Cigarette smoking reduces food intake, and a carbohydrate-specific craving often develops after cessation of smoking. The effect of nicotine administration on hypothalamic Neuropeptide Y (NPY) levels, an endogenous potent appetite stimulant, particularly for carbohydrate was assessed in a 12 day study in rats.

Three groups of rats were implanted (s.c.) with mini-osmotic pumps, one group containing nicotine dihydrochloride (12mg/kg /day n=8) and two groups containing saline (0.9% n=8,8). The nicotine treated rats and one of the saline groups were allowed to free-feed for twelve days. The second saline treated group were pair-fed to the level of food intake of the nicotine treated rats. Food intake in the nicotine treated rats was reduced by 11% over the twelve days (p=0.02), and body weight gain reduced by 10% over the twelve days (p<0.02).

NPY levels were significantly lower in the nicotine treated and pair-fed rats compared with the control rats (PVN 62 ± 6.5 vs 91.2 ± 6.3 fmoVug protein p<0.01, ARC 33 ± 4.9 vs 49 ± 4.0 fmoVug protein p=0.01. pair-fed PVN 74 ± 3.7 vs 91.2 ± 6.3 p<0.03)

These results suggest that the hypophagia associated with nicotine treatment may be a result of reduced hypothalamic NPYergic activity.

158 ALTERATIONS IN NEUROPEPTIDE Y LEVELS IN THE HYPOTHALAMUS OF THE RAT FOLLOWING TREATMENT WITH METHYSERGIDE


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Methysergide (Meth) is a non selective 5-HT antagonist which stimulates feeding in rats. 5-HT has been suggested to induce satiety. Neuropeptide Y (NPY) is a 36 amino-acid peptide structurally related to pancreatic polypeptide, and one of the most abundant neuropeptide in the brain, 5-HT fibres project to the hypothalamus particularly the paraventricular(PVN) and arcuate (ARC) nuclei, sites of NPY action and synthesis respectively.

This study set out to examine the effect of acute and chronic administration of methysergide on hypothalamic NPY.

Male Wistar rats were used. In the acute experiment, rats were injected with either saline (0.9% n=8) or methysergide(10mg/kg n=8) and killed after four hours.

In the chronic experiment, rats were implanted with mini-osmotic pumps filled with either saline (n=8) or methysergide (10mg/kg/day n=8). Rats were killed after seven days. Food intake was greater in the methysergide treated rats after four hours compared with the saline treated rats (p<0.01).

NPY levels were significantly increased in the PVN and ARC in the methysergide treated rats (PVN 61 ± 3.2 vs 47 ± 3 fmoVug protein p<0.01, ARC 49 ± 4.2 vs 27 ± 3.2 p<0.01)

In the chronically treated rats food intake was raised by 13% over seven days (p<0.01).

Again NPY levels were significantly increased in the methysergide treated rats (PVN 66 ± 6.2 vs 47 ± 3.1 fmoVug protein p=0.01, ARC 38.5 ± 3 vs 27.4 ± 3.2 p=0.02).

These results suggest that methysergide induced feeding is associated with changes in NPYergic activity in critical hypothalamic areas.

159 EFFECTS OF CHRONIC NICOTINE ADMINISTRATION ON HYPOTHALAMIC NEUROPEPTIDE Y LEVELS IN THE RAT


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Nicotine administration has an inverse relationship with body weight.

160 NEUROPEPTIDE Y CONCENTRATIONS IN CEREBROSPINAL FLUID ARE UNCHANGED IN OBESITY

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Neuropeptide Y (NPY) is a potent centrally acting appetite-stimulating peptide implicated in the regulation of energy balance. It induces hyperphagia and obesity when injected into the rat hypothalamus. Hypothalamic NPY and NPY mRNA levels are increased in spontaneously obese rats, suggesting that it may be involved in causing obesity in rodents. It is not known whether NPY has a role in the pathogenesis of obesity in man. NPY is found in human cerebrospinal fluid (CSF) and we have therefore compared CSF NPY levels in normal obese and non-obese individuals, to determine whether NPY concentrations might be increased in obesity.

We studied 25 clinically normal subjects (age 67 ± 5 years, male 11, female 14) undergoing spinal anaesthesia. None had any significant illness. Samples of 1 ml were freeze-dried and reconstituted to 100 ul, and 35-ul aliquots were assayed for NPY using an in-house RIA. CSF NPY levels were not correlated with body mass index (BMI) (r=0.088, p=0.673) and there were no differences in NPY concentrations between groups of subjects stratified for BMI: BMI <22 (n=7), 22-25 (n=11), 25-29 (n=7). 30+ (n=11), 702 ± 53 fmoVml (differences between all groups p=0.1).

CSF NPY levels are therefore not increased in human obesity. NPY is found in many brain regions outside the hypothalamic appetite-regulating nucleus, which could contribute to CSF levels. This negative observation does not therefore exclude a role of the peptide, acting specifically in the hypothalamus, in contributing to human obesity.

161 ACUTE COLD EXPOSURE INCREASES NEUROPEPTIDE Y LEVELS IN SPECIFIC REGIONS OF THE RAT HYPOTHALAMUS WHICH REGULATE ENERGY BALANCE

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Neuropeptide Y (NPY) is implicated in the regulation of energy balance and reduces energy expenditure, by inhibiting activation of