Cross-talk mechanisms of substance P and VIP-evoked chloride secretion in guinea-pig distal colon

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Summary

Enteric nervous system contains various neuropeptides such as substance P (SP) and VIP, which coexist with other classical transmitters or neuropeptides. The morphological evidence raises the possibility that enteric neurons may simultaneously release these neuropeptides and neuropeptides may cooperate with each other to modify the effector cell functions. We have examined this possibility using the isolated guinea-pig distal colon and dissociated crypt cells. Muscle-stripped preparations consisting of submucosal ganglia and mucosa were set up in Ussing flux chambers to measure the short-circuit current (Isc). All tissues were treated with tetrodotoxin (TTX)(2×10^{-7} M) to prevent neural activity. VIP or SP alone increased Isc, primarily due to chloride secretion in the presence of TTX. These responses were greatly reduced by the depletion of extracellular calcium. The SP-evoked increase in Isc was significantly enhanced by pretreatment with GP-VIP (10^{-6} M) and *vice versa*. The protein kinase A inhibitors, H-8 and H-89 significantly decreased the VIP-evoked response. H-8 and H-89 also decreased GP-VIP enhanced SP-evoked response. The augumentation of chloride secretion from epithelial cells by SP and VIP suggests a existence of cross-talk mechanism in the epithelial cells and the augumentation on chloride secretion by SP and VIP may occur in the process after protein kinase A activation.