Urocortin in the lateral septal area modulates feeding induced by orexin A in the lateral hypothalamus

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Wang, ChuanFeng, and Catherine M. Kotz. Urocortin in the lateral septal area modulates feeding induced by orexin A in the lateral hypothalamus. Am J Physiol Regulatory Integrative Comp Physiol 283: R358–R367, 2002; 10.1152/ajpregu.00558.2001.—The intermediate portion of the lateral septum (LSi) contains high levels of urocortin (UCN) peptide and type 2 corticotropin-releasing hormone (CRH) receptor (CRHR2) and has anatomic and functional connections with the lateral hypothalamus (LH). We tested the effect of UCN in the LSi on feeding. Injection of 10 or 30 pmol UCN into LSi significantly decreased feeding in food-deprived rats for 24 h without producing conditioned taste aversion (CTA). Pretreatment with a CRH receptor antagonist, α-helical CRH (α-hCRH), blocked the inhibitory effect of UCN on deprivation-induced feeding at 1 and 2 h postinjection. Furthermore, UCN in the LSi significantly decreased feeding induced by LH-injected orexin A at 2 and 4 h postinjection, and addition of α-hCRH blocked the inhibitory effect of UCN on orexin A-induced feeding. In conclusion, UCN significantly inhibits feeding induced by deprivation and LH-injected orexin A without producing a CTA, an effect that is mediated by CRHR2. These data define the LSi as an important site for UCN-induced anorexia and indicate that LSi UCN may influence orexin A feeding signals in the LH.

intermediate portion of lateral septum; corticotropin releasing hormone receptor; satiety

UCN may be the endogenous ligand for CRHR2 (25, 48). Ventricular injection of UCN decreases feeding with an ED$_{50}$ 25 times less than that for CRH (42) and with attenuated anxiogenic responses compared with that observed after CRH administration. However, the difference in magnitude of feeding inhibition by UCN and CRH in the PVN was not as profound as that observed after intracerebroventricular injection, which suggests the presence of other, potentially more sensitive sites for UCN action.

The lateral septum (LS) is part of the limbic system and is important in memory, learning, reward, stress, and defense mechanisms. The LS may also be important to the regulation of feeding. Lesioning the septum results in increased feeding behavior (24), greater licking responses to sucrose solutions, and exaggerated facilitatory and inhibitory behavior when various solutions (palatable or aversive) or tastants are offered, suggesting that the LS may be involved in the rewarding aspects of feeding (18, 47). Several pieces of evidence suggest that the intermediate portion of the LS (LSi) is an important site of UCN action: UCN has a dense fiber network in the LSi (6, 25); UCN peptide and CRHR2 coexist within the LSi (16, 25, 35, 48); and intracerebroventricular administration of UCN elevates c-Fos expression (an indicator of cellular activation) in CRHR2-containing cells within the LSi (48). Recent data indicate that the LSi is innervated by fibers containing the recently identified UCNIII (also known as stresscopin), suggesting that UCNIII may have important actions in this area (26).

The lateral hypothalamus (LH) is a central feeding center. Electrical stimulation of the LH increases feeding behavior whereas chemical lesions in this region result in anorexia and death (5). There is a predominance of orexin A (also referred to as hypocretin 1) and orexin receptors within the LH (7, 14, 40), and injection of orexin A into the LH induces feeding (15, 43). Neuroanatomic tracing studies indicate that the LH receives neural inputs from the LS and sends monosynaptic projections to the LH (37), which provides an anatomic basis for LS-LH signaling. Several studies...
METHODS

The treatment of animals in these studies fully conforms with the Guiding Principles for Research Involving Animals and Human Beings of the American Physiological Society (1), and these studies received local institutional animal care and use committee approval.

Animals

Male Sprague-Dawley rats (Harlan, Madison, WI) weighing 280–325 g were housed individually in cages with a 12:12-h light-dark photocycle (lights on at 0700) in a room at 21–22°C. Teklad lab chow and water were allowed ad libitum, except where noted.

 Cannulation and Verification of Placement

Rats were anesthetized with Nembutal (40 mg/kg) and were fitted with a 28-gauge stainless steel guide cannula placed just above the LSi and/or LH. Stereotaxic coordinates for the LSi were determined from the rat brain atlas by Paxinos and Watson (33) and were as follows: 0.4 mm lateral and 0.8 mm anterior to bregma, and 4.8 mm below the skull surface. For experiments 1a and 2-5, injections were unilateral on the right side. For experiment 1b, injections were bilateral into the LSi. Stereotaxic coordinates for the LH were 2.0 mm lateral and 2.1 mm posterior to bregma, and 7.3 mm below the skull surface. These coordinates were based on our previous studies indicating that this region of the LH is sensitive to the feeding effects of orexin A (43). Injectors extended 1 mm beyond the end of the guide cannula. The animals were given at least 1 wk to recover after surgery before experimental trials. After the experiments brains were dissected out and stored in a 10% formaldehyde solution for histological placement verification. A cannula was deemed incorrect if the injection site was outside of the region targeted and further than 0.75 mm away from the targeted site. Most injections (~85%) occurred within a 0.5-mm radius from the targeted site. Data from animals with incorrectly placed cannulas were excluded from the final analysis. The number of rats listed in the specific experimental protocols represents the number of rats in the final analysis (all cannulas correctly placed). Figure 1 illustrates examples of histological verification of correct location of injections into the LSi and into the LH. Figure 2 illustrates a map of actual injection sites and demonstrates those injections deemed correctly and incorrectly located for one study (experiment 5). This map is representative of placement verification for all studies and represents the widest possible variation in injection sites for all studies.

Drugs

UCN and orexin A were purchased from Phoenix Pharmaceuticals (Mountain View, CA), and α-helical CRH (α-hCRH) was purchased from Sigma (St. Louis, MO). These compounds were dissolved in artificial cerebrospinal fluid (aCSF) just before use.

Injections

A volume of 0.5 μl was injected slowly over 30 s, with injector left in place an additional 10 s to ensure extrusion from the tip and to minimize distribution of drug upward on the cannula tract. The total number of injections for each animal was <12. In previous studies, we demonstrated a lack of extensive tissue damage after 50 repeated injections as measured by gliosis around the injection site (10) and light microscopy at ×100. Injection sites were examined by light microscopy at
microscopy for extensive tissue damage in the present studies and none was found.

Specific Experimental Protocols

Experiment 1a: effect of unilateral injections of UCN and CRH in the LSi on deprivation-induced feeding. Seven LSi-cannulated rats were food deprived for 18 h and injected with 0 (vehicle = aCSF), 3, 10, or 30 pmol UCN. Food was given immediately after injection, and food intake was measured at 1, 2, 4, and 24 h after injection. Body weight was measured at 24 h after injection. Each animal received each treatment once with at least 72 h between treatments to allow for clearance of drug from the central nervous system (CNS) and for normal feeding patterns to be reestablished. Treatments were given in a randomly selected counterbalanced design. After a 1-wk washout period after the first feeding study, these animals were injected with the same doses of CRH under the same protocol.

Experiment 1b: comparison between unilateral vs. bilateral injections of UCN in the LSi on deprivation-induced feeding.

Fig. 2. Illustration of actual injection sites vs. incorrectly placed injections from experiment 5. Correct injections in the LSi (A) and LH (C), and incorrectly placed injections in the LSi (B) and LH (D). Eight of thirteen rats had correctly placed injections in both the LSi and the LH.
Nine bilaterally LSi-cannulated rats were food deprived for 18 h and injected with 0 (vehicle = aCSF), 10 or 30 pmol UCN unilaterally or bilaterally. For the bilateral injection, 10 or 30 pmol UCN were injected on each side and thus the total dose was 20 or 60 pmol. Food was given immediately after injection, and food intake was measured at 1, 2, 4, and 24 h after injection. Body weight was measured at 24 h after injection. Each animal received each treatment once with at least 72 h between treatments to allow for clearance of drug from the CNS and for normal feeding patterns to be reestablished. Treatments were given in a randomly selected counterbalanced design.

Experiment 2: CTA. The two-bottle preference test was used to determine whether UCN is aversive when administered into the LSi. The basis for this is as follows. When rats are exposed to water and saccharin solutions they show a preference for saccharin. When animals are exposed to saccharin for the first time and concurrently injected with a drug that has aversive properties, saccharin is associated with the aversive stimuli. Subsequently, when given water and saccharin at the same time, drinking of saccharin is reduced. Reduced consumption of the drug-paired flavor indicates that the drug administered has aversive properties. Twenty rats were water deprived for 23.5 h and had water access for 0.5 h each day for 7 days. They were then randomly divided into four groups (with an even distribution of body weight) and given 15 ml of saccharin immediately followed by injection with 0 (vehicle = aCSF), or 10, 30, or 100 pmol UCN. This conditioned stimulation was repeated once after 2 days, and the animals were then given the choice of water and saccharin in the absence of drug administration 2 days later. Twenty-four-hour intake of water and saccharin was measured.

Experiment 3: pretreatment of the LSi with CRH receptor antagonist: effect on LSi UCN-induced feeding inhibition. Nine LSi-cannulated rats were food-deprived for 18 h and randomly assigned to four treatments: 1) aCSF + aCSF, 2) aCSF + UCN (30 pmol), 3) α-hCRH (1 μg) + UCN (30 pmol), or 4) a-hCRH (1 μg) + aCSF. The first injection was given 15 min before the second injection. Food was given immediately after the second injection. The dose of 30 pmol of UCN was chosen based on its inhibitory effect on feeding in the absence of a CTA in experiment 2. The dose of α-hCRH was based on published doses used for intracerebroventricular (28) and PVN (20) administration. Each animal received each treatment once with at least 72 h between treatments.

Experiment 4: effect of UCN in the LH on feeding induced by orexin A in the LH. Eighteen nondeprived LSi and LH double-cannulated rats were randomly assigned to one of four treatments: 1) aCSF + aCSF, 2) aCSF + orexin A (1,000 pmol), 3) UCN (30 pmol) + orexin A (1,000 pmol), or 4) UCN (30 pmol) + aCSF. Animals were given the first injection 15 min before the second injection. Injections were carried out during the light cycle between 1230 and 1400. Each animal received each treatment once with at least 72 h between treatments.

Experiment 5: pretreatment of the LSi with a CRH receptor antagonist: effect on LSi-injected UCN inhibition of feeding produced by LH-injected orexin A. Eight nondeprived LSi and LH double-cannulated rats were randomly assigned to one of four treatments: 1) LSi (aCSF + aCSF) + LH (α-hCRH), 2) LSi (aCSF + aCSF) + LH (orexin A, 1,000 pmol), 3) LSi (aCSF + UCN, 30 pmol) + LH (orexin A, 1,000 pmol), or 4) LSi (α-hCRH (1 μg) + UCN (30 pmol)) + LH (aCSF). The first LSi injection was given 15 s before the second LSi injection. The LH injection was given 15 min after the second LSi injection. Food intake was measured at 1, 2, and 4 h after the LH injection. Injections were carried out during the light cycle between 1230 and 1400. Each animal received each treatment once with at least 72 h between treatments.

Statistical Analyses

For experiments 1a and 3–5, the data were analyzed by repeated-measures ANOVA, and thus each rat served as its own control. When main effects were observed, post hoc analysis was performed using multiple-comparison contrasts. For experiment 2b, data were analyzed by a two-factor ANOVA followed by Fisher’s least-significant difference t-test to compare means. For experiment 2, data were analyzed by a one-factor ANOVA followed by Fisher’s least-significant difference t-test to compare means.

RESULTS

Experiment 1a: Effect of LSi-injected UCN and CRH on Deprivation-Induced Feeding

In the first hour, LSi-injected UCN at 3, 10, and 30 pmol significantly inhibited deprivation-induced feeding by 20.6% (P = 0.015), 42.8% (P < 0.0001), and 49.4% (P < 0.0001), respectively (Fig. 3). Two hours after injection, these same doses of UCN inhibited feeding by 22.8% (P = 0.0203), 24.4% (P = 0.014), and 44.3% (P < 0.0001), respectively (Fig. 3). At 24 h postinjection, UCN at 10 and 30 pmol significantly inhibited feeding by 9.1% (P = 0.0358) and 10.6% (P = 0.0163), respectively (Fig. 3). UCN at 10 and 30 pmol significantly reduced body weight gain by 24.4% (P = 0.0037) and 17.3% (P = 0.0307), respectively (Fig. 5).

LSi-injected CRH at 3, 10, and 30 pmol significantly inhibited feeding by 29.9% (P = 0.0053), 48.7% (P < 0.0001), and 48.9% (P < 0.0001), respectively, at 1 h after injection (Fig. 4). However, there was no significant feeding inhibition after the first hour, and CRH did not significantly influence body weight gain measured 24 h after injection (Fig. 5).

Fig. 3. Effect of urocortin (UCN) in the LSi on deprivation-induced feeding at 1, 2, and 24 h after injection. *P < 0.05 compared with control [animals treated with artificial cerebrospinal fluid (aCSF)]; n = 8.
Experiment 1b: Effect of Unilateral vs. Bilateral Injection of UCN in LSi on Deprivation-Induced Feeding

Two-factor ANOVA, with injection type (bilateral or unilateral) and UCN doses representing factors, indicates no significant difference in feeding response to unilateral and bilateral injection of UCN at 1, 4, and 24 h after injection (P = 0.503, P = 0.8593, and P = 0.5899, respectively; Fig. 6). However, there was a main effect of UCN treatment at 1, 4, and 24 h after injection (P = 0.0078, P = 0.0126, and P = 0.0078, respectively).

Experiment 2: Effect of LSi-Injected UCN on Preference for Saccharin Solution

There were main effects of UCN on the percentage of fluid intake attributed to saccharin solution. Intake of saccharin solution in the group treated with 100 pmol UCN was significantly lower than that in the animals treated with aCSF (P = 0.0092, Fig. 7). There was no significant difference in saccharin solution intake among the groups receiving 0, 10, and 30 pmol of UCN (Fig. 7).

Experiment 3: Pretreatment of the LSi with CRH Receptor Antagonist and Effect on LSi UCN-Induced Feeding Inhibition

In this experiment, α-hCRH was injected into the LSi 15 min before LSi injection of UCN in food-deprived animals. In the first hour after injection, UCN at 30 pmol significantly inhibited deprivation-induced feeding by 29.3% (P = 0.0007, Fig. 8) compared with control levels, and addition of 1 µg α-hCRH significantly blocked the inhibitory effect of UCN (P = 0.0006, Fig. 8), resulting in a food intake value that was 42.4% greater than the level observed after UCN treatment (aCSF + UCN). At 2 h after injection, UCN decreased feeding by 26.3% (P = 0.0034, Fig. 8), and addition of α-hCRH blocked the anorectic effect of UCN, increasing feeding by 31.3% (P = 0.0088, Fig. 8) compared with UCN treatment alone (aCSF + UCN). α-hCRH treatment alone (α-hCRH + aCSF) did not increase feeding above control levels at any time point.

Experiment 4: Effect of LSi-Injected UCN on Feeding Induced by LH-Injected Orexin A

In the first hour postinjection, orexin A administered into the LH significantly increased feeding by 3.2-fold above control levels (P = 0.0001, Fig. 9), and UCN at 30 pmol did not significantly block orexin A-induced feeding (Fig. 9). In the second hour after injection, UCN significantly inhibited orexin A-induced feeding by 64.3% (P = 0.0208, Fig. 9). Thus within 2 h postinjection, LSi UCN blocked LH orexin A-induced feeding by 30.9% (P = 0.057, Fig. 9). At 4 h postinjection, orexin A insignificantly increased feeding, and UCN blocked LH orexin A-induced feeding by 34.7% (P = 0.028), resulting in a level of food intake that was not significantly different from controls (Fig. 9).

Experiment 5: Pretreatment of the LSi with a CRH Receptor Antagonist and Effect on LSi-Injected UCN Inhibition of Feeding Produced by LH-Injected Orexin A

In the first hour, orexin A in the LH significantly increased feeding by 2.1-fold above control levels (P = 0.005), and LSi-injected UCN blocked LH orexin A-induced feeding by 56.2% (P = 0.0156, Fig. 10). However, addition of α-hCRH into the LSi did not block the anorectic effect of UCN. By 2 and 4 h postinjection, α-hCRH in the LSi significantly blocked the inhibitory effect of LSi UCN on LH-orexin A-induced feeding (P = 0.0426 and P = 0.0047, respectively, Fig. 10).

DISCUSSION

The current data demonstrate for the first time that UCN acts within the LSi to inhibit feeding behavior.
Previously there had been no identified neurochemical basis for the anorectic response to stimulation of the LS (32). Our studies show that UCN in the LSi inhibits deprivation-induced feeding without producing a CTA, inhibits feeding induced by orexin A in the LH, and mediates feeding inhibition by CRH receptor stimulation. These findings are consistent with the strong neurochemical and neuroanatomic basis for UCN action within the LSi: UCN peptide is heavily distributed in the LSi and matches the presence of CRHR2 in the LSi. Moreover, intracerebroventricular administration of UCN activates c-Fos expression in CRHR2-containing cells within the LSi (48). The LS area lines the lateral cerebroventricles and may be relatively accessible to cerebrospinal fluid components and ventricular injectates. It is possible that the profound feeding-inhibitory effects observed with lateral ventricular injection of UCN and/or CRH represent actions within the LSi. Furthermore, the LS had been previously implicated in feeding behavior by lesioning and electrical stimulation studies: lesions of the LS resulted in stimulation of feeding (24) and increased sensitivity to specific tastants (18, 47), whereas electrical stimulation of the LS decreased feeding (24). As part of the limbic system the LS may relay signals about sensory and reward properties of feeding, and due to the large hippocampal input to the LS there may also be an association with the learning and memory aspects of feeding (44).

Unilateral administration of UCN in the LSi decreased feeding induced by deprivation (Fig. 3), which was associated with changes in body weight (Fig. 5) and is consistent with studies demonstrating that electrical stimulation of LSi inhibits feeding (24). Bilateral injection of UCN did not result in further reduction of deprivation-induced feeding (Fig. 6), indicating that the level of reduction observed with unilateral injection is the maximal response. This lack of complete abolition of the feeding response to food deprivation is not surprising given the multitude of feeding signals generated in response to food deprivation. LSi-injected CRH also inhibited deprivation-induced feeding (Fig. 4). However, the feeding inhibition by CRH lasted only 1 h, much shorter than the 24-h feeding inhibition observed after UCN injection, which is consistent with the higher affinity of UCN for CRHR2 than that of CRH for CRHR2 (48). The enhanced efficacy of LSi-injected UCN vs. CRH in feeding inhibition (Figs. 3–5) and the heavy distribution of UCN peptide in the LSi suggests that UCN, rather than CRH, is the endogenous ligand for CRHR2 in the LSi. Involvement of CRHR2 in feeding is in agreement with studies in which both CRHR2 knockout mice and rats treated with CRHR2 antisense or other CRH-selective antagonists (antisauvagine-30) display alterations in feeding behavior (3, 11, 12, 22, 41).

To verify that the feeding inhibition observed after LSi-injected UCN is not due to potential aversive effects of UCN, a CTA study was performed. UCN at doses equal and less than 30 pmol, doses for which significant feeding inhibition is observed, did not induce taste aversion, and this indicates that feeding inhibition by these doses of UCN is not due to malaise or other aversive sequelae (Fig. 7). Animals conditioned to associate saccharin consumption with a high dose of UCN (100 pmol) significantly reduced consumption of saccharin in subsequent exposures, indicating...
that saccharin had become aversive as a result of high-dose UCN administration (Fig. 7).

To establish that feeding inhibition induced by LSI-injected UCN is mediated via CRHR2, we tested the effect of α-hCRH on feeding inhibition produced by UCN administration in the LSI. α-hCRH is a synthetic antagonist of CRH receptor and binds to both the type 1 CRH receptor (CRHR1) and to CRHR2. Because CRHR2 is the only CRH receptor subtype within the LSI (6, 8, 45), α-hCRH injected in the LSI would bind to CRHR2 exclusively. As shown in Fig. 8, α-hCRH blocks UCN inhibition of deprivation-induced feeding, suggesting that UCN action in the LSI is mediated by CRHR2. However, as demonstrated in Fig. 8, blockade of CRHR2 in the LSI without concurrent UCN treatment did not enhance deprivation-induced feeding. It is possible that blockade of CRHR2 in the LSI in non-deprived rats may enhance normal feeding, but this was not tested in the current study.

We also sought to determine whether UCN in the LSI influences feeding signals generated by stimulation of the LH with orexin A. Orexin-containing neurons in the LH project throughout the neuroaxis (34), and the two receptors for the orexins, type 1 (OX1R) and type 2 (OX2R), are also widely distributed. Orexin A has a high affinity for OX1R (39, 40), and recent evidence indicates that OX1R is present in the LH (2). The neural mechanism by which LH-injected orexin A stimulates feeding is unknown. In the LH, OX1R has been demonstrated in cells containing melanin-concen-

**Fig. 8.** Effect of α-helical CRH (α-hCRH) on UCN-induced feeding inhibition in the LSI in food-deprived rats. *P < 0.05 compared with all other treatment groups; n = 9.

**Fig. 9.** Effect of UCN in the LSI on feeding induced by orexin A in the LH. *P < 0.05 compared with control [animals treated with aCSF (aCSF + aCSF)]; #P < 0.05 compared with animals treated with aCSF + orexin A; $P < 0.05 compared with animals treated with UCN + orexin A; n = 18.

**Fig. 10.** Effect α-hCRH on LSI-UCN inhibition of LH orexin A-induced feeding. *P < 0.05 compared with control [animals treated with aCSF (aCSF + aCSF + aCSF)]; #P < 0.05 compared with animals treated with aCSF + aCSF + orexin A; $P < 0.05 compared with animals treated with aCSF + UCN + orexin A; n = 8.
trating hormone (MCH), which coexpress cocaine-amphetamine related transcript (17), and in cells expressing orexin (2), which coexpress prodynorphin (9). A recent study indicates that orexin may interact with MCH-containing neurons (4), and it is possible that orexin stimulation of the LH enhances feeding via activation of MCH-containing neurons, as MCH elicits feeding on central administration (36). However, the presence of several feeding-related neuropeptides in the LH and the wide distribution of orexin-containing neurons throughout the brain in areas implicated in a variety of functions suggest that the stimulation of feeding by orexin A in the LH likely involves multiple mechanisms.

Several studies suggest communication between the LS area and the LH in the regulation of feeding behavior. The LSi sends monosynaptic projections to the LH (37), and the LH has a well-established role in feeding behavior (38). Lesions of the LS enhance LH-stimulated feeding behavior, whereas stimulation of the LS inhibits LH-stimulated feeding (32). Furthermore, a recent demonstration that electrical stimulation of the LSmI (adjacent to the LSi) results in elevated c-Fos immunoreactivity in the LH suggests that these two regions are functionally connected (46). A recent study showing elevated thresholds for LH self-stimulation after ventricular administration of UCN and CRH also suggests that UCN and/or CRH may modulate LH reward processes (27). On the basis of these anatomic and functional connections between the LSi and LH, we hypothesized that UCN may decrease feeding by influencing LH-induced feeding signals. As demonstrated in Fig. 9, orexin A in the LH significantly increased feeding, and this increase was blocked by injection of UCN in the LSi. Furthermore, we found that addition of α-hCRH in the LSi before UCN injection blocked the inhibitory effect of UCN, and food intake in the animals treated with α-hCRH, UCN, and orexin A alone (Fig. 10). Although the specific neurons activated by UCN in the LS are unknown, there are several cell types present in the LS region, including gonadotropin-releasing hormone (13), GABAergic calbindin cells, orphanin FQ (21, 29), somatostatin, and neurotensin (23), and it is possible that stimulation of CRHR2 influences some of these neurons. However, whether these specific neurons project to the LH region we targeted is unknown.

These data suggest that when signaling mechanisms in the LSi are increased (via UCN), feeding response to LH stimulation (by orexin A) is decreased, suggesting that UCN stimulation of the LSi transmits feeding inhibitory signals to the LH. Conversely, when signaling mechanisms in the LSi are decreased (via α-hCRH), feeding response to LH stimulation (by orexin A) is increased, suggesting that communication of inhibitory messages received by the LH are prevented. These data agree with reports by Oliveira et al. (32), who demonstrated that when signaling in the LSi is increased by electrical stimulation, feeding response to LH stimulation is decreased. Conversely, when signal-

References

7. Broberger C, De Lecce L, Sutcliffe JG, and Hokfelt T. Hypocretin/orexin- and melanin-concentrating hormone-expressing cells form distinct populations in the rodent lateral hypothal-
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