EFFECT OF HYPOTHALAMIC PEPTIDES ON SECRETION OF SQUALUS ACANTHIAS RECTAL GLAND

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Rat hypothalamic growth releasing factor (rGRF), a 43-amino acid member of the family of peptides related to vasoactive intestinal peptide (VIP) was found last year to stimulate rectal gland secretion (Bulletin MDIBL 1986; 26:23). In parallel experiments performed by J. Abucham and S. Reichlin, New England Medical Center, immunoreactivity to an antibody specific for rGRF (and unreactive to VIP) was detected in acid homogenates of shark brain and rectal gland. These results suggested that other brain peptides and their homologues might have effects on rectal gland secretion. We therefore assessed the effects of the following peptides (kindly supplied by Drs. Jean Rivier and Wylie Vale of the Salk Institute's Clayton Foundation Laboratories for Peptide Biology): carp GRF-like immunoreactive peptide (cGRF-LIP (1-45)-OH); human growth releasing factor (hGRF (1-29)-NH_2); hGRF (1-40)-OH; PHI (a component of the pro-VIP molecule); neurotensin; rat calcitonin gene related peptide (rCGRP); and gonadotropic releasing hormone (GnRH).

Isolated rectal glands were perfused at 16°C with shark Ringer's solution containing 5 glucose and gassed with 99% O_2, 1% CO_2 at a pH of 7.5 as previously described (Silva et al, Am J Physiol 1977; 233:F298-F306). Compounds to be tested were dissolved in 1 ml of shark Ringer's solution and injected as a bolus over a period of 1 minute into the arterial circulation of the perfused gland, without interrupting the normal flow of perfusate (about 4 ml/min). The concentration of hormone reaching the gland was calculated as the quantity injected divided by the volume of perfusate flow in one minute. The hormones were usually injected after 3 basal collection periods lasting 10 minutes each and the stimulatory effect upon the rectal gland was defined as the output of chloride in μEq/g wt/hr during the 10 minutes immediately following the bolus. The secretion induced by bolus injections reached its peak during the first 10 minutes after the injection and returned to its baseline level during the second or third 10 minute collection periods. Results are summarized in Figure 1. Each point represents the mean ± s.e. of 4 to 10 separate experiments.

Neurotensin, rCGRP and GnRH (not shown in the Figure) had no effect on rectal gland secretion at concentrations up to 10^{-4}M. PHI (a constituent of the pro-VIP molecule that is identical to VIP except for a carboxyl-terminal histidine and an amino-terminal isoleucine) was an effective stimulator at approximately 10x the effective concentration of VIP. Interestingly, rat growth-releasing factor was a more potent agonist in the elasmobranch than human GRF. On the other hand, cGRF-LIP, a peptide isolated from the hypothalamus of the common carp, Cyprinus carpio, which has 18 amino acid residues in common with VIP and 17 in common with rat GRF, had no stimulatory effect at all.

These data suggest that stimulatory receptors linked to adenylate cyclase in the shark rectal gland can respond to several VIP-like peptides. The native VIP-like neurotransmitter is likely to have a molecular structure closely resembling but not precisely replicating VIP, and an antigenic configuration that permits it to react with antibodies to rGRF.

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