic sucrose solution of a resistivity higher than 1 MΩ/cm. The experiments were performed at 35°C. Under these conditions Ang II at 10^{-7} M (Figure 1b) which already produces a maximal contraction (Worcel *et al.*, 1971) induced a depolarization and an increase in membrane conductance. This increase in membrane conductance is not potential dependent since it is observed even when the membrane potential is reset at the baselevel electrically. At a 10^{-6} M concentration which produces a supramaximal contraction, Ang II maximally depolarizes the preparations (Figure 1a). When all Na^+ in the test solution is replaced by either Li^+ or Mg^{2+} the depolarizing effect of 10^{-6} M Ang II disappears. Under these conditions Ang II produces a slight initial hyperpolarization. When all Cl^- is replaced by either NO_3- or cyclohexane-sulfamate Ang II 10^{-6} M still produces a 20 mV depolarisation. The suppression of extracellular Ca^{2+} or K^+ does not have any effect on the depolarizing action of Ang II, which is not changed either by ouabain 10^{-3} M.

In conclusion Ang II produces a depolarization of the uterine smooth muscle membrane, through an increase in the membrane conductance to Na^+ accompanied by a small increase in potassium conductance. These results confirm previous findings using isotope fluxes (Villamil, Nachev & Kleeman, 1970; Hamon & Worcel, 1973) but not the results of Turker, Page & Khairallah (1967) who considered that Ang II might stimulate the Na^+–K^+ pump in rat myometrium.

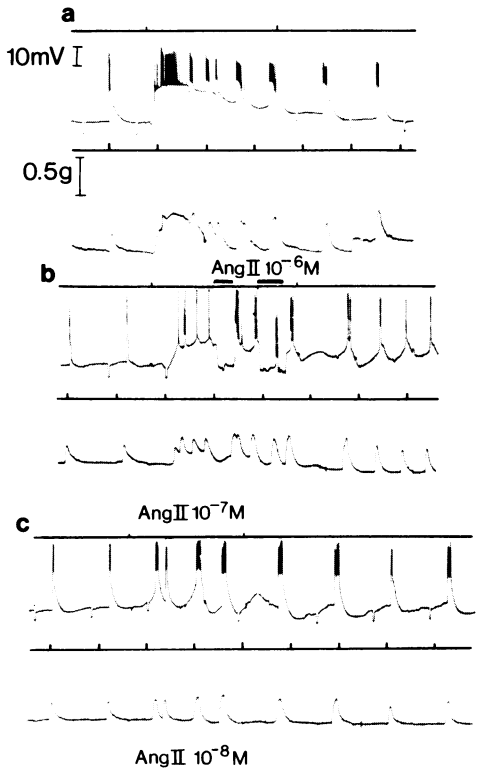

Figure 1 Angiotensin II (Ang II) in physiological solution. (a) Effects of Ang II 10^{-6} M; (b) Effects of 10^{-7}M. Electrical repolarization was performed at times marked by the horizontal bars. (c) Effects of Ang II 10^{-8} M. The vertical marks on the time scale indicate minute intervals.

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