rissia and *Physella* (Pulmonata); and *Eubrianix* (Psephenidae)], except for midge (Chironomidae) larvae, on the top and bottom of each tile. Midges were counted on only one tile because of their high abundance. We collected benthic algae (largely a mixture of *Cladophora glomerata, Nostoc* spp., and *Epithemia* spp.) from one randomly selected tile in each treatment by scraping the tile with a razor blade and measuring ash-free dry weight in the laboratory. All floating algal mats in a channel were collected with an aquarium net, spun in a salad spinner for a standard 50 turns to remove excess water, and weighed. Subsamples of floating algae were collected, dried, weighed, and analyzed through measurement of ash-free dry weight to calibrate wet mass with ash-free dry weight. We used a blocked, two-way MANOVA to test for community-wide differences among treatments, and then tested for the specific differences predicted a priori by the model, using one-tailed paired *t* tests.

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Appetite-Suppressing Effects of Urocortin, a CRF-Related Neuropeptide

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The neuropeptide corticotropin-releasing factor (CRF) is well known to act on the central nervous system in ways that mimic stress and result in decreases in exploration, increases in sympathetic activity, decreases in parasympathetic outflow, and decreases in appetitive behavior. Urocortin, a neuropeptide related to CRF, binds with high affinity to the CRF_2 receptor, is more potent than CRF in suppressing appetite, but is less potent than CRF in producing anxiety-like effects and activation. Doses as low as 10 nanograms injected intracerebroventricularly were effective in decreasing food intake in food-deprived and free-feeding rats. These results suggest that urocortin may be an endogenous CRF-like factor in the brain responsible for the effects of stress on appetite.

Corticotropin-releasing factor, a neuropeptide isolated from the mammalian brain (*1*), has been implicated in the mediation of the integrated physiological response to stress (*2*, *3*). When released from the median eminence into the hypophysial portal system, CRF exerts powerful effects to stimulate the release of adrenocorticotropic hormone (ACTH) from the pituitary; thus, as a hypothalamic-releasing factor, CRF regulates glucocorticoid responses to stress (*2*). When infused within the central nervous system, CRF mimics most of the behavioral responses to stress (*3*). Central administration of CRF increases arousal, as measured by changes in cardiovascular parameters (*4*) and locomotor activity (*5*), and, like stress, produces "anxiogenic-like" and anorectic effects in a variety of behavioral paradigms (*3*, *6*). These effects are largely independent of the activation of ACTH and corticoids (*7*), suggesting a direct action on brain CRF receptors implicated in behavioral responses to stressors. Until recently, only one endogenous CRF had been isolated from the mammalian brain, suggesting that only CRF itself was directly involved in stress-induced behavioral changes, including anorexia. However, the identification in the mammalian brain of another neuropeptide of the CRF family, urocortin (UCN) (*8*), has reopened the question, suggesting a potential physiological role for endogenous UCN in activating central CRF receptors.

The major cellular sites of expression of UCN in the rat brain were detected in the Edinger-Westphal nucleus, the lateral superior olive, the lateral hypothalamus, and the supraoptic nucleus, all regions that do not contain CRF mRNA (*8*). Binding studies have shown that UCN binds with very high affinity to both the identified CRF receptors, CRF_1 (*9*) and CRF_2 (*10*), but has a much higher affinity for the CRF_2 receptor than CRF, and the distribution of UCN fibers correlates well with the distribution of the CRF_2 receptor but not the CRF_1 receptor (*8*). These observations led to the hypothesis that central infusion of UCN may produce behavioral effects that only partially overlap with those produced by CRF. To test this hypothesis, we analyzed the effects of a wide range of concentrations of UCN, urotensin I, and r-h CRF (0.01 to 10.0 μg per animal) after they were infused into the cerebral ventricle (ICV) of rats previously implanted with intracerebroventricular cannulas.

Rats were food-deprived for 24 hours and food consumption was tested for 2 hours after ICV injection of vehicle or different doses of the peptide. UCN consis-

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Table 1. Effect of central and peripheral administration of urocortin on mean blood pressure. Data are represented as mean ± SEM ($n = 5$). Changes in mean arterial blood pressure (ΔMAP) were calculated as the difference between the basal values taken before urocortin administration. Mild hypertensive effects were obtained after central injection, whereas peripheral administration exerted prolonged hypotensive effects. No significant change in myocardial contractility was recorded after central administration (*22*). Data were analyzed by using analysis of variance (ANOVA) followed by Tukey's test. ICV, intracerebroventricular; SC, subcutaneous.

Urocortin dose (μg)	Time course of ΔMAP (mm Hg)		
	30 min	60 min	90 min
Central (ICV) administration			
0	−0.9 ± 0.04	1.5 ± 0.02	0.8 ± 0.11
1.0	6.9 ± 2.50	0.8 ± 0.12	0.2 ± 0.05
10.0	12.2 ± 1.32*	6.3 ± 0.15	1.8 ± 0.14
Peripheral (SC) administration			
0	1.5 ± 0.04	1.2 ± 0.02	−0.8 ± 0.15
10.0	−17.8 ± 1.44*†	−26.7 ± 2.31*†	−32.7 ± 2.61*†

*$P < 0.01$ versus vehicle; †$P < 0.01$ versus central administration, at the same urocortin dose.

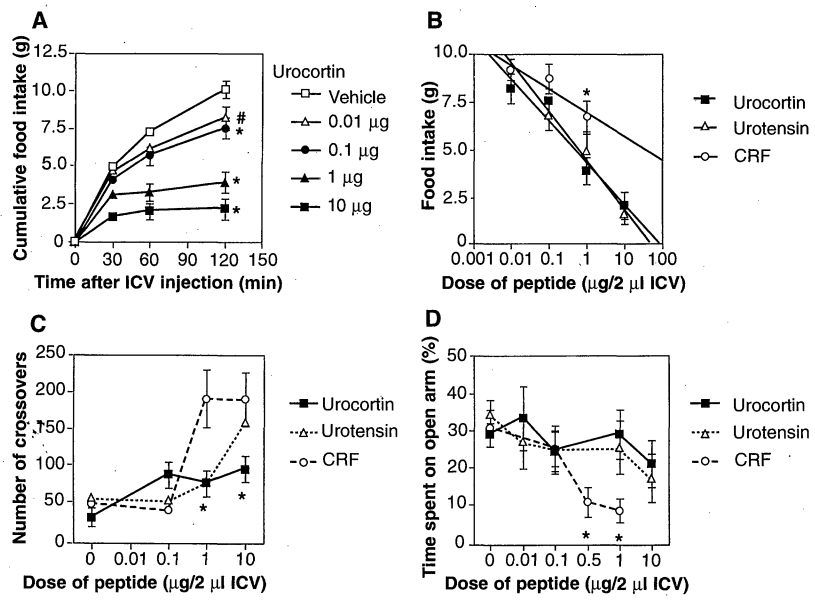

Fig. 1. (**A**) Effects of various doses of UCN on food intake in rats previously food-deprived for 24 hours. UCN at doses greater than 0.1 μg significantly attenuated food consumption (*, $P < 0.05$ compared with the vehicle value, Newman-Keuls test; #, $P < 0.05$ Student's t test, vehicle versus treatment). (**B**) Comparison of the effects of various doses of UCN, urotensin, and CRF on food intake as measured 120 min after peptide ICV infusion. Regression analysis and test for parallelism indicates that CRF was significantly ($P < 0.05$) less effective than UCN and urotensin in suppressing food intake after 24-hour food deprivation. (**C**) Effects of various doses of UCN, urotensin, and CRF on locomotor activity [measured as the number of crossovers during a 3-hour period (*18*)]. All peptides produced significant increases in crossovers at the doses of 1 μg and 10 μg ($P < 0.01$, Newman-Keuls test when compared with vehicle). At these doses, UCN locomotor scores were significantly lower than those of CRF (*, $P < 0.05$, Newman-Keuls test compared with CRF values). (**D**) Effects of UCN, urotensin, and CRF on the elevated plus-maze. For UCN and urotensin, the rats were injected ICV with the peptides and tested for 5 min in the maze. The time spent in the open arm was used as dependent measurement to estimate the drive to explore the mildly aversive open arms. The data for CRF is redrawn from (*21*). Here the rats were injected 30 min before testing, and CRF reduced the time spent in the open arm at doses of 0.5 to 1 μg, whereas no significant effect was seen in the same dose range for UCN and urotensin (*, $P < 0.05$ compared with vehicle values, Newman-Keuls test).

Table 2. Effect of urocortin (ICV) on water intake in water-deprived animals. Data are represented as mean ± SEM ($n = 7$ for each group) of cumulative water intake in rats deprived of water for 24 hours.

Urocortin dose (μg)	Time after injection		
	30 min	60 min	90 min
Vehicle	14.4 ± 1.1	16.9 ± 0.8	19.3 ± 1.5
0.01	15.6 ± 0.8	17.3 ± 1.5	17.6 ± 1.6
0.1	14.7 ± 1.7	15.0 ± 1.7	16.0 ± 1.8
1.0	10.6 ± 0.9*	10.7 ± 0.9**	10.7 ± 1.0**

*$P < 0.05$; **$P < 0.01$, Student's t test.

Table 3. Effect of urocortin (ICV) on food intake in nondeprived animals. Values represent mean ± SEM of the number of 45-mg food pellets ingested over each time period ($n = 6$ rats). Each rat received each dose (*16*).

Urocortin dose (μg)	Time after injection			
	0 to 3 hours	0 to 6 hours	0 to 12 hours	7 to 12 hours
Vehicle	113.2 ± 12.6	235.3 ± 16.7	399.8 ± 37.5	164.5 ± 24.9
0.01	125.3 ± 11.0	242.2 ± 26.8	398.3 ± 33.5	156.2 ± 32.5
0.1	69.2 ± 15.4**	142.2 ± 22.8**	303.8 ± 48.0*	161.7 ± 33.2
1.0	18.2 ± 4.9**	54.8 ± 19.1**	123.7 ± 32.1**	68.0 ± 26.4*

*$P < 0.05$; **$P < 0.01$, paired t test preplanned comparison after a significant overall within-subjects analysis of variance.

tently suppressed food consumption in a dose-related manner (Fig. 1, A and B) (*11*), showing a potency similar to urotensin [UCN ED_{50} (median effective dose) = 0.19 μg; urotensin ED_{50} = 0.27 μg]. UCN was significantly more potent than CRF in producing its anorectic effects (CRF ED_{50} = 6.82 μg; Fig. 1B). Indeed, previous studies have shown that 5 μg of CRF is required to produce major effects on food intake in food-deprived rats (*12*).

To rule out the possibility that the suppression of food intake obtained with central infusion of UCN is produced by indirect effects due to the leakage of the peptide into the peripheral blood stream, we measured arterial blood pressure in freely moving rats after central administration of UCN (1 to 10 μg) (*13*). UCN and the other CRF-related peptides are known to produce prolonged hypotension when administered systemically (intravenously) and transient hypertension when administered centrally (*4*, *8*). In the present experiment, mild hypertensive effects were recorded after UCN ICV infusion, whereas prolonged hypotensive effects were observed only after subcutaneous administration of the same dose (Table 1). These observations support the hypothesis that UCN-induced anorexia is not mediated by nonspecific central effects associated with reduced blood pressure. UCN did not decrease water intake in fluid-deprived rats at doses of 0.01 and 0.1 μg (Table 2), further illustrating the specificity of the appetite-suppressing effects. UCN also failed to produce a taste aversion except at the dose of 1 μg ICV (*14*), again suggesting selective and specific appetite suppression effects at low doses.

The appetite-suppressing effects of UCN were further studied in rats that were not deprived of food. After a period of training, six animals were allowed to work to obtain 45-mg pellets and 100 μl of water ad libitum during the dark phase of the light-dark cycle using a nose-poke response (*15*). We observed significant decreases in food and water intake with doses as low as 100 ng ICV, and UCN decreased food and water intake for up to 12 hours, depending on the dose (Table 3). UCN decreased the meal size (number of pellets per bout) and frequency of meals (bouts) with significant effects at 10 ng for meal size and 1 μg for meal bouts (Table 4). At 1 μg, meal bouts were virtually abolished for 6 hours (*15*). Water intake paralleled that of food intake with and without peptide treatment. This selective effect on meal size with no effect on the number of bouts at the low doses of UCN is identical to that observed with the appetite-suppressing drug *d*-fenfluramine (Table 4), thus demonstrating a behavioral profile of an endogenous brain peptide identical to that of a known anti-appetite agent (*16*).

More interesting was the observation that ICV administration of UCN did not produce "anxiogenic-like" behavior when rats were tested in the elevated plus-maze (Fig. 1D), a test of emotionality in rodents that has been shown to be sensitive to CRF (*17*). In this paradigm, urotensin was active only at the highest dose tested (10 μg), whereas CRF displayed a significant effect at low doses (0.5 μg) (*3*). UCN was also significantly less effective than CRF in activating locomotor behavior in a familiar environment (Fig. 1C) (*18*).

These results suggest that UCN at low doses has mildly activating, powerful anorectic effects with very low anxiogenic-like activity or aversive effects. This profile of behavioral activity partially overlaps with the effects of urotensin, a nonmammalian peptide, and to a lesser extent, with those of CRF.

The neuropharmacological mechanisms accounting for the differential behavioral effects of UCN compared with CRF are at present difficult to explain. However, the higher affinity of UCN and urotensin for the CRF_2 receptor with respect to CRF may partly explain some of the differences between UCN and CRF in their central effects (*8*). In addition, the brain distribution of the 411–amino acid variant of CRF_2, $CRF_{2\alpha}$, is restricted to a limited set of brain areas, including lateral septum, ventromedial hypothalamus, and medial amygdaloid nucleus (*10*), and is consistent with fibers and terminals stained with antiserum to UCN or urotensin (*8*). Interestingly, all these brain regions have been implicated in the control of food consumption and digestive functions (*19*).

Finally, UCN has a high affinity for the CRF binding protein (*8*); thus, a particular combination of differential binding protein–CRF_2 receptor distribution (*20*) could explain the selective functional effects. For example, there is some evidence that the CRF binding protein and the CRF_1 receptor are more localized cortically than subcortically, which would decrease the effective concentration of UCN at sites where CRF_1 receptors are localized. Thus, in subcortical regions where CRF_2 receptors are primarily localized, the binding protein is less abundant and these subcortical CRF_2 sites may mediate the anorexic effects of UCN.

The involvement of an endogenous ligand for CRF receptors in anorexia was also suggested by the effects of the CRF antagonist α-helical CRF(9–41) in reversing the attenuation of food consumption induced by stress and in enhancing the increase of food consumption induced by food deprivation or central administration of neuropeptide Y, a potent orexigenic agent (*6*). Because α-helical CRF(9–41) blocks the effects of UCN, CRF, urotensin, and sauvagine on both CRF_1 and CRF_2 receptors in vitro (*8*, *10*, *11*), definitive selective antagonist effects are still unavailable. However, these data do suggest that the role of UCN in the behavioral responses previously attributed to CRF may be ultimately assessed pharmacologically with selective CRF antagonists (*3*) or in mice having null mutations for specific receptors and ligands. The selective functional effects on food intake of this mammalian peptide member of the CRF family opens up opportunities for the exploration of the role of stress and the CRF systems in appetite regulation.

Table 4. Effect of urocortin (ICV) and *d*-fenfluramine (administered intraperitoneally) on meal bouts and meal size from 0 to 6 hours in nondeprived rats. Meal bouts were arbitrarily defined as continuous nose pokes for food pellets with no inter-poke interval greater than 60 s and a minimum inter-bout interval of 15 min (*17*). Meal size was defined as the number of pellets earned per bout. For urocortin, six rats were tested at 3-day intervals with all doses of urocortin in a Latin-square design. For *d*-fenfluramine, six rats were tested at 5-day intervals in a Latin-square design. Dose of *d*-fenfluramine is in milligrams per kilogram of body weight.

Dose	Number of bouts	Mean pellets per bout
	Urocortin	
Vehicle	5.5 ± 0.8	29.5 ± 5.8
0.01 μg	6.3 ± 0.7	21.0 ± 2.0*
0.1 μg	5.8 ± 1.1	18.2 ± 1.1**
1.0 μg	2.3 ± 0.7**	11.0 ± 3.1**
	d-*Fenfluramine*	
Vehicle	6.2 ± 0.5	33.5 ± 4.7
0.75 mg/kg	6.5 ± 0.7	25.8 ± 5.8
1.5 mg/kg	5.0 ± 0.3	16.3 ± 0.8*
3.0 mg/kg	1.7 ± 0.8**	9.8 ± 3.7**

*$P < 0.05$; **$P < 0.01$, paired *t* test.

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11. For the deprivation-induced feeding experiment, rats (Wistar) were implanted with unilateral guide cannulas (7 mm long) 1 mm above the lateral ventricle while under halothane anesthesia. The side of the brain for implantations was alternated so as to eliminate hemispheric biases. After at least 7 days of recovery from surgery, the animals were food-deprived 24 hours before the experiment with free access to water. Six hours before the beginning of the experiment they were individually housed in cages without bedding. Animals were injected ICV with UCN (0.01, 0.1, 1, or 10 μg/2 μl) or vehicle. Injections were unilateral and performed over a 1-min period by gravity, that is, the tubing containing the peptide was raised until flow began. No asymmetries, or untoward effects, were observed with these volumes and rate of injection. A few minutes after the injection, preweighed food (20 g) was provided. The remaining food, including the spillage, was weighed 30, 60, and 120 min after the injection, and behavior was observed. Weight of the food at different times and cumulative amount of food eaten were calculated. For the water deprivation–induced drinking experiment, the animals were prepared as above and water-deprived for 24 hours. After the ICV injections, water was provided in Richter tubes, and water intake was measured at 30, 60, and 120 min after the injection. Food was not available during this period.
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13. Experiments were performed on individually housed, conscious, freely moving Wistar rats 24 hours after implantation of femoral arterial catheters for monitoring blood pressure. Food and water were available ad libitum. One hour before injection, the catheter was connected with a transducer. Arterial blood pressure was monitored on a pen recorder, and heart rate was computed from the blood pressure pulses with a biotachometer. The ICV injection unit was put in place 15 min before injection, and UCN (1 and 10 μg/2 μl) or vehicle were infused ICV in a randomized sequence. Depending on the dose, injections were spaced at 30-min to 1-hour intervals after the complete recovery of arterial blood pressure to the basal value. Subcutaneous injection of UCN (10 μg/ml) or vehicle at the scapular region was performed after the ICV injection session.
14. Rats were subjected to a two-bottle taste aversion test where UCN was injected ICV after exposure to a highly palatable saccharin ingestion session two times. Animals (vehicle $n = 7$; 0.1 μg of UCN, $n = 8$;

1.0 μg of UCN, $n = 8$) had 30-min access to water (days 1 through 6, 8, and 10) or saccharin solution (days 7 and 9) daily for the duration of an 11-day multiple-pairing test conditioning procedure. UCN was administered ICV on days 7 and 9 immediately after access to the saccharin. On day 11, all rats chose between two choices (water or saccharin). A significant taste aversion was observed only at 1.0 μg of UCN. Mean ± SEM milliliters of saccharin intake during the two-bottle test was as follows: vehicle, 16.4 ± 4.5 ml; 0.1 μg of UCN, 12.3 ± 3.5 ml; and 1.0 of μg UCN, 1.1 ± 0.6 ml. Water intake during the same two-bottle test was as follows: vehicle, 8.1 ± 3.1 ml; 0.1 μg of UCN, 9.6 ± 2.3 ml; and 1.0 μg of UCN, 20.3 ± 1.2 ml. Water intake baseline on days 1 through 6, when the animals had access only to water, was 19.1 ± 1.3 (vehicle), 21.2 ± 1.5 ml (0.1 μg of UCN), and 22.2 ± 1.8 ml (1.0 μg of UCN).

15. The nose-poke apparatus consists of an acrylic plastic chamber and wire mesh floor (25 cm by 25 cm by 25 cm) enclosed within a sound- and light-attenuating box. Two holes, one for food and one for water, were made (2 cm above the floor) in two opposite side walls of the chamber. Each nose poke in either the food or water hole activated the delivery of a 45-mg pellet or 100 μl of water, respectively, into a food or water tray situated next to each hole. Nose pokes were recorded by photocell beam interruptions and a microcomputer. Rats (Wistar) were exposed to one session daily for 20 hours and trained during several days to obtain an appropriate baseline level (±20% total food intake from day to day). Six animals were injected ICV with UCN in a within-subjects design; for example, each rat received each dose (0.01, 0.1, and 1.0 μg/2 μl) and vehicle according to a Latin-square design with a minimum of 3 days between injections. Injections were made at 19:30 hours, 90 min after the onset of the dark cycle (12 hours, 6 p.m. to 6 a.m.). Water intake followed food intake on a prandial basis. Results showed that nose pokes for water showed the same decrease as food intake at the same doses of UCN. The data were analyzed at 3, 6, and 12 hours after the injections. Meals or bouts of feeding were defined as continuous sequences of nose-poking for 45-mg food pellets with no inter-poke interval greater than 60 s and a minimum inter-bout interval of 15 min. This analysis is similar to that reported by others, and meals or bouts corresponded to those of visual inspection of the event recorded. J. A. Grinker, A. Drewnowski, M. Enns, H. Kissileff. *Pharmacol. Biochem. Behav.* **12**, 265 (1980).
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18. The locomotor apparatus consisted of 16 wire mesh cages (20 cm by 25 cm by 36 cm) with two horizontal infrared photocell beams located across the long axis of the cage 2 cm above the floor and 16 cm from one another. Beam interruptions and crossovers were recorded (beam 1 broken followed by beam 2 and vice versa) by computer and printed out every 10 min. Activity was recorded over 3 hours, and behavior was observed every 30 min. The day before the experiment, rats were habituated for 1 hour to the room and then for 5 hours to the testing cages. On the testing day, after a 90-min habituation period, rats were injected ICV with UCN (0.1, 1, and 10 μg/2 μl) or vehicle, and the locomotor activity was monitored for the next 3 hours.
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The Mental Representation of Hand Movements After Parietal Cortex Damage

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Recent neuroimagery findings showed that the patterns of cerebral activation during the mental rehearsal of a motor act are similar to those produced by its actual execution. This concurs with the notion that part of the distributed neural activity taking place during movement involves internal simulations, but it is not yet clear what specific contribution the different brain areas involved bring to this process. Here, patients with lesions restricted to the parietal cortex were found to be impaired selectively at predicting, through mental imagery, the time necessary to perform differentiated finger movements and visually guided pointing gestures, in comparison to normal individuals and to a patient with damage to the primary motor area. These results suggest that the parietal cortex is important for the ability to generate mental movement representations.

Prediction is essential to many aspects of motor behavior, from postural compensation to the tracking of moving objects and the planning of a complex trajectory. The capacity of the central nervous system to simulate and anticipate the behavior of the motor apparatus is a central issue not only in experimental and computational studies of motor control (*1*), but also in the study of mental processes. Humans can use this capacity to improve a motor skill or induce sensorimotor plasticity through mental rehearsal (*2*). Decety and his colleagues have shown that motor imagery can be used to predict the time needed to complete a movement, and that the mental reenactment of an effortful exercise causes the same vegetative changes as its actual performance (*3*). Studies of cerebral metabolic activity have demonstrated that most of the regions that are active during overt movement execution such as the parietal and premotor cortices, the basal ganglia, and the cerebellum are active during mental simulation as well (*4*).

These results suggest that motor impairments caused by a cerebral lesion might also affect mentally simulated actions. We reported a case of a patient with motor cortex damage where the simulation of a movement with the affected limb produced a sensation of mental drag and matched that limb's reduced motor efficiency (*5*). Parallel impairments in imagined and executed movements were also observed in patients with basal ganglia dysfunction due to Parkinson's disease (*6*). This observation suggests that the excitatory output produced in the cortico-striatal pathways during motor imagery closely mimics what occurs during movement execution, and that it is accessible to conscious evaluation. Furthermore,

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