## SUBSTANCE K MOLECULAR FORMS IN RAT BRAIN

H ARAI and P C EMSON

AFRC Institute of Animal Physiology, Babraham, Cambridge CB2 4AT U.K.

Using recently developed neurokinin α (substance K) directed radioimmunoassays we detected one major peak of substance K like immunoreactivity on reverse phase HPLC (μBondapak $C_{18}$ column). However, separation of this peak on Sephadex G25 revealed that this single peak contained one major form eluting at the position expected for synthetic bovine substance K but also a higher molecular form with substance K like immunoreactivity. The relative amounts of the high and low molecular weight forms of substance K like immunoreactivity are similar whether a cell body rich area (caudate/dorsal root ganglia) or a terminal region is sampled (substantia nigra/ substantia gelatinosa). It is likely that the high molecular weight form of substance K immunoreactivity corresponds to neuropeptide K (Tatemoto et al 1985).

## GIP AND THE ENTEROINSULAR AXIS IN HYPERINSULINAEMIC AND HYPOINSULINAEMIC DIABETIC MICE

C J Bailey, P R Flatt, P Kwasowski, V Marks, Department of Molecular Sciences, Aston University, Birmingham B4 7ET, UK, and Department of Biochemistry, University of Surrey, Guildford GU2 5XH, UK

Studies of gastric inhibitory polypeptide (GIP) in human type 1 and type 2 diabetes mellitus have yielded equivocal information. This study compares plasma GIP concentrations in hyperinsulinaemic obese hyperglycaemic Aston ob/ob mice and hypoinsulinaemic streptozotocin (STZ) diabetic mice under different physiological conditions. Plasma GIP was elevated in both diabetic models, 5-15 fold in fed ob/ob mice and about 2 fold in fed STZ mice, although food intake was approximately doubled in the two groups. GIP concentrations fell promptly during fasting, but concentrations in fasted ob/ob mice remained higher than in fasted lean controls. GIP responses to orally administered lipid were similar in magnitude in the diabetic mice, exceeding those of control mice about 2 fold. Although glucose tolerance was impaired in both groups of diabetic mice, plasma glucose concentrations were consistently lower after oral than intraperitoneal (ip) glucose. Oral (but not ip) glucose evoked a well defined insulin response in ob/ob mice, whereas neither route of glucose administration produced a significant insulin response in STZ mice. The results indicate that increased activity of the enteroinsular axis, associated with raised GIP concentrations, promotes the hyperinsulinaemia in hyperglycaemic ob/ob mice. However, raised GIP concentrations appear to be ineffective in promoting insulin secretion in severely diabetic STZ mice, possibly reflecting an inadequate pancreatic insulin reserve. Raised GIP concentrations in both diabetic models are due in part to the hyperphagia, but a lack of insulin in STZ mice and a lack of responsiveness to insulin in ob/ob mice may result in impaired insulin feedback on GIP secretion.