SHORT COMMUNICATION

Kassinin and substance P stimulate somatostatin release in the rat

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Summary

1. The effect of the tachykinin dodecapeptide kassinin, which has been extracted from the skin of several African frogs, on somatostatin release was examined in the rat and compared with that of the neuropeptide substance P.

2. Equimolar doses of the two peptides were injected intravenously and the animals killed at specified intervals after injection. Somatostatin was measured by a specific radioimmunoassay.

3. Kassinin and substance P had no effect when given in low doses (0.1 and 1.0 pg). However, when administered in a dose of 10-0 μg, both peptides significantly increased plasma somatostatin, by 31 and 22% respectively.

4. These findings suggest that kassinin and substance P have common endocrine actions. The effect on somatostatin release may be specific for tachykinins, since other neuropeptides such as the enkephalins have no effect.

Key words: kassinin, neuropeptides, somatostatin, substance P, tachykinin.

Introduction

Kassinin is a tachykinin dodecapeptide which has been isolated recently from the skin of the African frog Kassina senegalensis [1]. Kassinin shares with all other known tachykinins the C-terminal tripeptide. It also lacks the N-terminal pyroglutamyl residue, a feature which it shares only with substance P. Thus kassinin and substance P are structurally closely related. Little information is available regarding the biological activity of kassinin, although it has been shown to possess, like all tachykinins, hypotensive effects and on salivary secretion and smooth muscle contraction [2]. It has been shown recently that kassinin has profound endocrine effects in the rat (H.-G. Güllner, unpublished work). In fact, it is equipotent with substance P in its effects on follicle-stimulating hormone (FSH), luteinizing hormone (LH) and prolactin secretion.

Substance P has been localized in neurons in close proximity to somatostatin-containing neurons [3], suggesting some functional relationship. It has been reported that substance P and neurotensin, when injected intravenously in the rat, elevate serum growth hormone, but suppress growth hormone when given intraventricularly (this effect is abolished when the rats are pretreated with an antiserum to somatostatin) [4]. This finding has been taken as evidence that the effect of substance P on growth hormone secretion is mediated by somatostatin. Furthermore, substance P has been shown to stimulate somatostatin release from the rat hypothalamus in vitro [5]. In contrast, the neuropeptides Met-enkephalin or Leu-enkephalin do not affect somatostatin release. Because of the striking structural similarities between substance P and kassinin, we examined the effects of the two tachykinin peptides on plasma somatostatin in the rat.

Methods

Male, adult Fischer 344 rats (250–300 g, obtained from the Small Animal Section, Veterinary
Resources Branch, National Institutes of Health), which were maintained on standard rat chow and water ad libitum, were used for the experiments. The animals were anaesthetized with ketamine HCl (100 mg/100 g body weight) and equimolar doses of the peptides were injected intravenously in a volume of 0.2 ml. Synthetic substance P was purchased from Beckman Instruments Inc. (Palo Alto, CA, U.S.A.). Synthetic kassinin [6] was kindly donated by Professor Haruaki Yajima of Kyoto University. Vehicle alone (phosphate buffer, 0.01 mmol/l) was injected in the control groups. The rats were killed at specified intervals after injection and blood was collected into chilled tubes containing EDTA and aprotinin [500 kallikrein-inactivating units/ml of blood]. The plasma was immediately separated and stored at -40°C until analysis. Somatostatin-like immunoreactivity was measured by a modification [7] of previously published methods [8, 9]. The antibody used was directed against the central portion of the somatostatin molecule. It had been established previously by multiple criteria that the material measured in this assay is immunologically related to somatostatin rather than reflecting interfering substances [7]. The results were analysed by Student's t-test for non-paired observations. All values reported represent means ± SEM of seven animals.

Results

Injections of the two low doses of either peptide (0.1 and 1.0 µg) did not significantly change the plasma concentrations of somatostatin (Fig. 1). In contrast, the highest dose of kassinin or substance P (10 µg) increased plasma somatostatin concentrations significantly (216.0 ± 10.6 pg/ml, control; 281.5 ± 27.0 pg/ml, kassinin, P < 0.01; 262.0 ± 20.5 pg/ml, substance P, P < 0.05). The increase with the high dose occurred 30 and 20 min after injection respectively.

Discussion

The recently discovered frog skin dodecapeptide kassinin and substance P are unique among the tachykinins since they share, in addition to the C-terminal tripeptide, a free N-terminal residue. In the present study both peptides had similar effects on somatostatin release. It has been shown that kassinin has potent effects on the secretion of FSH, LH and prolactin in the rat (H.-G. Gullner, unpublished work). The dose−response curves obtained for kassinin resembled very closely those obtained for substance P. These findings and the close structural similarities between the two peptides suggest that a search for the presence of kassinin in mammalian neuronal and extra-neuronal tissues, such as the gastrointestinal tract, might be justified and that kassinin may serve functions similar to those of substance P. Should this be the case, another member would have to be added to the growing family of the neuropeptides.

Several neuropeptides have been shown to stimulate or suppress the release of a variety of hypothalamic, hypophysyal and of non-pituitary hormones. The nature of this function and the physiological significance of these interactions, if any, are not understood. Specifically, it is not clear if neuropeptides are direct regulators of hormone release or if their biological role is one of modulating the secretory response of hormones to physiological perturbations. The available data are not sufficient to answer these questions.

References


