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Is vasoactive intestinal peptide an inhibitory transmitter in the circular but not the longitudinal muscle of guinea-pig colon?

A. BENNETT*, S. R. BLOOM, J. CH'NG, N. D. CHRISTOFIDES, L. E. PEACOCK, J. A. RENNIE, *Department of Surgery, The Rayne Institute, King's College School of Medicine and Dentistry, London SE5 9NU, and Department of Medicine, Royal Postgradute Medical School, London W12 0HS, UK*

Circular muscle strips of guinea-pig isolated colon relaxed with vasoactive intestinal peptide or peptide histidine methionine, whereas the longitudinal muscle contracted. The non-adrenergic-non-cholinergic inhibitory nerves may therefore be different in these two muscle layers.

The identity of the non-adrenergic-non-cholinergic (NANC) transmitter is a controversial subject. Some favour a purine, and others suggest vasoactive intestinal peptide (VIP) as a candidate (Polak et al 1982). There are numerous studies showing VIP-induced relaxation of gastrointestinal muscle (Furness & Costa 1982), but these have mainly been in circular muscle. In contrast, evidence against VIP as an inhibitory transmitter has been obtained using longitudinal muscle from guinea-pig and rabbit small intestine (Cohen & Landry 1980).

We have studied the longitudinal and circular muscles of guinea-pig colon, often in simultaneous experiments, using hog VIP (gift from V. Mutt, Karolinska Institute, Stockholm) and the related human neuropeptide PHM (peptide histidine methionine, synthesised by Peninsular Laboratories, California, USA) which is closely similar to PHI (peptide histidine isoleucine) first isolated from hog intestine (Bloom et al 1983). Adult guinea-pigs of either sex were stunned and exsanguinated, and the colon removed. Whole segments 2–3 cm long were used for experiments on the longitudinal muscle, and cuts were made transversely (Brownlee & Harry 1963) to produce strips for studying the circular muscle. The preparations were suspended in 5 or 10 ml Krebs solution (g litre^{-1}: NaCl 7·1, $CaCl_2.6H_2O$ 0·55, KH_2PO_4 0·16, KCl 0·35, $MgSO_4.7H_2O$ 0·29, $NaHCO_3$ 2·1, dextrose 1·0) at 37 °C under a load of 0·5 –1 g, and bubbled with 5% CO_2 in O_2. Isotonic responses (×10 –15) were measured using transducers and pen recorders. Constant submaximal contractions were obtained to acetylcholine in contact with the tissue for 0·5 or 1 min with a cycle time of 3 min. Doses of VIP or PHM were then added to the bathing fluid and left in contact with the tissue for 2 min (occasionally 5 min for VIP); in some cases acetylcholine was then added in the presence of the peptide.

The circular muscle preparations were concentration-relatedly inhibited by VIP or PHM whereas the longitudinal muscle preparations were stimulated. VIP 200–500 ng ml^{-1} relaxed the circular muscle and/or reduced the submaximal contraction to acetylcholine by up to 45% (n = 4; Fig. 1A). PHM, in some cases with concentrations as low as 20 ng ml^{-1}, acted similarly (n = 6 tissues from 4 guinea-pigs). Vehicle controls had little or no effect.

VIP 100–500 ng ml^{-1} contracted the longitudinal muscle preparations and/or increased the response to added acetylcholine (n = 6, tissues from 5 guinea-pigs; Fig. 1B). PHM was often more potent than VIP, with concentrations sometimes as low as 10 ng ml^{-1} causing contraction (n = 5 tissues from 4 animals).

Thus the results are consistent with the possibility that in guinea-pig colon VIP and/or a related peptide

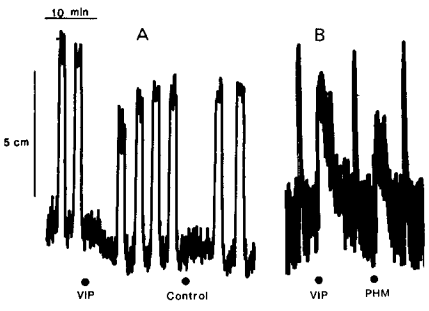

FIG. 1. A: Guinea-pig colon circular muscle. VIP 500 ng ml^{-1} in contact with the tissue for 5 min caused a small relaxation, and reduced contractions to acetylcholine 100 ng ml^{-1} (unlabelled faster responses). Lower concentrations of VIP were also effective in this and other experiments, and PHM was even more potent. B: Guinea-pig colon longitudinal muscle. VIP or PHM, both 100 ng ml^{-1} in contact with the tissue for 2 min, caused a contraction. Lower concentrations were effective in this and some other experiments, particularly with PHM. The unlabelled faster contractions were responses to acetylcholine 5 ng ml^{-1}.

* Correspondence.

may transmit the responses to non-adrenergic-non-cholinergic nerve stimulation in the circular muscle but not in the longitudinal muscle. Perhaps the latter transmitter is purinergic. It is interesting that ATP and adenosine relaxed transverse (circular muscle) strips of guinea-pig trachea, but contracted spiral strips containing longitudinal muscle fibres (Satchell & Smith 1984).

Could both the purinergic and the peptidergic hypotheses be correct, with different non-adrenergic-non-cholinergic transmitters in the longitudinal and circular muscle layers?

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