

RECENT ADVANCE IN MOTILIN AND hPP RESEARCH

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We studied the relationship between plasma motilin levels and gastric motor activity in conscious dogs and healthy subjects. Plasma motilin levels were measured by sensitive radioimmunoassay while gastric motor activity was recorded by means of chronically implanted force transducer in dogs and intragastric balloon tubing in man.

When the gastric contractile activity was in the interdigestive state, plasma motilin levels were always elevated in all dogs, furthermore it fluctuated in complete association with hunger contractions during the interdigestive state. Ingestion of food lowered the plasma motilin concentration and this low levels of motilin lasted as long as the gastric motor activity was in the digestive pattern. In human study, the similar findings were obtained between fasting motilin levels and gastric motor activity, furthermore gastric borborygmus closely associated with high motilin concentration in the fasting state.

Human pancreatic polypeptide (hPP) is newly recognized pancreatic hormone described Chance et al. Using radioimmunoassay, we studied fasting plasma levels of hPP and responses to food stimuli in healthy subjects and patients of chronic pancreatitis. Basal level of hPP in young control subjects was 50 ± 5 pg/ml, although older subjects showed high level of hPP according to each decade of age. There was a significant correlation of basal hPP and age. After ingestion of food plasma hPP increased promptly and showed biphasic secretory pattern in healthy subjects, these postprandial high level was sustained for 5 to 6 hours. Impaired release of hPP to food stimuli in patients with chronic pancreatitis were observed. So to study the hPP secretion to food stimuli is very useful and noninvasive tool for pancreatic exocrine and endocrine function.

RADIOIMMUNOASSAYS OF NEUROPEPTIDES

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Recently, it was reported that many bioactive substances were present in the central nervous system of several species including man. These substances are considered to function to convey information between the adjacent neurons (e.g. nor-epinephrine, dopamine and acetylcholine) or to modify, stimulate or inhibit, chemical neurotransmission (e.g. neuropeptides such as enkephalins, β -endorphin, LH-RH and TRH), which are called neurotransmitters and neuromodulators respectively. For the measurements of these compounds, relatively non-specific and insensitive bioassays have been used so far. However, recently, very specific and sensitive radioimmunoassays of these compounds, especially neuropeptides, have been developed and applied for analyses of these substances in the brain, the visceral organs, the cerebrospinal fluid and the blood.

We have developed a radioimmunoassay for β -endorphin using an anti-serum obtained in a rabbit immunized with β -endorphin obtained in the crude porcine ACTH preparations (Organon). The minimal detectable amount was 5 pg per tube. The antiserum used reacted with β_3 -LPH as equally as β -endorphin on a molar base but showed negligible cross-reactivity with other peptides including α -endorphin β -MSH, α -MSH and enkephalins, indicating that this antiserum was directed to 17-31 amino acid sequence of β -endorphin. Using this assay we have confirmed the presence of β -endorphin in the pituitary extracts of human, rat and cow in addition to β -LPH after fractionations by Sephadex G-100 column. Furthermore, we have measured the content of β -endorphin in the various brain regions and several visceral organs of the Japanese monkeys. The interpeduncular nucleus had the highest content of β -endorphin activity except for the pituitary, among the brain regions analyzed, followed by the habenula and the hypothalamus. Considerably higher amounts were found in the preoptic areas, the substantia nigra, the pallidum, the superior and the inferior colliculi, the olfactory tract, the corpus callosum, the pyramis and the ventral as well as the dorsal roots of the spinal cord. In contrast, no significant amount of immunoreactive β -endorphin was detected in the visceral organs such as the

liver, the pancreas, the duodenum and the colon. The fractionation studies of these brain extracts on Sephadex G-50 column indicated that approximately half of β -endorphin activity detected were attributable to specific β -endorphin. We also observed a concomitant production of β -endorphin in 6 ectopic ACTH-LPH producing tumors and confirmed the presence of β -endorphin immunoreactivity in plasma from Addison's disease and Nelson's syndrome after gel filtration on Sephadex G-50. Very small amount of β -endorphin in plasma was also detected in a normal subject.

Anyway, the roles of neuropeptides including β -endorphin in the central nervous system, the peripheral tissues as well as the blood have to be elucidated further using the specific and sensitive radioimmunoassays of these neuropeptides.

ENDORPHINS AND ITS RECEPTOR

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Peptides with opiate-like properties (endorphins) have been isolated from brain and pituitary, but the physiological significance of these peptides remain to be defined. Three sensitive and specific assay systems, opioid radioreceptor assay (RRA), Met⁵-enkephalin radioimmunoassay (RIA) and β -endorphin RIA, have been developed. Using these three assay systems, regional distribution of opioid receptors and concentrations of endorphins in rat brain has been determined. Total enkephalins activity by RRA and immunoreactive Met⁵-enkephalin found in rat brain have the regional distribution correlating with that of opioid receptors, with highest levels in corpus striatum and negligible amounts in the cerebellum. On the other hand, β -endorphin-like immunoreactivity has a different regional distribution from that of opioid receptors and that of enkephalins, with highest levels in hypothalamus and negligible amounts in corpus striatum. These observations suggest that β -endorphin might have no relationship to brain enkephalins, and that it seems to require several assay systems for studying physiological significance of enkephalins and endorphins.