SEVERAL GUT PEPTIDES ACTIVATE MYENTERIC NEURONS IN THE GASTRIC ANTRUM OF THE GUINEA-PIG.

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Several gut peptides have a modulatory effect on antral contractility, partly through their actions on enteric neurones. We used conventional intracellular recording methods to study the actions of several gut peptides on 114 myenteric neurons in the guinea-pig gastric antrum. Peptides were applied either by pressure micro-ejection from micro-pipettes or by addition to the superfusion solution. Substance P, Vasoactive intestinal polypeptide (VIP), Neurokinin A, Neurokinin B, Neurotensin, Motilin, Somatostatin and Calcitonin gene-related peptide (CGRP) each evoked similar responses in different subsets of antral myenteric neurons. This response consisted of a depolarization of the membrane associated with enhanced excitability and increased input resistance (IR). The reversal potential for the depolarization was -80 to -90 mV, suggesting closure of K^+ channels as a final mechanism. Additionally, synaptic activity was often enhanced, as was apparent by an increased incidence of spontaneous fast excitatory postsynaptic potentials. The effects of all peptides still occurred in the presence of 0.2 μM tetrodotoxin, indicating a direct action on the impaled neurons. Dose-related responses occurred during application in the superfusion solution at concentrations of 0.1nM to 0.1μM. **Conclusion:** Antral myenteric neurons display a prolonged excitatory response to several gut peptides. These findings directly confirm the neural component in the influence of these modulatory substances on antral contractility. Peptides that enhance antral contractility, such as the tachykinins and Motilin, may act by exciting excitatory motor neurons. Peptides with an inhibitory effect on antral contractility, such as VIP, Somatostatin, CGRP and Neurotensin, may act by exciting inhibitory motor neurons.

HYPERGLYCEMIA BUT NOT HYPERINSULINEMIA PREVENTS THE SECRETION OF GLUCAGON-LIKE PEPTIDE-1 (7-36AMIDE) STIMULATED BY FAT INGESTION .

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We examined the effect of insulin and glucose to the secretion of fat-induced gastric inhibitory polypeptide (GIP) and Glucagon-like peptide-1 (7-36amide) (GLP-1 (7-36amide)) in five healthy subjects during continuous glucose infusion (Protocol 1) and during hyperinsulinemic euglycemic clamp (Protocol 2). In Protocol 1, 50 g fat was orally ingested and glucose was infused at a rate of 0.7 g/kg/h for 2 h continuously from the time of fat ingestion. Either glucose infusion alone or fat ingestion alone was carried out in the same subjects. Fat ingestion augmented insulin release in the hyperglycemic state but not in the euglycemic state. The release of GIP and GLP-1 (7-36amide) was suppressed in the hyperglycemic hyperinsulinemic state. But the integrated response of GLP-1 (7-36amide) was far less than that of GIP, and negligible. Therefore, GLP-1 (7-36amide) can not be responsible for the augmented insulin response, and may not be a incretin. In Protocol 2, 50 g fat was ingested and insulin was infused at a rate of 0.1 U /kg/h in the euglycemic clamp to obtain the normoglycemic hyperinsulinemic state. The release of GIP was significantly suppressed in the normoglycemic hyperinsulinemic state as well as in the hyperglycemic hyperinsulinemic state. However, the release of GLP -1 (7-36amide) was suppressed in the hyperglycemic hyperinsulinemic state but not in the euglycemic hyperinsulinemic state. We concluded that insulin prevents fat-induced GIP, but not GLP-1 (7-36 amide), secretion and that glucose itself is likely to prevents GLP-1 (7-36 amide) secretion.