These results indicate that metabolic control is related to 2.77±0.38 g/l, p=0.07; vWF, 1.15±0.35 IU/ml to 1.07±0.28 IU/ml, p=0.003 and Alb, 103±10±1, p=0.04. There was no significant change in FVII:C levels. There was a significant linear association between changes in HbA1c and FVII:C, r=0.71, p=0.001; fibrinogen, r=0.72; PC 10 and vWF, r=0.47, p=0.001. These results indicate that metabolic control is related to FVII:C, vWF and fibrinogen levels and that abnormalities of haemostasis may provide a link between glycemic control and vascular disease.

PC 10 IMMUNOSTAINING OF HUMAN PITUITARY ADENDOMAS IN VITRO MAY BE AN UNRELIABLE MARKER OF PROLIFERATION

The labelling index in 9 human anterior pituitary adenomas (6 GH, 2 FSH/LH and 1 LH) was determined after 4 days in serum free medium employing monoclonal antibody against PC 10 and bromodeoxyuridine (BUD) labelling. The monoclonal antibody PC 10 has a strong affinity for proliferating cell nuclear antigen (PCNA), an auxiliary factor to DNA polymerase &. PCNA has been used as a marker of proliferation being detected throughout the cell cycle from G1 phase to S phase which is specific for the S phase. Human pituitary adenomas were dispersed to single cells and plated out at 10^5 cells/ml in 24 well plates in Iscoves modified Dulbecco's medium (IMDM) supplemented with 10% foetal calf serum and allowed to attach. Cells were washed and the medium replaced with serum free IMDM. After 4 days in situ viability was assessed using a graticule and fluorescence in 24 well plates in Iscoves modified Dulbecco's medium (IMDM) supplemented with 10% foetal calf serum and allowed to attach. Cells were washed and the medium replaced with serum free IMDM. After 4 days in situ viability was assessed using a graticule and fluorescence in situ. We then immunostained with either anti-enolase to identify proliferation and the adenoma cells respectively. The labelling index (LI) was the number of proliferating cells per 1000 pituitary cells studied. Two tumours were negative for both BUD and PCNA staining, 2 tumours were negative for BUD but positive for PCNA staining (LI 0.8% and 3.6%) and 1 tumour gave comparable results (LI 0.1% BUD, 0.2% PCNA). Marked positivity in 4 tumours (3 GH + 1 LH) was found with PCNA (LI 9.4%, 47.5%, 80%, 87%) compared to BUD (LI 0.3%, 1.4%, 1%, 1%) respectively. Antigen cross reactivity is the most likely explanation for the very high PCNA labelling index compared to that found with BUD. We conclude that the monoclonal antibody PC 10 against PCNA is a less reliable marker of proliferation than the use of BUD in this in vitro system.

EXAGGERATED VASCULAR SENSITIVITY TO NORADRENALINE: A CONTRIBUTORY FACTOR TO HYPERTENSION IN PHAEOCHROMOCYTOMA

A 31-year old man presented with a 6-month history of night sweats; high blood pressure had been noted on one occasion two years previously but not followed up. Blood pressure at presentation was 154/112 mm Hg. Phaeochromocytoma was diagnosed by grossly elevated urinary catecholamine excretion (27,370 nmol/24h; normal range 120-590), with normal adrenaline and dopamine. Neuropeptide Y, a powerful vasoconstrictor, is secreted by some phaeochromocytomas and by Glomus Iike cells were normal in our patient. MIBG and abdominal CT scans indicated two large para-aortic pheochromocytomas, which were successfully removed at surgery, with resolution of the symptoms and hypertension. We examined the vasoconstrictor responses to locally-infused noradrenaline (NA) before and after surgery. A dose-response curve was constructed using a stepped infusion of NA (1-128 ng/min) into a dorsal hand vein using an established technique, and the dose causing 50% of maximal vasoconstriction (ED50) was calculated. The patient was hyper-responsive to NA, showing a significant left-shift of his dose-response curve, with an ED50 of 3.6 ng/min (range for 20 normal subjects 5-157). Sensitivity was normal following tumour removal (ED50 15.9 ng/min). We suggest that hypersensitivity to the vasoconstrictor effects of NA may exacerbate hypertension in phaeochromocytoma. However, the mechanism is unknown.

IS INSULIN A SATIETY SIGNAL? INSULIN TREATMENT ANTAGONISES STARVATION-INDUCED INCREASES IN NEUROPEPTIDE Y CONCENTRATIONS IN THE ARCULATE NUCLEUS OF THE RAT HYPOTHALAMUS

Neuropeptide Y (NPY), the most powerful appetite stimulant known, is synthesised in hypothalamic arcuate nucleus (ARC). NPY levels rise in the ARC and in appetite-regulating hypothalamic nuclei in food-deprived rats, and may drive compensatory hyperphagia in starvation. Circulating insulin levels fall in starvation and insulin deficiency has been postulated to stimulate hypothalamic NPY: this supports the suggestion that insulin acts on the brain to inhibit feeding. We tested this hypothesis by determining whether the increase in NPY in the ARC of starved rats was suppressed by insulin treatment.

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Adult male Wistar rats were studied. Controls (n=8) were fed and two other groups were food-deprived for 72 hours, both losing 20% of initial weight (pc0.001 vs controls). One food-deprived group (n=10) received insulin (5 U/kg/day) injected subcutaneously twice daily and both other groups received saline. Mean blood glucose values (measured in tail-prick samples) were 5.9±0.1 mmol/l in controls, 4.6±0.3 mmol/l in food-deprived (p<0.001 vs controls) and in insulin-treated 4.4±0.3 mmol/l (p<0.001 vs controls; NS vs food-deprived group). Final plasma insulin levels in insulin-treated rats were higher than in saline-treated food-deprived rats (46.6±8.9 vs 28.9±4.5 pmol/l; p<0.001) and comparable with controls (52.6±16.2 pmol/l; NS). ARC NPY concentrations rose significantly above controls in food-deprived rats (14.18±7.9 vs 8.4±2.16 fmol/kg protein; p<0.001) and were intermediate in the insulin-treated food-deprived group (11.19±3.63 fmol/kg protein; p<0.01 vs controls and p<0.001 vs saline-treated, food-deprived). Other hypothalamic regions showed no differences between groups.

In conclusion, insulin antagonises fasting-induced increases in NPY concentrations in the ARC. This is consistent with the hypotheses that insulin deficiency stimulates hypothalamic NPY synthesis, and that peripheral insulin acts as a satiety factor by inhibiting hypothalamic NPY.

D-FENFLURAMINE (D-FEN) IMPROVES INSULIN SENSITIVITY AND GLUCOSE TOLERANCE IN INSULIN-DEFICIENT RATS

D-Fenfluramine (D-Fen), a widely used anorectic drug, is reported to improve insulin sensitivity and glycaemic control in human non-insulin dependent diabetes independently of its anorectic effect. A dose range of 0.5-1.0, 2.5, 5.0 mg/kg of D-fen was given by gavage to male Wistar rats (n=10) that had been made diabetic by streptozotocin (55 mg/kg) for 3