Pharmacology Biochemistry & Behavior, Vol 38, pp 379–384 © Pergamon Press plc, 1991 Printed in the U S A 0091-3057/91 $3 00 + 00

Differential Feeding Responses Evoked in the Rat by NPY and NPY_{1-27} Injected Intracerebroventricularly

XIMENA PAEZ,[1] J. W. NYCE AND R. D. MYERS[2]

Departments of Pharmacology and Psychiatric Medicine, School of Medicine East Carolina University, Greenville, NC 27858

Received 2 October 1990

PAEZ, X , J W NYCE AND R D MYERS. *Differential feeding responses evoked in the rat by NPY and NPY_{1-27} injected intracerebroventricularly* PHARMACOL BIOCHEM BEHAV **38**(2) 379–384, 1991 —Neuropeptide Y (NPY) given by the intracerebroventricular (ICV) route in the rat evokes hyperphagic-like feeding. To examine the molecular nature of action of NPY, comparisons were made between the central effects of this peptide and a newly synthesized amino-terminus fragment, NPY_{1-27} A single guide tube was implanted stereotaxically to rest just above a lateral cerebral ventricle so that ICV injections in a volume of 10 μl of either CSF control vehicle or peptide could be given in the unrestrained rat Native NPY or NPY_{1-27} was given in doses of 5 0 or 10 0 μg, whereas nondeprotected NPY was infused in a dose of 10 0 μg. The intakes of either regular commercial rat diet or specially prepared chocolate-flavored biscuits as well as water were recorded intermittently for 4 0 h following each ICV infusion Although a clear-cut dose response with a latency of similar magnitude emerged for both molecules, NPY was found to be nearly twice as potent as NPY_{1-27} in inducing spontaneous feeding A corresponding infusion in the same volume of either nondeprotected NPY or CSF control vehicle was without effect When chocolate-flavored biscuits were provided to the rat, an ICV infusion of a 10 0 μg dose of NPY enhanced significantly both rate of eating and total cumulative intake of flavored food in comparison to that after a similar infusion of NPY_{1-27} or either control solution These results suggest that native NPY acting centrally affects gustatory and/or olfactory systems to a much greater degree than does NPY_{1-27} Consequently, the carboxy terminus amino acids 28–36 appear to be essential in shifting the sensory threshold for food ingested by the rat and thus may govern the overall magnitude of its intake.

Neuropeptide Y Feeding Intracerebroventricular infusion Food intake Neuropeptide Y_{1-27} Hunger Peptides Hypothalamus Water intake Satiety mechanism

THE central action of neuropeptide Y (NPY) in inducing an intense feeding response has been localized anatomically to the medial and other hypothalamic areas (10). When microinjected into the paraventricular nucleus (PVN), NPY evokes a dose-dependent feeding response which, when compared to norepinephrine-induced feeding, is characterized by a longer latency but far greater potency and longevity (28). By repeated perfusions of NPY intermittently within medial hypothalamic sites of the rat, nonsatiable feeding is evoked in which up to twice the normal 24 hour intake of food is consumed in less than five hours (22,23). Evidence also exists that NPY produces carbohydrate selective feeding in a choice situation since the rat preferentially consumes this micronutrient over that of fat or protein (29).

Although the part of the NPY molecule which is functionally active has not yet been clarified, differences between the potencies of several fragments have been demonstrated in different neurobiological systems. For example, the deletion of tyrosine at the amino terminus (NPY_{2-36}) decreases by three-fold the agonist action peripherally of NPY on adrenergic transmission in the vas deferens preparation, whereas successively cleaved fragments of the NPY molecule (i.e., 5–26, 11–36, 25–36) are proportionally less potent (3). Substitution of tyrosine in position 20 and 21 and of alanine in the first 10 residues generally diminishes the binding affinity for NPY receptors in the brain of the rat (14). However, the 2–36 fragment of NPY, but not the 5–36 moiety is even more effective in evoking feeding when it is injected into the PVN (13). Although NPY_{26-36} and $_{20-36}$ given ICV in the mouse are without any effect on feeding behavior, the latter carboxy terminus fragment reportedly improves memory retention in a manner similar to that of NPY (5) Further, NPY_{13-36} given ICV is without any anxiolytic effect on the rat placed in conflict tests in contrast to that of NPY (6); however, this fragment does elevate the levels of DA and DOPAC in the cortex of the rat similarly to that of NPY (7). In this connection, carboxy terminus fragments also are more potent than NPY in inhibiting calmodulin-stimulated phosphodiesterase activity (8).

In the present study, we compared the central effect on feeding of a cleaved portion of the amino terminus of the molecule,

[1]Laboratorio de Fisiologia de la Conducta, Facultad de Medicina, Universidad de Los Andes, Merida, Venezuela.
[2]Requests for reprints should be addressed to R D Myers, Department of Pharmacology, ECU School of Medicine, Greenville, NC 27858-4354.

NPY_{1-27}, with that of native NPY. Two doses of both NPY and NPY_{1-27} were injected by the intracerebroventricular (ICV) route to induce feeding in the fully satiated rat (1, 12, 15). As a control for its molecular specificity, nondeprotected NPY was also injected ICV following the same experimental procedures.

METHOD

Male Sprague-Dawley rats (N = 5) weighing 409–456 g at the time of surgery were kept in an individual cage with a 12.12 hour light-dark cycle (0630–1830 h). Water and Purina rat pellets were provided ad lib throughout the experiments.

Surgical Procedures

After the rat was anesthetized with sodium pentobarbital (35–45 mg/kg) intraperitoneally and placed in a stereotaxic instrument, a 20-ga thin-walled guide tube 10 mm in length was implanted just dorsal to the right lateral cerebral ventricle according to methods described previously (18). The incisor bar was set 3 0 mm ventral to the interaural line, and the stereotaxic coordinates of Paxinos and Watson (25) were as follows: 0.8 mm caudal to bregma, 1.4 mm lateral to the sagittal sinus, and 3.0 mm below dura mater. To prevent occlusion of the guide, a 23-ga stylet was inserted in the tube. A period of 5 days or more elapsed prior to an experiment. The patency of each ventricular cannula was verified physiologically both at the beginning as well as at the end of a series of experiments. The test injection consisted of an ICV infusion by gravity flow of 10 μl of a standard artificial CSF solution (19) containing 10 μg NE-HCl (Sigma) which evokes spontaneous feeding in the fully satiated rat (20)

Synthesis of Peptides

Using Fmoc-BOP chemistry, NPY was synthesized by one of us (J.W N.) by means of an automated BioSearch model 9600 peptide synthesizer. The side chain protected amino acids (Milligen BioSearch) were· Tyr (tBu [tert-butyl]), Thr (tBu), Ser (tBu), Glx (Tmob [2,4,6-trimethoxybenzyl]), Asx (Tmob), Arg (Mtr [4-methoxy-2,3,6-trimethylbenzenesulfonyl]), His (Trt [triphenylmethyl]), Asp (Ot Bu [t-butyl ester]) and Lys (Boc [t-butyloxycarbonil]). The nonprotected amino acids used were Ile, Leu, Ala, Met, Pro and Gly. The final product was deprotected with a molar excess (10 ml/g) of TFA/thioanisole/ethanedithiol/anisole which serves to separate the peptide from the PAL resin and consequently removes side-chain protecting groups. After completion of the deprotection process, the compound was purified by means of a Waters model 600-E HPLC system using a 1 × 25 cm VYDAC 5 micron C_{18} column with 0.1% TFA->60% acetonitrile in 0.1% TFA, applying a linear gradient over 45 min The main peak detected by UV absorbance at 215 nm was collected and lyophilized repeatedly. Purity of the final product was estimated to be >95%. The NPY_{1-27} fragment of native NPY was synthesized identically except for premature termination of the sequence at amino acid position 27.

As a molecular control for the newly synthesized NPY used for these experiments, a portion of the synthesis was undertaken leaving the protected groups intact. This nondeprotected form of the native peptide was infused ICV in an identical manner so as to parallel that of the deprotected NPY. Commercial NPY, used as a test substance in selected pilot experiments and for comparison of purity of synthesized product, was obtained from Peninsula Laboratories.

ICV Injection of Compounds

Both NPY and NPY_{1-27} were given ICV in doses of either 5.0 or 10 μg/10 μl, whereas 10 μl of artificial CSF vehicle or 10 μg/10 μl of NPY nondeprotected were used as control solutions All solutions were prepared freshly on each day and filtered through a 0.22 μM millipore filter just prior to an ICV infusion which was made at 0700–0800 h.

A 23-ga injector needle was attached to the end of a length of PE 50 tubing which was filled with the respective control or peptide-containing solution Gravity flow into the ventricle was established in each rat by adjusting the depth of the injector needle to 1.0 mm or more below the tip of the guide tube (18). Following an ICV infusion of 10 μl of the solution over an interval of 30–40 s, the injector needle was kept in place for an additional 30 s, then removed and replaced by the stylet The tubing and each injector needle were always kept in 70% ethanol and flushed several times prior to their use.

To determine the effects on feeding behavior of native NPY compared to NPY_{1-27}, each rat was tested in the presence of the regular commercial diet (Purina Rat Chow) as well as chocolate-flavored biscuits (23) comprised of a wetted mixture of 38% ground Purina rat chow, 30% sucrose, 14% commercial evaporated milk and 18% instant chocolate powder (Nestle Quik). Each rat received both native NPY and NPY_{1-27} as well as the two control solutions, CSF and nondeprotected NPY in a randomized order. One week before the initiation of the experiments the rats were acclimated to a palatable food ration which was presented together with the standard commercial rat pellets. Fresh food was always inserted in the test chamber 1 0 hour before the ICV injection commenced. The cumulative food intake was recorded at 30 minutes and then every hour for 4 hours.

Histological and Statistical Analysis

In addition to the NE patency test (vide supra), at the end of the experiments the position of the ventricular cannula was verified following standard histological procedures. After the rat was perfused transcardially with 10% buffered neutral formalin, the brain was removed, sectioned and stained with cresyl violet to visualize the cannula track.

The data were analyzed by computer using the Stat-Mate software program One-way analyses of variance were performed by Newman-Keuls tests when appropriate. For comparisons of the results of two sets of food intake measures, Student *t*-tests also were performed. In both cases, a p value of <0.01 was considered to be statistically significant.

RESULTS

The ICV injection of either native NPY or the amino terminus peptide, NPY_{1-27}, induced behavioral activation of the rat which was followed by the spontaneous ingestion of its regular food. As shown in Fig. 1, the rate of feeding over the first 0.5 h of both NPY- and NPY_{1-27}-treated rats was virtually identical. However, throughout the 4.0 h period of observation (Table 1), the overall differences among all groups were statistically significant during the remaining time course of the experiments [e.g., $F(5,48) = 20.29$, $p<0.01$ at 0.5 h and $F(5,48) = 29.62$, $p<0.01$ at 1.0 h]

Following the ICV administration of either the lower 5.0 μg or higher 10.0 μg dose of NPY, the mean total intake of food consumed by the rats was greater than that after injections of the equivalent doses of NPY_{1-27}, i e., 2.4 ± 0.7 g versus $4\ 5 \pm 1.0$ g and 3.2 ± 0.4 g versus 6.5 ± 1.3 g, respectively (Table 1). Similarly, significant dose-related differences in feeding evoked by the ICV infusion of native NPY and NPY_{1-27} emerged by the 1 0 h interval, $F(3,35) = 21.34$, $p<0\ 01$, and persisted over the course of the test period In comparison to the central effect of the lower

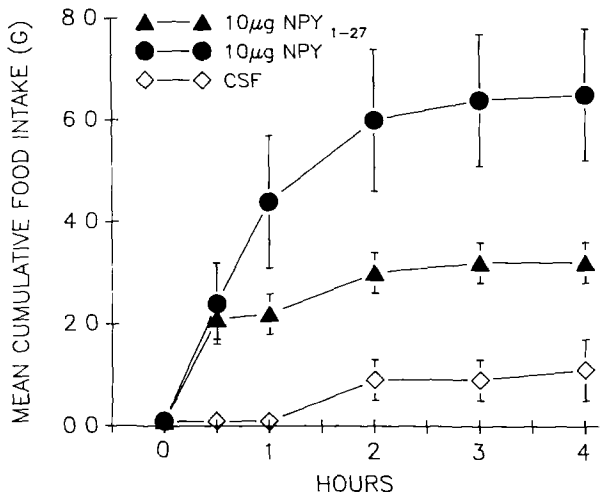

FIG 1 Mean ± S E cumulative intake of food in rats in which an ICV infusion of 5 0 or 10 0 μg NPY and NPY_{1-27} or CSF control vehicle was given in a volume of 10 μl at zero h Rats were provided regular commercial diet before the experiment and throughout the 4 0 h test interval

doses of NPY_{1-27} and NPY, ICV injection of either the control vehicle or nondeprotected NPY (Fig. 1) induced a significantly lower cumulative intake of food of 1.1 ± 0.6 and 1.8 ± 1.4 g, respectively (Table 1), by the 4 0 h period, $F(3,30) = 20.29$, $p<0.01$.

The latency of feeding in response to both lower and higher doses of NPY administered ICV was 12.8 ± 3.3 min and 12 5 ± 3.9 min, respectively. However, the latency to feed following the injection of NPY_{1-27} was 16 1 ± 6 3 min after the 5 0 μg dose but only 4.4 ± 0.8 min following the higher 10 μg dose. In contrast, the latencies of the feeding response after injection of the control solutions were substantially longer 47.3 ± 14.4 min after 10 μg nondeprotected NPY and 3.4 ± 0.5 h following the CSF vehicle.

As presented in Table 2, the ICV infusion of the 10 μg dose of NPY evoked an immediate and significantly greater intake of the chocolate-flavored food than that following the same dose of NPY_{1-27}, $F(1,23) = 122.86$, $p<0.01$. As shown in Fig. 2, the intake of the more palatable food increased sharply at the beginning of the test interval over that ingested by the rats given ICV injections of either NPY_{1-27} or control solutions [e g., $F(3,48) = 89.01$, $p<0$ 01 at 0.5 h]. Nevertheless, by the 4 0 h interval, the NPY_{1-27} induced a higher intake of the more palatable food than that evoked by the control CSF, $F(1,24) = 9.55$, $p<0.01$, but not following injection of the nondeprotected NPY (Fig 2).

A comparison of the mean intakes of the two foods offered to the rats is presented in Fig 3. Although the consumption of chocolate-flavored food induced by the 10 μg dose of NPY was greater within the first 0 5 h after the ICV injection than that of regular diet, $F(1,21) = 23$ 43, $p<0.01$, as well as at 1.0 h, $F(1,21) = 11.76$, $p<0$ 01, the intakes were not significantly different thereafter. Similarly, the rats' intake of the flavored food after injection of NPY_{1-27} was less than that of regular diet at 0.5 h but significantly greater at the 4.0 h interval, $F(1,19) = 20.25$, $p<0$ 01. The control rats ate significantly higher amounts of the chocolate-flavored food than the regular diet (Fig. 3) following the ICV administration of either CSF or nondeprotected NPY at the 4 0 h interval, $F(1,14) = 12.40$, $p<0.01$ and $F(1,22) = 53.97$, $p<0.01$, respectively

DISCUSSION

The present results demonstrate that the central administration of NPY_{1-27}, an amino terminus fragment of NPY, induces spontaneous feeding in the rat with a response latency similar to that of NPY. However, the dose response analysis showed that NPY is essentially twice as potent as NPY_{1-27} in evoking ingestive behavior Whereas NPY seems to produce a selective preference for chocolate-flavored food to the apparent point of nonsatiabil-

TABLE 1

MEAN ± S E CUMULATIVE INTAKE (GRAMS) OF COMMERCIAL DIET IN RATS AFTER ICV INJECTION OF NPY OR NPY_{1-27} (DOSE PER 10 μl VOLUME)

	Time Course (hours)				
Injection	0 5	1 0	2 0	3 0	4 0
NPY					
10 0 μg (N = 8)	2 4 ± 0 8	4 4 ± 1 3	6 0 ± 1 4	6 4 ± 1 3	6 5 ± 1 3
NPY_{1-27}					
10 0 μg (N = 10)	2 1 ± 0 4	2 2 ± 0 4	3 0 ± 0 4	3 2 ± 0 4	3 2 ± 0 4
NPY					
5.0 μg (N = 8)	1 6 ± 0 5	2 6 ± 0 4	4 0 ± 0 9	4 1 ± 0 9	4 5 ± 1 0
NPY_{1-27}					
5 0 μg (N = 10)	1 4 ± 0 6	1 7 ± 0 6	2 1 ± 0 8	2 3 ± 0 7	2 4 ± 0 7
NPY nondeprotected					
10 0 μg (N = 5)	1.0 ± 0 6	1 6 ± 1 2	1 6 ± 1 2	1 8 ± 1 4	1.8 ± 1 4
CSF Controls					
(N = 8)	0 0	0 0	0 9 ± 0 4	0 9 ± 0 4	1 1 ± 0 6

N = Number of experiments

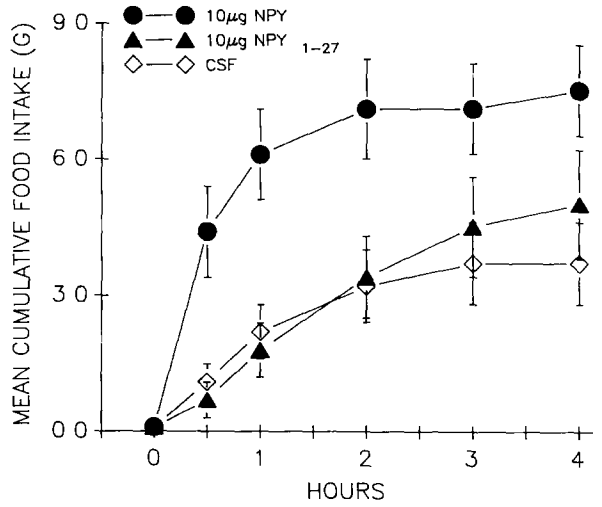

FIG 2 Mean ± S E cumulative intake of food in rats given an ICV infusion of NPY, NPY_{1-27} or nondeprotected NPY, all in a dose of 10 0 μg, or CSF control vehicle at zero h The regular food was replaced by chocolate-flavored biscuits offered to the rats before the experiment and throughout the 4 0 h test interval

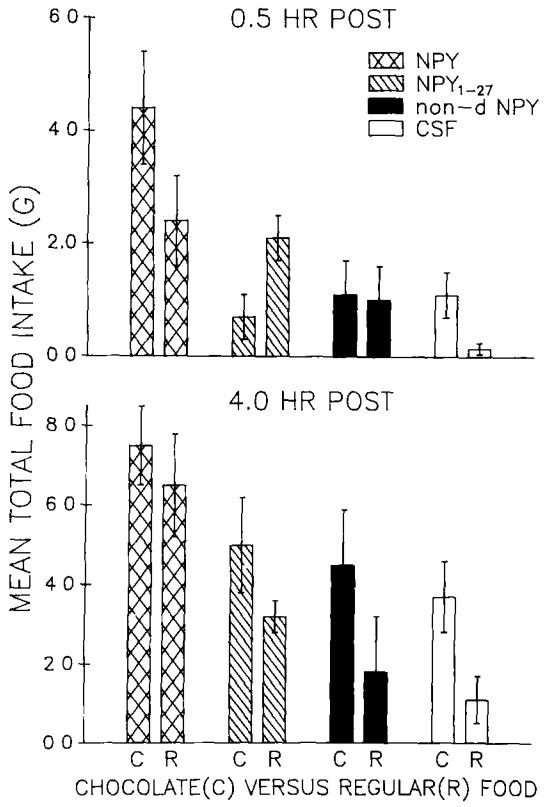

FIG 3 Histogram comparing mean ± S E total intakes of chocolate-flavored food (C) versus regular diet (R) at 0 5 h (top) and 4 0 h (bottom) after ICV infusion at zero h of 10 0 μg NPY, NPY_{1-27} or nondeprotected NPY or of the CSF control vehicle

ity (22,23), NPY_{1-27} does not arouse a special preference for this highly palatable and nutritionally enriched food. Apparently, therefore, the segment of feeding behavior mediated by gustatory and/or olfactory stimuli appears to be affected to a much greater degree by native NPY than NPY_{1-27}. This suggests that amino acids 28–36 play an important role in governing the magnitude of food ingested by the rat.

We envisage that NPY possesses a dual function in the central mechanism underlying the regulation of feeding behavior. First, the peptide ostensibly modifies the intrinsic carbohydrate-contingent drive for calories in that the rat consumes its regular food readily after NPY is injected ICV. In fact, Leibowitz and colleagues showed that NPY injected in the PVN of the rat evokes a discrete preference for carbohydrate over fat and protein (29). Secondly, the peptide apparently shifts the gustatory or olfactory or both thresholds underlying the sensory component of feeding, because the central action of NPY is augmented significantly by the palatability of the food. Since NPY_{1-27} appears to stimulate only the drive for calories and its effect is relatively unchanged

TABLE 2

MEAN ± S E CUMULATIVE INTAKE (GRAMS) OF CHOCOLATE-FLAVORED FOOD IN RATS AFTER ICV INJECTION OF NPY OR NPY_{1-27} (DOSE PER 10 μl VOLUME)

	Time Course (hours)				
Injection	0 5	1 0	2.0	3 0	4 0
NPY					
10 0 μg (N = 14)	4 4 ± 1 0	6 1 ± 1 0	7 1 ± 1 1	7 1 ± 1 0	7 5 ± 1.0
NPY_{1-27}					
10 0 μg (N = 10)	0 7 ± 0 4	1 8 ± 0.6	3 4 ± 0.9	4 5 ± 1 1	5 0 ± 1 2
NPY nondeprotected					
10.0 μg (N = 10)	1 1 ± 0 6	2 0 ± 1 0	4 0 ± 1 3	4 5 ± 1 4	4 5 ± 1 4
CSF Controls (N = 15)	1 1 ± 0 4	2 2 ± 0 6	3 2 ± 0 8	3 7 ± 0 9	3.7 ± 0.9

N = Number of experiments.

by the flavor of the proffered food, the amino acids 28–36 moiety of the NPY molecule must contribute, therefore, to gustatory-olfactory mechanisms involved in the control of feeding. In terms of the issue of palatability, the neuronal mechanism could revolve about a sensory system upon which NPY acts either to increase the acceptability of a less appetizing food substance or to further enhance the intake of an already palatable food.

Because of the 10-min latency preceding feeding after an ICV injection of NPY, it is probable that the peptide does not act directly on either pre- or postsynaptic elements of neurons within the paraventricular or ventromedial nuclei or other periformical structures implicated in the ingestion of food (11). One possibility is that NPY reciprocally stimulates the synthesis and/or release of a catecholamine or serotonin within medial hypothalamic neurons. Recently, phasic changes in the in vivo profile of activity of these monoamines in NPY-containing perfusate collected from the PVN of the feeding rat have been demonstrated (22,24). This could explain the delay in the intracerebral effect of the peptide on the feeding response since NE given either directly into the PVN (10,11) or by the ICV route (20) evokes feeding characterized by a much more rapid onset and shorter duration than that of NPY Interestingly, an olfactory stimulus coupled with an odorous food such as peanut butter exerts an intense effect on the release of a catecholamine neurotransmitter from the same area of the medial hypothalamus (21) at which NPY exerts its potent action on the feeding response. The coexistence of NPY and norepinephrine (NE) in neurons of the brainstem with their ascending fibers innervating the medial hypothalamus (4,26) would support this supposition.

In terms of the cellular mechanism whereby NPY or NPY_{1-27} mobilizes the feeding response, we envisage that the peptide may inhibit the local activity of medial hypothalamic neurons which comprise the rostral terminal input from vagal afferent neurons of gastric origin and which signal the condition of satiety (27). Such an inhibition of satiety neurons by NPY would thus suppress the satiety mechanism and consequently result in feeding. In this connection, when NPY is injected ICV, the ingestive response is not blocked by cholecystokinin injected either peripherally or centrally (9,17). This suggests that the hunger-sensory signals generated centrally by an elevated intracerebral level of NPY may override peripheral satiety sensors. In this connection, structurally related analogues of NPY given ICV to the rat evoke different cumulative intakes of food as well as significant differences in time spent eating (2) This corresponds to our finding in which both NPY and NPY_{1-27} evoke the same sharp increase in feeding initially, but the latter peptide is essentially without effect after 30 min.

In summary, the present results show that NPY_{1-27} did not augment the intake of chocolate-flavored food above that of the control level. Amino acids $_{28-36}$ of native NPY are likely involved in an alteration of the sensory threshold for a given foodstuff and may be as important as the nature of the micronutrient itself Thus, the distinction between the mechanism of action of NPY_{1-27} and native NPY may rest simply in the greater shift in sensory threshold so that the food presented to the animal either tastes better or smells better or both.

ACKNOWLEDGEMENTS

This research was supported in part by National Science Foundation Grant BNS 84-10663 to R D M We thank Amy K Roscoe, Miles F Lankford and Sherry A Leonard for their excellent technical assistance

REFERENCES

1 Clark, J. T , Kalra, P S , Crowley, W R , Kalra, S P Neuropeptide Y and human pancreatic polypeptide stimulate feeding behavior in rats Endocrinology 115 427–429, 1984
2 Clark, J T , Sahu, A , Kalra, P S , Balasubramaniam, A , Kalra, S P Neuropeptide Y (NPY)-induced feeding behavior in female rats comparison with human NPY ([Met[17]]NPY), NPY analog ([norLeu[4]]NPY) and peptide YY Regul. Pept 17 31–39, 1987
3 Donoso, V., Macarena, S , St-Pierre, S , Huidobro-Toro, J. Neuropeptide Y (NPY), an endogenous presynaptic modulator of adrenergic neurotransmission in the rat vas deferens Structural and functional studies Peptides 9 545–553, 1988
4 Everitt, B J , Hokfelt, T , Terenius, L , Tatemoto, K., Mutt, V , Goldstein, M Differential coexistence of neuropeptide Y (NPY)-like immunoreactivity with catecholamines in the central nervous system of the rat. Neuroscience 11 443–462, 1984
5 Flood, J F , Morley, J E Dissociation of the effects of neuropeptide Y on feeding and memory Evidence for pre- and postsynaptic mediation Peptides 10 963–966, 1989
6. Heilig, M , Soderpalm, B , Engel, J A , Widerlov, E Centrally administered neuropeptide Y (NPY) produces anxiolytic-like effects in animal anxiety models Psychopharmacology (Berlin) 98·524–529, 1989
7 Heilig, M , Vecsei, L , Wahlestedt, C.; Alling, C., Widerlov, E Effects of centrally administered neuropeptide Y (NPY) and NPY_{13-36} on the brain monoaminergic systems of the rat J Neural Transm 79 193–208, 1990
8 Ishiguro, T , Fujita, S , Okano, R., Kato, N , Eguchi, C , Matsuo, H Synthesis of peptide fragments of neuropeptide Y Potent inhibitors of calmodulin-stimulated phosphodiesterase Chem Pharm Bull 36 2720–2723, 1988
9 Kalra, S P , Dube, M. G , Kalra, P S Continuous intraventricular infusion of neuropeptide Y evokes episodic food intake in satiated female rats Effects of adrenalectomy and cholecystokinin Peptides 9 723–728, 1988
10 Leibowitz, S F. Hypothalamic neuropeptide Y and galanin Functional studies of coexistence with monoamines In Mutt, V , Fuxe, K , Hokfelt, T , Lundberg, J M , eds Neuropeptide Y New York Raven Press, 1989 267–281
11 Leibowitz, S F , Myers, R D The neurochemistry of ingestion Chemical stimulation of the brain and in vivo measurement of transmitter release In Toates, F M , Rowland, N E , eds Techniques in the behavioral and neural sciences, vol 1, Feeding and drinking Amsterdam Elsevier, 1987
12 Levine, A S., Morley, J E Neuropeptide Y A potent inducer of consummatory behavior in rats Peptides 5 1025–1029, 1984
13 Magdalin, W , Stanley, B G , Fournier, A , Leibowitz, S F A structure-activity analysis of neuropeptide Y-induced eating behavior Soc Neurosci Abstr 15 895, 1989
14 Martel, J C , Fournier, A , Forest, M , St-Pierre, S., Quirion, R Structure-affinity study of neuropeptide Y analogs in the rat brain Soc Neurosci Abstr. 15 987, 1989
15 Miner, J L , Della-Fera, M A , Paterson, J A , Baile, C A Lateral cerebroventricular injection of neuropeptide Y stimulates feeding in sheep Am J Physiol 257 R383–R387, 1989
16. Morley, J E , Flood, J F Effects of NPY on memory processing and ingestive behaviors In· Mutt, V , Fuxe, K , Hokfelt, T , Lundberg, J M , eds Neuropeptide Y. New York Raven Press, 1989 303–312
17 Morley, J E., Levine, A S., Gosnell, B A , Kneip, J , Grace, M Effect of neuropeptide Y on ingestive behaviors in the rat Am J Physiol 252 R599–R609, 1987
18 Myers, R. D Chronic methods Intraventricular infusion, cerebrospinal fluid sampling and push-pull perfusion In Myers, R D , ed Methods in psychobiology, vol III New York Academic Press, 1977 281–315
19 Myers, R D Handbook of drug and chemical stimulation of the brain New York Van Nostrand Reinhold Company, 1974
20 Myers, R D , Yaksh, T L Feeding and temperature responses in the unrestrained rat after injections of cholinergic and aminergic substances into the cerebral ventricles Physiol Behav 3 917–928, 1968

21 Myers, R D , McCaleb, M L , Hughes, K. A. Is the noradrenergic "feeding circuit" in hypothalamus really an olfactory system? Pharmacol. Biochem. Behav 10:923–927, 1979
22 Paez, X , Myers, R D Non-satiable feeding induced by multiple perfusions of neuropeptide Y (NPY) in medial hypothalamus of the rat FASEB J 4 882, 1990
23 Paez, X., Myers, R D Non-satiable feeding evoked in rats by neuropeptide-Y perfused repeatedly in the hypothalamus Peptides, in press, 1991
24 Paez, X , Lankford, M , Myers, R D Temporal profile of norepinephrine, dopamine and serotonin activity during feeding induced by NPY perfused in medial hypothalamus in rats Am J Physiol , in preparation, 1991
25 Paxinos, G , Watson, C The rat brain in stereotaxic coordinates Sydney Academic Press, 1982
26 Sawchenko, P E , Swanson, L W , Grzanna, R , Howe, P R C , Bloom, S. R , Polak, J M Colocalization of neuropeptide Y immunoreactivity in brainstem catecholaminergic neurons that project to the paraventricular nucleus of the hypothalamus. J Comp Neurol 241 138–153, 1985
27 Smith, G P , Jerome, C , Norgren, R Afferent axons in abdominal vagus mediate satiety effect of cholecystokinin in rats. Am J Physiol 18 R638–R641, 1985
28 Stanley, B G , Leibowitz, S F Neuropeptide Y Stimulation of feeding and drinking by injection into the paraventricular nucleus Life Sci 35.2635–2642, 1984
29 Stanley, B G , Anderson, K. C , Grayson, M H , Leibowitz, S F Repeated hypothalamic stimulation with neuropeptide Y increases daily carbohydrate and fat intake and body weight gain in female rats. Physiol. Behav 46 173–177, 1989