EFFECTS OF VIP ON SECRETORY RESPONSES TO CCK-8 IN RAT EXOCRINE PANCREAS

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Effects of VIP on CCK-8-induced exocrine secretion were examined in isolated perifused pancreatic acini and isolated perfused whole pancreas of rats. Furthermore, changes in cytosolic Ca^{2+} concentrations ($[Ca^{2+}]_c$) in pancreatic acini were detected by microspectrofluorometry using Fura-2.

In pancreatic acini, VIP (1-10nM) alone failed to induced an increase of amylase release. Stimulation by 100pM CCK-8 in combination with 1nM VIP significantly prevented a decay in the response to 100pM CCK-8, and maintained the peak level during the continuous stimulation. Stimulation by 30pM CCK-8 in combination with 10nM VIP caused continuous amylase release, the plateau level of which was significantly greater than the level induced by 30pM CCK-8 alone. Stimulation by 10pM CCK-8 in combination with 1nM VIP caused an elevation of the initial rapid phase of the response, which was greater than the corresponding initial phase of the response to 10pM CCK-8 alone.

In isolatad perfused pancreas, 1nM VIP alone caused few, if any, secretory responses (juice flow and protein output). Continuous stimulation by 10pM or 30pM CCK-8 in combination with 1nM VIP caused secretory responses that were greater than the responses to CCK-8 alone. The potentiation of protein output was larger than that of juice flow. Stimulation by 100pM CCK-8 in combination with 1nM VIP, however, failed to potentiate the secretory responses.

In pancreatic acini, 10pM CCK-8 induced continuous oscillation of $[Ca^{2+}]_c$. VIP (1nM) alone caused no change in $[Ca^{2+}]_c$. Stimulation by 10pM CCK-8 in combination with 1nM VIP decreased the frequency of CCK-8-induced $[Ca^{2+}]_c$ oscillation.

These results show that VIP, a second neurotransmitter candidate of the vagus nerve, may play a physiological role in regulating the secretory function of the rat exocrine pancreas in concert with CCK, a gut hormone. A possible mechanism of the potentiating effect of VIP may be in decreasing the frequency of $[Ca^{2+}]_c$ oscillation, which may be a cardinal intracellular signal for maintaining recurrent exocytosis of zymogen granules, and the efficiency of $[Ca^{2+}]_c$ dynamics might be amplified by cAMP, a possible intracellular signal of VIP.