The effects of neuroactive peptides on growth hormone release

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The plasma concentration of growth hormone fluctuates rhythmically over a 24 h period; in humans a major peak of release follows the onset of sleep and smaller peaks occur during 'unstressed sedentary wakefulness' (Parker *et al.* 1979). It can also be altered acutely by insulin-hypoglycaemia, amino acids, neurotransmitters or their precursors agonists or antagonists and by some peptides. These changes in concentration are thought to be mediated by changes in the release from the median eminence of the inhibitory peptide somatostatin or the postulated stimulatory GH-RH.

Rhythmic release of growth hormone is attributed to changes in GH-RH release, mainly because it was not prevented by passive immunization of rats with antisomatostatin serum. However, active immunization of monkeys with somatostatin abolished it (Steiner *et al.* 1978). Recently larger forms of somatostatin, which are more active than somatostatin-14, have been identified in the hypothalamus (Bohen *et al.* 1980) and they may be present in hypophysial portal blood. It is not clear whether these larger peptides would have been neutralized by the antisomatostatin sera used for passive immunization.

The actions of naturally-occurring peptides on growth hormone release in vivo are complex and occasionally conflicting and explanations must await the measurement of GH-RH and somatostatin concentrations in hypophysial portal blood. Stimulation of growth hormone release by opioid peptides may involve decreased release of somatostatin (Drouva *et al.* 1981). However, morphine increased growth hormone release in rats injected with antisomatostatin serum, so opioid peptides are thought to suppress inhibitory control on GH-RH release. Intravenously, substance P and neurotensin at high doses cause hyperglycaemia and alter insulin and glucagon release as well as increasing plasma growth hormone, whereas intraventricularly they have been reported both to increase and to decrease growth hormone release (Vijayan & McCann, 1980). Gastrin, CCK and VIP are most effective when administered intraventricularly, but gastrin and CCK at high concentrations increase growth hormone release in vitro (Morley *et al.* 1979). TRH increases the low plasma growth hormone concentration in urethane-anaesthetised rats which have high portal somatostatin, but decreases the high plasma growth hormone concentration after pentobarbital-anaesthesia (Brown & Vale, 1975). It is unlikely that any of these peptides is a physiological GH-RH acting directly on the pituitary in vivo. Recently low-energy computation of peptide conformation has been used to design a number of peptides which are highly active and selective stimuli for in vitro and in vivo growth hormone release (Momany *et al.* 1981). Their relationship to the actual GH-RH remains to be determined.

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