superficial touch and pressure, hair bending, pinching the skin, deep pressure, and joint movement; (iii) auditory: white noise, clicks, and pure tones; and (iv) optic: diffuse illumination intensity changes and movement of contrast patterns in various directions.

Seventy-four units were thoroughly tested. All units responded, but none exclusively to vestibular stimulation. There were no responses to either auditory or optic stimuli. Vestibular units fitted two groups—group 1, those responding to both vestibular and kinesthetic (joint) stimuli; and group 2, those responding to vestibular stimulation and deep muscle pressure.

Group 1 units (convergence of vestibular and kinesthetic afferents) responded to vestibular polarization with different patterns of adaptation: (i) slow adaptation following a short phasic activation peak (dynamic transient), (ii) phasic on-activation followed by phasic off-inhibition or vice versa, and (iii) tonic inhibition with rebound activation.

The activity of these units was invariably influenced by joint movement and the response was always direction specific, that is, activation in one direction and inhibition in the other. When a joint was moved from its resting position toward the activation direction and held there, most frequently unit activation peaked during movement (dynamic transient). In the new static position, the firing frequency (slowly adapting) was higher than that for the resting joint position. Proximal and forelimb joints were more frequently effective than distal and hindlimb joints (Fig. 2). Contralateral joints were more influential than ipsilateral joints were. Often neighboring joints activated the same unit. One unit was seldom influenced by many joints; however, when this did occur, the activation pattern appeared to mimic a moment in a coordinated movement (Fig. 3).

Group 2 units were influenced by vestibular polarization and deep muscle pressure. Effective muscle groups included the proximal flexors and extensors of the contralateral fore- and hindlimbs. Joint rotation also affected these units, but only when the effector muscle was attached to that joint. When the joint was held in a fixed position, pulling the tendon of the effector muscle also produced a response. The exact whereabouts of the afferents producing this effect remains uncertain. It is interesting that A1 muscle afferents have been found to project to the region of the cat's vestibular cortex (*1*).

Our results show that the primary vestibular cortex is not modality specific as classically described for the somatosensory, auditory, and visual systems. If we assume, however, that the cortex will only reflect the sensory specificity, which might be expected for differentiated conscious perception, then one should not expect modality-specific vestibular input. In contrast to the auditory, visual, and somatosensory systems, the perception of position requires integration of at least two different sensory modalities: the vestibular (head position) and the kinesthetic (joint position). Functionally, the afferent input to the primary vestibular projection field may be considered to be as "specific" for conscious orientation as the differentiated, strictly modality-specific inputs of other primary fields are for hearing, vision, and somatosensation.

It has been stated that the rhesus cortical vestibular field is probably located in area 2 of the somatosensory cortex as defined by Vogt and Vogt (*6*). If this were correct, one would expect units immediately rostral to the vestibular field to be affected by stimulation of body regions somatotopically similar to those influential in the vestibular field, since the S1 cortex is organized somatotopically in segmental strips across areas 3, 1, and 2 (*7*). However, single units immediately rostral to the vestibular field were responsive exclusively to tactile stimuli on small receptive fields in the mouth region and were strictly modality specific (*8*). Furthermore, the microelectrode tracts in the vestibular field were located in a cytoarchitectonic area not corresponding to that described for area 2 (*6, 9*), or PC (*10*). In fact, a thorough study of serial sections (Klüver-Barrera stain) of the brains of two rhesus monkeys, one sectioned horizontally and the other coronally, demonstrated that the vestibular field (Fig. 1) does not correspond to the other neighboring cytoarchitectonic areas of 5, 7, and 19 (*6, 9*) or PEm, PF, and OA (*10*).

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Norepinephrine: Reversal of Anorexia in Rats with Lateral Hypothalamic Damage

Abstract. *Injection of norepinephrine in the lateral ventricles of rats recovering from lateral hypothalamic anorexia caused immediate feeding and, frequently, overeating. Intraventricular administration of the α-noradrenergic blocker, phentolamine, suppressed feeding in both normal rats and rats that had recovered from lateral hypothalamic lesions. Feeding is reinforced by ascending medial forebrain bundle fibers that form α-noradrenergic synapses in the hypothalamus and forebrain. Damage to these fibers suppresses feeding by reducing noradrenergic transmission and, hence, the rewarding value of food. Recovery of feeding after hypothalamic lesions coincides with the recovery of noradrenergic reward function.*

Feeding is facilitated by neurons in the lateral hypothalamus (*1*). Electrical stimulation of this area induces feeding (*2*), whereas bilateral damage stops feeding and even causes death by starvation (*3*). On the chemical side, there is considerable evidence that norepinephrine is a transmitter in the feeding system. Injection of norepinephrine directly into the hypothalamus or limbic forebrain causes satiated rats to eat, whereas adrenergic blocking agents suppress feeding and antagonize the facilitating effects of noreprinephrine (*4*).

A relation between these physiological and biochemical facts about feeding is suggested by the findings of histochemical and psychopharmacological experiments. The histochemical work shows that most, if not all, of the noradrenergic terminals in the hypothalamus and forebrain originate from cell bodies in the lower brainstem; the axons of these cells ascend in the lateral hypothalmic area via the medial forebrain bundle to form noradrenergic synapses in the diencephalon and forebrain (*5*). The psychopharmacological work shows that self-stimulation of the brain and other rewarded behaviors depend heavily on this noradrenergic system. Therefore, it has been assumed than an important, if not primary, function of this system is to mediate rewarding or positively reinforcing effects on goal-directed behavior (*6*). We now present evidence that feeding also is positively reinforced by this ascending noradrenergic system.

According to this idea, the rewarding value of food is mediated, at least in part, by noradrenergic fibers in the medial forebrain bundle. Electrical stimulation of these fibers releases norepinephrine at hypothalamic and limbic forebrain synapses and increases the rewarding value of food. Hence, stimulated animals can be induced to eat nonpreferred foods or to feed after satiety. On the other hand, lateral hypothalamic damage produces a deficit in noradrenergic function and reduces the rewarding value of food. Hence, animals with lateral hypothalamic lesions are finicky eaters and accept only the most palatable foods or refuse to eat altogether. Finally, we assume that recovery of feeding after hypothalamic lesions depends on the restoration of noradrenergic function in reversibly damaged neurons as well as on development of compensatory mechanisms.

As a first test of the idea that lateral hypothalamic anorexia results from a norepinephrine deficit, we attempted to restore feeding in rats that had received hypothalamic lesions.

Seven rats under pentobarbital anesthesia received lesions in the lateral hypothalmus (at the level of the ventromedial nucleus) on both sides by a direct anodal current of 2 ma for 10 seconds. Two sham-operated controls did not receive lesions. All nine rats had a cannula for intraventricular injections permanently implanted in the lateral ventricle. The rats had been trained for 1 week prior to the operation to drink milk (1 part Borden's sweetened condensed milk and 2 parts water) rapidly from a calibrated tube. On the second day after the operation, they were given access to the milk tube for 3 minutes. The two control rats and one of the rats in the group that received lesions drank immediately, but the remaining six rats in the group failed to drink. The rats were then injected intraventricularly with 10 μg of *l*-norepinephrine hydrochloride dissolved in 10 μl of Ringer-Locke solution (adjusted to *p*H 7.5). The six aphagic rats drank immediately, and consumed, on the average, 17.6 ml of milk during the next 20 minutes. On the following day, all but one of the six again failed to drink in the first 3-minute period. The rats then were injected with 10 μl of Ringer-Locke solution. Drinking was immediately initiated in the five nonfeeders, but continued only for a few minutes. The mean consumption of all six rats in the 20-minute test was 6.8 ml, which was significantly less than the intake after norepinephrine ($P < .01$). Norepinephrine also increased the 20-minute intake of the three rats that were not aphagic (17.8 ml after norepinephrine compared to 12.7 ml after Ringer-Locke). Histological analysis indicated that the lesions invaded the dorsal aspect of the lateral hypothalamus and caused only partial damage to the medial forebrain bundle.

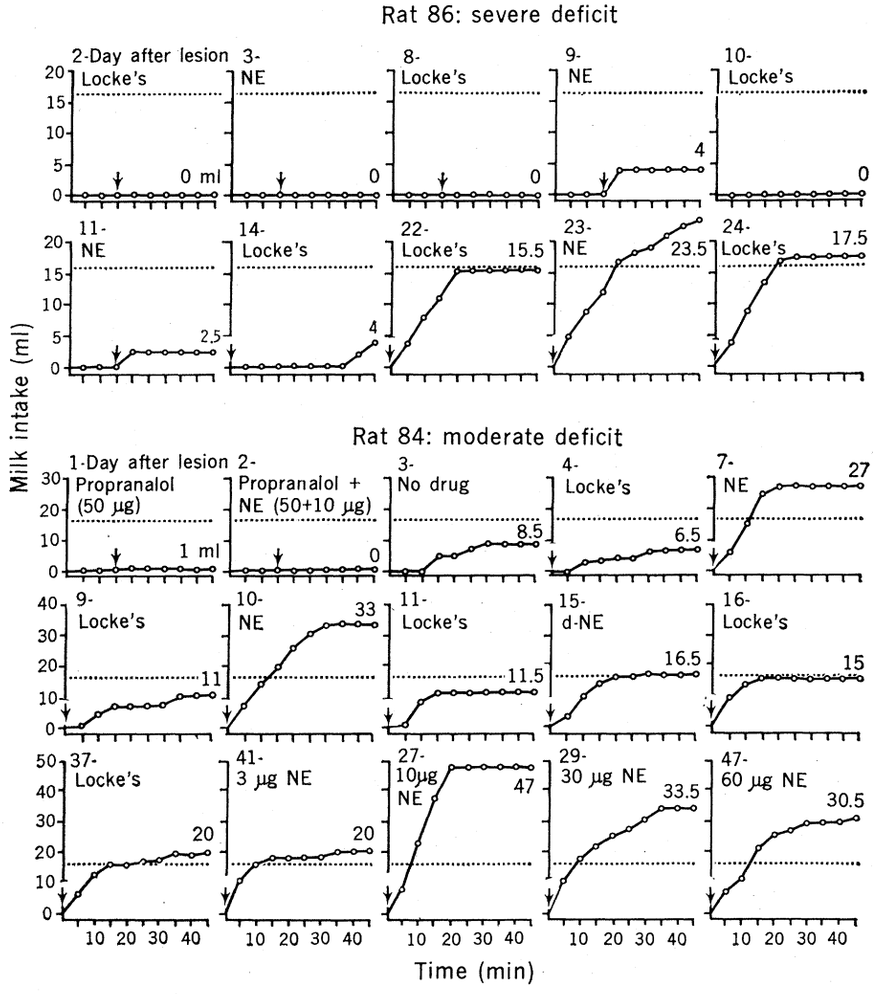

Fig. 1. Recovery of feeding in two rats during daily 45-minute tests after the rats had received lateral hypothalamic lesions. Curves are cumulative plots of milk intake in successive 5-minute periods. Numbers over curves indicate 45-minute intakes. Arrows indicate time of intraventricular injections. All doses are 10 μg unless noted otherwise. Dashed lines indicate intake prior to lesion placement. (Rat 86) Reversal of aphagia by *l*-norepinephrine (*NE*) in a rat with severe hypothalamic damage. Feeding after the operation occurs for the first time on day 9 as a result of the norepinephrine injection, although a similar injection on day 3 failed to induce feeding. (Rat 84) Reversal of anorexia and extensive overeating induced by *l*-norepinephrine in a case of moderate damage. On day 15, *d*-norepinephrine had no effect. The bottom row of plots indicates that norepinephrine is effective over a wide range of doses, with optimum effect at 10 μg.

In a second experiment, lesions were placed more ventrally in 26 rats. In many cases this caused a prolonged anorexia, which enabled us to trace the effects of norepinephrine and other drugs for several weeks. In the first stage of recovery after a severe lesion, while animals were aphagic and adipsic (*7*), norepinephrine usually failed to induce feeding, although frequently the animals were aroused by the injection and approached the tube. In three out of ten cases, however, animals ate for the first time as a result of a norepinephrine injection (Fig. 1.) As recovery proceeded into a second stage, in which animals fed spontaneously but consumed less than 75 percent of the intake prior to the placement of the lesions, norepinephrine significantly facilitated feeding (Table 1); indeed, in five out of ten cases, the intake after norepinephrine exceeded the level before the operation (Fig. 1). A similar pattern was observed in the fully recovered stage. Norepinephrine caused more eating than Ringer-Locke solution in 15 out of 17 cases, and in 10 of these it induced substantial overeating.

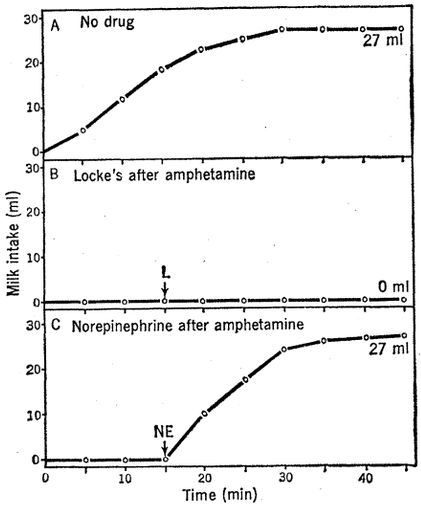

Fig. 2. Reversal of amphetamine-induced anorexia by an intraventricular injection of norepinephrine. (A) Control; (B) intraventricular injection of Locke's solution (*L*) 30 minutes after *d*-amphetamine sulfate (4 mg/kg, intraperitoneally); (C) 10 μg of norepinephrine (*NE*) 30 minutes after *d*-amphetamine sulfate (4 mg/kg, intraperitoneally). In this case, prior treatment with amphetamine increased the response to norepinephrine: 10-minute intake after norepinephrine is 18 ml with amphetamine compared to 12 to 13.5 ml without amphetamine. In a second test, the anorexic effects of a 2 mg/kg dose of *d*-amphetamine was similarly reversed by norepinephrine. Rat 80 (recovered from lateral lesion).

Table 1. Mean intake of milk during a 45-minute test of rats in various stages of recovery after having received lateral hypothalamic lesions. Drugs were injected in the lateral ventricle 15 minutes after the start of the feeding test in the aphagic stage, and immediately before the test in the anorexic and recovered stages (see text for definition of stages). Number of rats is indicated in parentheses; NE, norepinephrine.

Stage	Intake before lesion (ml)	Intake (ml) after ventricular injection of: 10 μl Ringer-Locke	10 μg *l*-NE	10 μg Dopamine	50 μg Propranolol	50 μg Propranolol + 10 μg NE	10 μg *d*-NE
Aphagic	16.4 (10)	0.2 (9)	3.0 (10)	0.9 (7)	0.0 (6)	0.2 (6)	
Anorexic	19.4 (10)	10.4 (10)	18.5* (10)	12.3 (3)	12.0 (2)	19.2* (5)	
Recovered	17.9 (17)	20.5 (17)	26.7* (17)	19.5 (4)	22.3 (8)	29.4* (13)	21.7 (6)

* Differs from Ringer-Locke at $P < .01$ (*t*-test for related measures).

Neurochemical specificity is suggested by the observations that dopamine hydrochloride and *d*-norepinephrine hydrochloride did not significantly facilitate feeding or cause overeating (Table 1).

Suppressive effects on feeding were obtained with the α-noradrenergic antagonist, phentolamine hydrochloride (Table 2). The effects of phentolamine were cumulative and often persisted for a day or more. Specificity of α-receptor blockade was suggested by the failure to obtain suppressive effects with the β-receptor antagonist, propranolol hydrochloride. Indeed, in two animals that had recovered from lateral lesions, propranolol induced overeating, and the combination of propranolol and norepinephrine had a greater facilitating action than norepinephrine alone in 9 out of 13 cases.

Our experiments show that norepinephrine reverses the suppression of feeding induced by lateral hypothalamic damage, and that the α-noradrenergic antagonist phentolamine resuppresses feeding after recovery. These findings support the idea that lateral hypothalamic anorexia is due in large measure to a noradrenergic deficit. More generally, because the food intake of normal rats also is increased by norepinephrine and decreased by phentolamine, we conclude that feeding is facilitated by a system of noradrenergic neurons that ascend in the lateral hypothalamus and terminate at synapses of the α-receptor type. Furthermore, because the intraventricular route was highly effective in our experiments, it is likely that these synapses are located in limbic forebrain and hypothalamic sites close to the lateral ventricle.

In parallel experiments, we found that intraventricular norepinephrine facilitates, and that intraventricular phentolamine suppresses, self-stimulation of the lateral hypothalamus (*8*). These results suggest that the lateral hypothalamic reward system, like the lateral hypothalamic feeding system, contains noradrenergic synapses of the α-receptor type.

The foregoing considerations make it reasonable to suggest that the noradrenergic feeding system is a component of the ascending noradenergic reward system in the medial forebrain bundle. The advantages of such an idea with respect to theory have been discussed by Hoebel (*9*) and Mendelson (*10*). Furthermore, the system of food reward proposed here may provide a physiological and neurochemical basis for Teitelbaum's (*1*, *11*) concept that the same process of encephalization underlies the development of feeding during maturation and the recovery of feeding after hypothalamic damage. Specifically, in the infant organism, the intake of food is regulated by feeding centers in the lower brainstem. During

Table 2. Suppressant action of intraventricular phentolamine on the milk intake (milliliters in a 45-minute test) of rats that had recovered from lesions and rats that had not received lesions. Ringer-Locke control tests were made on the days immediately preceding and following the phentolamine test. In four cases, a second phentolamine test was made on the day following the first (indicated in parentheses).

Rat No.	Intake (ml) immediately after: Ringer-Locke (pre)	Phentolamine (30 μg)	Ringer-Locke (post)
63	24	2	24
54*	14	5	14
58	19	8	18
52*	18	9	6
61	22	10	28
57	26	12	24
59	19	14	20
60	28	18	20
65	29	25	22
46	12	2 (2)	8
45*	31	13 (12)	9
80	34	19 (10)	18
82	38	38 (12)	22
Mean	24.2	13.5† (9.0)†	17.9†

* No lesions. † Differs from Ringer-Locke control prior to phentolamine at $P < .01$ (*t*-test for related measures).

maturation, the feeding reflexes come under the inhibitory control of suppressor cells in the medial hypothalamus and the limbic forebrain. The activity of these cells, in turn, is inhibited by the noradrenergic food reward system in the lateral hypothalamus. In the mature organism, appetizing foods disinhibit the feeding reflexes from forebrain suppression by activating the noradrenergic food reward system. Lateral hypothalamic damage stops feeding because the forebrain suppressor cells no longer may be inhibited in this way and, in fact, may be in rebound activation. Finally, during recovery from hypothalamic damage, the noradrenergic regulation of suppressor cell activity is gradually and at least partially restored.

However, opposite effects of amphetamine on self-stimulation and feeding apparently contradict the view that the noradrenergic feeding and reward systems may be identified. This norepinephrine-releasing drug lowers thresholds of self-stimulation but raises thresholds of elicited feeding from the same lateral hypothalamic probe (*12*). According to our theory of food reward, a drug that lowers reward thresholds by release of norepinephrine (*6*) should facilitate feeding by the same action.

Although amphetamine generally suppresses feeding and is used clinically as an anorexic agent, it also facilitates feeding under some conditions. Thus, amphetamine increases food intake if eating is induced by high intensity stimulation of the lateral hypothalamus (*13*), or if severely deprived rats are offered a wet and highly palatable food (*14*). These observations may be reconciled with the anorexic action of amphetamine if the drug exerts multiple and antagonistic effects on feeding. Under most circumstances, the anorexic effect of amphetamine will obscure its facilitating action; however, facilitation may predominate if the noradrenergic feeding system is activated by electrical stimulation or if it is sensitized by severe food deprivation.

As one test of this idea, we attempted to activate the noradrenergic feeding system of amphetamine-treated rats by intraventricular administration of norepinephrine. Figure 2 shows, in a responsive animal, that norepinephrine rapidly reverses the anorexia induced by amphetamine. This result fits our noradrenergic theory of food reward, and suggests, furthermore, that the anorexic action of amphetamine does not depend on the release of norepinephrine at α-noradrenergic synapses in periventricular regions of hypothalamus and forebrain (*15*).

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14. Twenty rats were reduced to 75 to 80 percent of normal body weight by limited feedings of dry food, and ten controls had free access to food. *d*-Amphetamine sulfate (2 mg/kg, intraperitoneally) or saline was administered in a balanced sequence 15 minutes before a 30-minute feeding test, in which the rats (food deprived for 24 hours) were offered a wet mash of Purina Lab Chow and water. Mean intakes in grams $\pm$ S.E.M. were: amphetamine, free access, 15.4 ± 3.8 compared to starved, 37.1 ± 2.2 ($P < .001$); saline, free access, 32.5 ± 1.3 compared to starved, 33.6 ± 0.9 ($P > .2$). For another example of amphetamine-induced feeding, also see S. F. Leibowitz, *Proc. 78th Annu. Mtg. Amer. Psychol. Ass.* **5**, 813 (1970).
15. Our findings apparently pose difficulties for a recent model [D. Margules, *Life Sci.* **8**, 693 (1969)] in which it is assumed that α-noradrenergic synapses in the hypothalamus mediate satiety rather than feeding. It is possible to reconcile this idea with the view of Miller (*4*), that α-receptors mediate feeding if one assumes that satiety depends on the accumulation of a fixed number of reward messages from the α-noradrenergic feeding system. If so, Margules' finding that the α-antagonist phentolamine increases the intake of a palatable food could be explained. In moderate doses, phentolamine would partially block the noradrenergic reward message, and thus require that a larger than normal number of messages (overeating) be received before the satiety cutoff criterion was reached. More complete blockade of the reward message by phentolamine (higher doses, intraventricular rather than intrahypothalamic administration) should of course reduce intake (see Table 2).
16. We thank H. Morris, W. J. Carmint, and A. Rothchild for technical assistance, and A. T. Shropshire for devising an improved intraventricular injection technique.

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Height and Antisocial Behavior in XY and XYY Boys

Abstract. *The observed association of the XYY genotype with both (i) large height in childhood and (ii) institutionalization for antisocial behavior suggested that large size per se in childhood might tend to establish personality patterns leading to eventual incarceration for delinquency. To investigate this question, the height distributions of four groups of XY boys in institutions for nonpsychotic, nonretarded juvenile offenders were compared with the published standards as well as the predicted gaussian distributions calculated from the mean and variance of the age-adjusted heights of each group. In none of these groups was there evidence for an increased number of large individuals. But three XYY individuals in the same institutions all had heights greater than the 90th percentile of XY boys of the same race.*

Almost all reports of XYY individuals with antisocial behavior have noted the presence of large height. Furthermore, while many descriptions are incomplete, the available published evidence indicates that tall stature has been present from childhood on. Thus a question of some interest is whether large size per se has been the factor accounting for the increased frequency of XYY individuals in institutions for antisocial behavior. There are at least four possible explanations as to why increased height might predispose to misbehavior. (i) Larger children would be more likely to be successful in fights with children of their own age and are more likely to find that threats or acts of aggression would succeed. (ii) Larger children, appearing older than their age, might elicit greater social and intellectual expectations from their elders than their ability would warrant. This might lead to greater opportunities to enter into mischief outside of school, as well as frustration resulting in disruption in school. (iii) Larger children may be more likely to be sin-