

Angiotensin II positively modulates the spontaneous contractile activity of mouse and human colon *via* activation of AT₁ receptors.

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Objective: Angiotensin II (Ang II) is a potent smooth muscle contractile neurohumoral agonist but has not been much investigated with regard to gastrointestinal motor activity. Ang II effects are mediated by specific receptors, the Ang II type 1 (AT₁) and the Ang II type 2 (AT₂) receptors, which are well expressed in the gut. In this study we evaluated the effects of Ang II on the contractile activity of longitudinal muscle from mouse and human colon and we analysed the subtype(s) of receptors involved in the observed effects. **Methods:** Mechanical responses to Ang II, in the absence or in the presence of different drugs, were assessed *in vitro* in colonic longitudinal muscle from mice and humans, as changes in isometric tension. **Results:** **In the murine proximal and distal colon** Ang II induced a concentration-dependent muscular contraction, which was reduced by the AT₁ receptor antagonist, losartan, but it was not affected by the AT₂ receptor antagonist, PD123319. Pretreatment with TTX, sodium voltage-gated neural channel blocker, partially reduced the contractile response to Ang II in the proximal colon, while abolished it in the distal colon. Atropine, muscarinic receptor antagonist, or SR140333, NK₁ receptor antagonist, reduced the TTX-sensitive excitatory effects induced by Ang II in both preparations. On the contrary, hexamethonium, nicotinic receptor antagonists, ondansetron, 5-HT₃ receptor antagonist, or SR48968, NK₂ receptor antagonist, were ineffective. The contraction induced by a selective NK₁ receptor agonist was reduced by atropine, whilst SR140333 did not affect carbachol inducing muscular contraction. Ang II induced a muscular contraction even in the **human distal colonic longitudinal** muscle preparations. The concentration–response curve was shifted to the right by losartan but it was unaffected by PD123319. TTX and atropine partially antagonized the response to Ang II. **Conclusion:** In the longitudinal muscle preparations from mouse and human colon Ang II positively modulates the spontaneous contractile activity *via* activation of post-junctional and pre-junctional AT₁ receptors, the latter located on the enteric nerves and modulating the release of tachykinins and acetylcholine. In mouse tachykinergic neurons and cholinergic neurons are sequentially recruited by Ang II to induce muscular contraction.