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Relationship of Adrenergic and Electrical Brain Stimulation Induced Feeding Responses[1]

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HALPERIN R, C L GATCHALIAN, T J ADACHI, J CARTER AND S F LEIBOWITZ *Relationship of adrenergic and electrical brain stimulation induced feeding responses* PHARMACOL BIOCHEM BEHAV **18**(3) 415–422, 1983 —Electrical and adrenergic brain stimulation can induce eating in satiated animals This report explores the interrelationship of brain feeding systems mediating eating in response to norepinephrine and electrical stimulation of the hypothalamus in rats It was found that simultaneous adrenergic and electrical brain stimulation resulted in a significant increase in food intake as compared to each stimulation condition alone Furthermore, pharmacological blockade of the α-adrenergic receptors in the hypothalamus attenuated feeding in response to adrenergic, but not electrical brain stimulation Results are interpreted to suggest that these feeding systems are independent at the level of the diencephalon The role of the vagus nerve as an efferent link through which these brain systems may influence feeding behavior is discussed

Feeding behavior Hypothalamus Norepinephrine Electrical brain stimulation Paraventricular nucleus Phentolamine Adrenergic receptors Vagal mediation of feeding Dopamine

A ROBUST eating response can be elicited in the rat by injecting *l*-norepinephrine (NE) directly into the anteromedial hypothalamus [5, 9, 18], or by electrically stimulating the lateral hypothalamus [22,24] Historically, the discovery of each of these elicited eating responses stimulated a somewhat independent line of investigation, and each has resulted in an elaborate description of a forebrain neural mechanism controlling feeding behavior (for examples see [14, 17, 37, 40]) No studies, however, have directly explored the interrelationship of these brain feeding mechanisms

Leibowitz [19] has proposed that eating elicited by central NE injection is mediated by α-adrenergic receptors in the hypothalamic paraventricular nucleus (PVN) It has been shown that the PVN is the most sensitive brain site for eliciting this eating response [9,18], and that a preceding injection of an α-adrenergic receptor blocking agent, such as phentolamine, attenuates the NE-elicited eating response [6, 16, 33] Exogenous NE may stimulate feeding by inhibiting hypothalamic neurons, since microiontophoretically applied NE has been shown to exert an inhibitory influence on hypothalamic neurons [3] Consistent with this hypothesis is the finding that PVN lesions result in hyperphagia and obesity [11,21], this suggests that the PVN may indeed play an important role in spontaneous feeding Recent evidence [13] also suggests that the PVN may be the rostral focal point of fibers coursing through the ventromedial hypothalamus which, when lesioned, result in the well-known syndrome of hyperhagia and obesity

Eating in response to electrical brain stimulation (EBS) occurs most effectively when electrodes are placed at the level of the ventromedial nucleus, in the perifornical hypothalamic area or in the lateral hypothalamic medial forebrain bundle [39] This response can also be elicited from brain loci extending caudally along the path of the medial forebrain bundle to the ventral tegmental area of Tsai [38] However, because of the diffuse organization of this area, the neural elements mediating the elicited eating response have not been positively identified It has been proposed, however, that EBS-elicited eating may be mediated by dopamine-containing fibers arising from midbrain cell groups, which course through the lateral hypothalamus and terminate in extrahypothalamic forebrain structures [26,31] This hypothesis is based on the findings that systemic injection of dopamine receptor blocking agents such as haloperidol [28], and the intraventricular injection of the neurotoxin 6-hydroxydopamine (6-OHDA) [26,27], each reliably attenuate feeding in response to EBS

While distinct hypothalamic mechanisms have been char-

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acterized as mediating the EBS- and NE-elicited eating responses, the possible interaction of these mechanisms has not been investigated Eating responses to central NE injection and EBS bear striking behavioral similarities For example, both responses can be viewed as motivated rather than reflexive, in that the animal will modify its sequence of motor responses in order to obtain and consume the food [7, 8, 36] Furthermore, both responses occur in conjunction with other prandial responses, such as drinking, sniffing, and grooming (17,37] In addition, chronic administration of both NE [30] and EBS [35] appear to induce eating that will override body weight regulation In light of these similarities, we have explored the possibility that the hypothalamic mechanisms mediating these responses are parts of a unitary forebrain feeding system In Experiment 1, we evaluated the effect on feeding of simultaneously stimulating both systems In Experiment 2, we attempted to determine whether the integrity of the α-adrenergic receptors in the anteromedial hypothalamic area is critical for the elicitation of eating in response to EBS We found a surprising degree of independence between the systems mediating these two elicited feeding responses

EXPERIMENT 1

METHOD

Subjects

Male Sprague-Dawley rats (325–375 g), anesthetized with Nembutal (50 mg/kg), were each implanted with a bipolar stainless steel electrode (Plastic Products MS 303/1) aimed at the left lateral hypothalamus (LH), and a 23-gauge cannula aimed at the ipsilateral anteromedial hypothalamic area For implantation of the electrode, the nose bar was set at 5 2 mm below the intra-aural line and the stereotaxic coordinates were the midpoint between lambda and bregma, 1 7 mm lateral to the midsagittal suture, and 8 5 mm below the surface of the skull For the cannula implantation, the nose bar was set 3 1 mm above the intra-aural line and the stereotaxic coordinates were 0 2 mm caudal to bregma, 0 3 mm lateral to the midsagittal suture, and 8 2 mm below the surface of the skull The electrode and cannula were cemented to the skull with dental acrylic Stainless steel screws anchored the acrylic fixture to the skull

The first half of all the animals used in the experiment were implanted with the cannula and electrode during a single operation For the remaining rats, we found that it was more efficient to implant each animal initially with the electrode only, after recovering from surgery, those rats exhibiting eating in response to electrical brain stimulation (EBS) underwent a second operation in which they were implanted with the drug injection cannula After surgery, the rats were housed individually and maintained on Purina pellet chow and water ad lib under a 12-hour light/dark cycle

Apparatus

During all testing procedures, animals were removed from the cages in which they were housed and placed in Plexiglas cages (20×20×20 cm) with stainless steel grid floors Prior to all feeding tests, the rats were each injected (over a period of a few seconds) with 40 nmoles of *l*-norepinephrine-d-bitartrate (NE) dissolved in 0 5 μl sterile physiological saline, or with the vehicle alone Drugs were injected through a 10-μl Hamilton syringe Immediately following the drug injection, each rat was connected to an electrical stimulator through a commutator which permitted the animal to move freely

Electrical brain stimulation consisted of 60 Hz sine waves delivered in 30-sec trains Each trial consisted of a 30-sec train of stimulation and was separated by a 30-sec inter-trial interval A daily test consisted of 20 trials During all trials, stimulation was continuously monitored through the use of a cathode ray oscilloscope, reading the voltage drop across the animal A 1 5 mΩ resistor was placed in series with the rat to achieve a relatively constant current During the inter-trial interval, the experimenter set the current intensity by reading the voltage drop across a 10 kΩ resistor The current flow was caluclated utilizing the root mean square of the peak to peak voltage

Screening

After a one- to two-week post surgery recovery period, each animal was screened for eating in response to EBS and NE The food used during all screening and testing procedures consisted of powdered lab chow and sweetened condensed milk mixed and then rolled into a ball For the EBS screening tests, the rat was placed in the test cage with fresh food for a 35-min adaptation and satiation period At the end of the satiation period, the rat was connected to the stimulator and tested for eating in response to EBS during a 20-trial session On the initial trial, the current intensity was set at four to eight μA On subsequent trials, the current was incremented in 1 5 μA steps until the animal exhibited arousal (locomotion or sniffing) or orientation toward the food Current levels within the range of intensities that elicited these responses were repeated until a total of 20 trials had been conducted Each rat was tested at least two times on separate days

Animals that ate in response to EBS were then screened (on a different day) for eating responsivity to NE injection under testing conditions comparable to those used to assess EBS-elicited eating After the satiation period and just prior to the 20-min test, each rat was injected with NE through the chronically implanted brain cannula The food was weighed before and after the 20-min test Rats that ate in response to both EBS and NE injection were tested daily either under EBS, NE or vehicle conditions until the eating responses became stable with respect to electrical threshold and the amount of food ingested

All animals used in the experiment exhibited a reliable eating response of one gram greater than baseline to (a) a consistent (within 9 μA) range of electrical stimulation intensities and (b) a central injection of 40 nmoles of NE over a period of several days Nine rats, of approximately 45 that underwent surgery, maintained both eating responses and were ultimately used in the experiment

Procedure

Animals were tested at the same time daily throughout the actual experiment A 35-min satiation period immediately preceded all tests The satiation procedure consisted of placing the animal in the test cage with a pre-weighed milk mash ball Food intake during this initial period averaged 3 9 g (±0 11) and did not differ across conditions Immediately following the satiation period, the animals were injected with NE (40 nmoles) or saline and then connected to the stimulator The 20-min test session, during which the rats received EBS or No-EBS, began immediately thereafter

During the EBS condition, a test consisted of 20 stimulation trials each of 30-sec duration, separated by a 30-sec inter-trial interval The experimenter recorded the latency and duration of eating during each trial and inter-trial interval The level of stimulation was varied between trials so that each rat received an approximately 10 μA range of current intensities spanning sub-threshold through supra-threshold levels The procedure was designed so that each rat ate during approximately 10 of the 20 test trials in response to EBS Each rat received identical levels of electrical stimulation during all EBS conditions During the No-EBS condition, identical procedures were followed, but no current was passed through the animal Food intake was measured at the end of each test session

The four conditions of the experiment were saline/No-EBS, NE/No-EBS, saline/EBS and NE/EBS The sequence of drug conditions, saline-NE-saline, was repeated four times in each animal Thus two "saline" days separated each "drug" day Two drug sequences were run in conjunction with the EBS condition, and two were run in conjunction with the No-EBS condition The order of the electrical stimulation conditions was counterbalanced

Three of the eight rats tested in this experiment exhibited EBS-elicited eating thresholds that were lower than 1 4 μA Since our stimulation apparatus did not permit us to deliver a current below that level, we stimulated them at 1 4 to 10 4 μA throughout the 20-trial test Thus, the animals received supra-threshold stimulation for all 20 test trials Because of this difference in treatment, these three rats were analyzed as a separate group (Subsequent to this experiment, we built a square wave stimulator which permitted us to deliver lower levels of stimulation (monophasic square waves of 0 1 msec duration) We tested rats exhibiting low thresholds for EBS-elicited eating, and found that, although they were unusually sensitive to EBS, they exhibited stable thresholds for EBS-elicited eating)

RESULTS

For the five rats exhibiting normosensitive eating in response to EBS, we found that food intake in response to simultaneous NE and electrical brain stimulation was significantly greater than to either stimulation condition alone Figure 1 represents mean food intake during the 20-min session in response to each experimental treatment A single-factor analysis of variance revealed a significant difference across conditions, $F(3,12)=22\ 084$, $p<0\ 01$ Tukey's test for paired comparisons revealed that food intake in response to the NE/EBS treatment was significantly greater than food intake in response to NE/No-EBS, $q(4,12)=20\ 3$, $p<0\ 01$, and saline/EBS, $q(4,12)=23\ 7$, $p<0\ 01$ Furthermore, food intake during simultaneous drug and electrical stimulation (NE/EBS) was almost precisely equal to the sum of the responses to each stimulation condition alone (NE/No-EBS and saline/EBS) A contrast analysis was performed to detect any significant deviation from additivity by comparing the differences between the sum of the mean food intake scores in response to NE/No-EBS and to saline/EBS with the sum of the scores in response saline/No-EBS and NE/EBS This comparison showed no significant deviation from additivity, $F(1,12)=0\ 176$, $p>0\ 25$

When a NE injection (as opposed to saline injection) preceded the test session, eating in response to EBS occurred more frequently and for longer durations both during trials and inter-trial intervals In the saline/EBS condition, eating

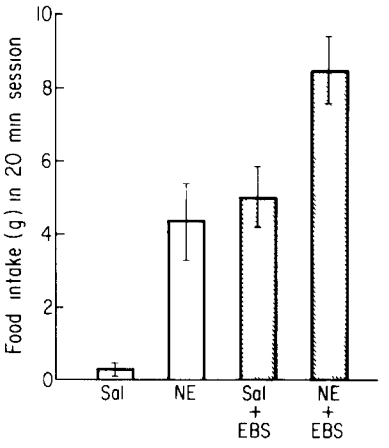

FIG 1 Feeding behavior in animals (n=5) exhibiting normosensitive current thresholds in response to electrical brain stimulation Food intake was measured in response to medial hypothalamic injection of saline and norepinephrine with and without simultaneous lateral hypothalamic electrical brain stimulation All rats were tested in each experimental condition

was confined almost exclusively to the stimulation periods of the test session, with the rats spending an average of 190 sec eating during the EBS trials as opposed to 35 sec during the inter-trial intervals This contrasts with the NE/EBS condition, in which the rats spent an average of 351 sec eating during the EBS trials and 204 sec during the inter-trial intervals Rats exhibited eating during more trials in the NE/EBS test session (15 2 positive trials) than in the saline/EBS session (10 4 positive trials), and the mean duration of the eating response during these positive 30 sec trials was greater in the NE/EBS test (22 0 vs 17 8 sec) The magnitude of the differences displayed on each of these measures (between saline/EBS and NE/EBS conditions), although generally large, was extremely variable across animals, and therefore failed to reach significance In some cases, during the NE/EBS condition, the animal would display a bout of eating that appeared to be continuous throughout stimulation trials and inter-trial intervals Interestingly, when the eating bout had ended, the current threshold for elicited eating on the remaining test trials appeared to be the same as that seen when saline injection preceded the EBS test

The additional three rats that exhibited uniquely low current thresholds for EBS-elicited eating received current levels that far exceeded threshold levels on almost all stimulation trials Figure 2 represents the mean food intake during the 20-min test session for each experimental condition During the saline/EBS condition, these animals exhibited a large eating response of approximately 12 7 g ($\pm$1 2) This response appeared unaltered by NE injection, which in the No-EBS condition produced an eating response of 3 7 g ($\pm$0 8) Since, under any circumstances, we have rarely observed satiated animals eating much more than 12 g during a 20-min test session, the failure of NE to potentiate the EBS response, in the manner demonstrated by animals with higher thresholds (Fig 1), may reflect a ceiling effect due to the large amount of food eaten The possibility of an interaction at high levels of stimulation cannot, however, be ruled out

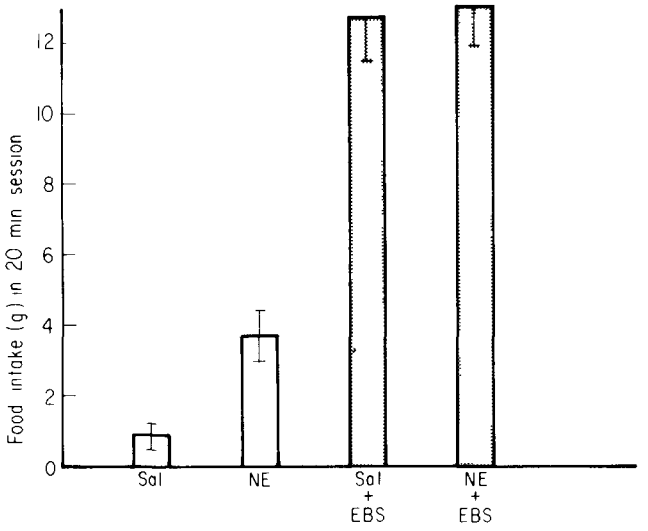

FIG 2 Feeding behavior in animals (n=3) tested only at suprathreshold current intensities in responses to electrical brain stimulation Food intake was measured in response to medial hypothalamic injection of saline and norepinephrine with, and without simultaneous lateral hypothalamic electrical brain stimulation All rats were tested in each experimental condition

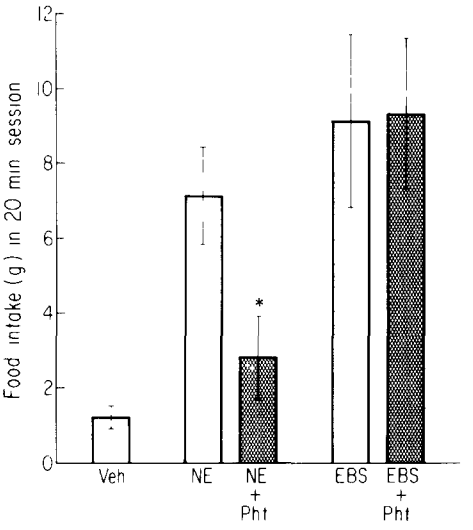

FIG 3 Food intake in response to hypothalamic norepinephrine injection and electrical brain stimulation with and without a preceding central injection of phentolamine All rats (n=5) were tested in each experimental condition

For these low threshold rats, the number of positive eating trials and the duration of eating during EBS trials did not appear to differ for the saline/EBS vs the NE/EBS conditions (17 8 vs 19 2 positive trials, and 21 4 vs 20 7 sec duration, respectively) These animals, however, appeared to spend more time eating during the inter-trial interval of the NE/EBS test than the saline/EBS test (108 vs 19 sec, respectively)

DISCUSSION

The fact that we could detect no strong evidence for an interaction between these stimulation conditions, at relatively high levels of drug and electrical stimulation, led us to hypothesize that the systems mediating eating in response to hypothalamic NE injection and EBS may be independently regulated Experiment 2 was conducted as a first attempt to explore this hypothesis

EXPERIMENT 2

In this experiment, we attempted to determine the impact on EBS-elicited eating of pharmacologically inactivating the α-adrenergic receptors of the PVN, which are believed to mediate the NE-elicited eating response We compared the effect of hypothalamic injection of phentolamine (Pht), an α-adrenergic receptor blocker on NE- and on EBS-elicited eating in the same animal

METHOD

Subjects

The five rats used in this experiment had previously been tested in the paradigm described in Experiment 1 Two were among the five rats whose data appear in Fig 1, two were among those who had displayed low current thresholds (Fig 2) One was tested but not used in Experiment 1 because its eating response to NE injection did not reliably exceed its response to saline in the No-EBS condition However, this rat's eating response to central NE injection subsequently stabilized, and it was therefore included in this experiment

Procedure

Testing procedures were identical to those used in Experiment 1 except for the modifications noted here To assess the effect of Pht on the NE-elicited eating response, we first injected the animals with Pht HCl (60 nmoles in 1 0 μl sterile water, injected over a period of approximately 7 seconds) or with the vehicle alone Five minutes later, they received another injection of either NE (40 nmoles in 0 5 μl of sterile saline, injected over a period of a few seconds) or the vehicle A 20-min test session identical to that used in the No-EBS condition of Experiment 1 immediately followed the second injection

To determine the effect of Pht on EBS-elicited eating, the animals were injected with either Pht (60 nmoles) or water just prior to a 20-min test A dose of 60 nmoles of Pht was selected because higher doses have been found to cause a suppression of spontaneous feeding [17] During each EBS test, the current intensity was varied to assess the threshold for elicited eating A modified method of constant stimuli was used A 10-μA range of current intensities spanning sub-threshold through suprathreshold levels was selected for each rat The 20-trial test session consisted of four ascending blocks of five trials Within a block, the intensity was incremented in 2 μA steps from one trial to the next A daily threshold was determined by calculating the arithmetic mean of the threshold for each block of trials

As in Experiment 1, the experimenter recorded the latency and duration of all eating responses during each trial and inter-trial interval Food intake was measured at the beginning and end of each test session

Thus eating in response to water/saline, water/NE and

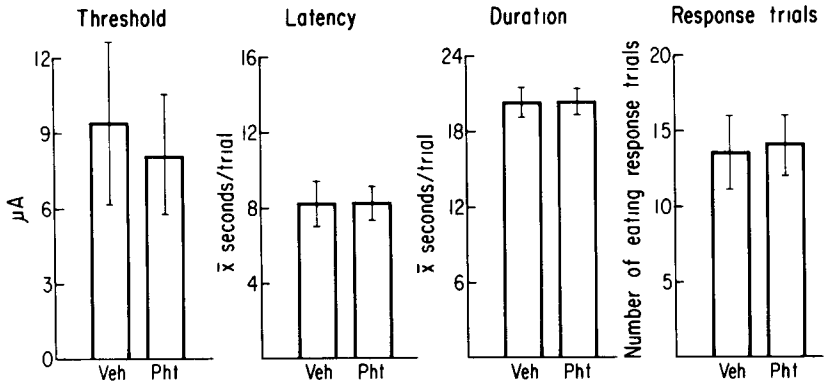

FIG 4 Effect of hypothalamic injection of phentolamine on four parameters of eating in response to electrical brain stimulation current threshold for elicitation of eating, latency to eat after onset of stimulation, duration of eating response during 30-sec stimulation trial, and number of positive response trials in a 20-trial test

Pht/NE was measured, in the absence of EBS, to determine the impact of Pht on NE-elicited eating Two water/saline days separated each drug day Drug conditions (water/NE and Pht/NE) were given in an ABBA sequence beginning with the water/NE condition The conditions used to determine the impact of Pht injection on EBS-elicited eating were water/EBS or Pht/EBS The sequence, water-Pht-water, was given two times to each animal in conjunction with EBS The order of NE vs EBS conditions was counterbalanced across animals All animals were tested in all treatment conditions

Histological Analysis

After completion of this experiment, the rats were anesthetized and guillotined Their brains were removed from the skull and placed in a 10% formalin solution containing 30% sucrose Alternate frozen sections, 50 μ thick, were stained with cresyl violet Cannula and electrode tips were localized with the aid of a stereotaxic atlas [15]

RESULTS

As can be seen in Fig 3, the food intake response elicited by NE was attenuated by 68 2% after injection of Pht into the anteromedial hypothalamic area This feeding suppression, observed when an injection of Pht preceded the NE injection, was significant, $t(4)=4\ 406, p<0\ 02$ This contrasts with EBS-elicited eating, which in the same rats remained unaltered by this α-adrenergic receptor antagonist, $t(4)=1\ 875$, $p>0\ 10$ Food intake was less in response to central NE injection than to EBS, although this difference was not statistically significant, $t(4)=2\ 178$, $p>0\ 05$ To determine whether the higher food intake response to EBS could account for the failure of Pht to suppress eating in this condition, we evaluated the effect of Pht in three rats with low food intake scores The mean food intake in response to EBS was 4 9 g ±0 40 and 4 6 g ±0 049 in the Pht and vehicle conditions, respectively To explore further any possible effect of Pht injection on EBS-elicited eating, we compared a variety of response parameters after central Pht and vehicle injection As shown in Fig 4, Pht produced no change in current threshold for elicitation of eating, mean latency to eat or the number of positive responses made during a test session

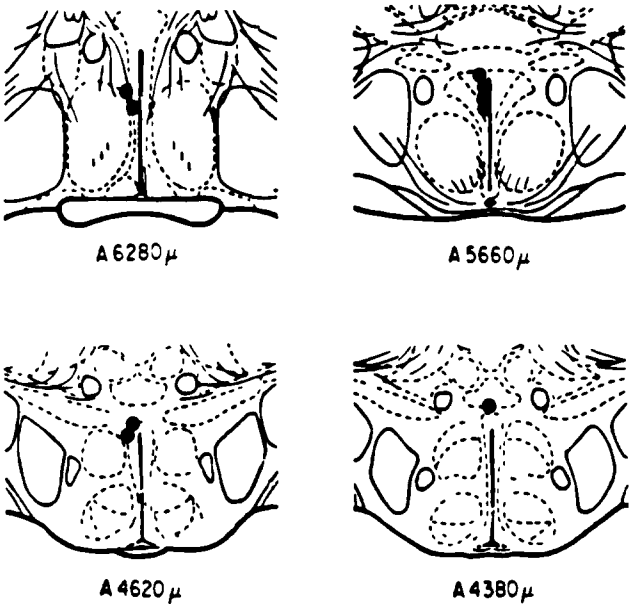

FIG 5 Schematic representation of cannula placements for central drug injections (Taken from [15])

Histological analysis of cannula placements was conducted by localizing what were judged to be the center points of the 23-gauge cannulas Four cannula tips were located either just above or along the dorsal edge of the PVN at its anterior portion Three cannula tips were more posteriorly placed, approximately 0 5 to 0 7 mm posterior to the PVN in the area of the nucleus reuniens or the periventricular nucleus Two cannula tips were approximately 0 4 mm anterior to the PVN bordering the anterior hypothalamus and the nucleus periventricular stellatocellularis All placements

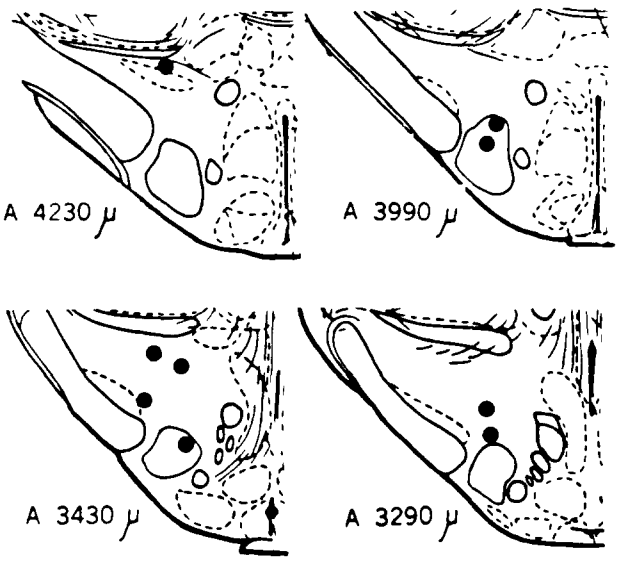

FIG 6 Schematic representation of electrode tips for EBS (Taken from [15])

were thus found to lie in the medial hypothalamic area where NE is most effective in eliciting eating [18]

The electrode tips were placed more posteriorly, two at the level of the ventromedial nucleus and seven at the level of the posterior hypothalamus Three tips were in the medial forebrain bundle, two were in the zona incerta, and three were in the H_2 field of Forel

DISCUSSION

Since the Pht injected into the anteromedial hypothalamus attenuated NE-elicited eating and, in the same animals, had no apparent effect on EBS-elicited eating, we suggest that the functional integrity of these α-adrenergic receptors, which appear to mediate NE-elicited eating, is not critical for the manifestation of EBS-elicited eating

GENERAL DISCUSSION

The fact that we could detect no interaction after simultaneous activation of the NE- and EBS-elicited eating mechanisms suggests that the brain systems mediating these responses may be independent Additive increases in food intake after simultaneous electrical and NE brain stimulation can be interpreted to reflect mediation by independent systems if the level of stimulation used (for each stimulation condition alone) yields close to a maximal behavioral response, i e , if one system were saturated, an increase in feeding due to an additional kind of stimulation would have to be the result of activation of a second system An additive increase would further suggest that the two systems involved are not mutually facilitative or inhibitory

An attempt was made to utilize high levels of stimulation in this study However, this goal was somewhat restricted by the requirements that the feeding response to each stimulation condition (1) did not outlast the 20-min test session, and (2) was not so high as to preclude the possibility of our observing (by virtue of a ceiling resulting from excessive food intake) an additive or multiplicative increase in feeding during the combined stimulation condition The magnitude of the eating response we observed to simultaneous NE and EBS exceeded the maximum feeding response we generally observe to the highest level of NE or EBS stimulation alone (unpublished data) Thus, the additive increase in food intake suggests that these responses are mediated by independent brain systems

In Experiment 2 we found that Pht, an α-adrenergic antagonist, attenuated NE-elicited eating, but had no impact on the EBS-elicited eating response This difference is not attributable to the difference in food intake scores resulting from these treatments since Pht did not suppress feeding in rats with low food intake scores Thus, the α-adrenergic receptors in the anteromedial hypothalamus, which appear to mediate the NE-elicited eating response, are not essential for manifestation of EBS-elicited eating Furthermore, the fact that these two similar eating responses can be differentially affected under comparable experimental conditions demonstrates that the response decrement produced by Pht on NE-elicited eating cannot be attributed to broad behavioral deficits

In this report, we have shown that the eating responses elicited by two different manipulations within the diencephalon may occur independently of each other Whereas this appears to indicate that the brain systems mediating these responses function independently at this level of the neuraxis it leaves open the question as to the extent of their interaction at other levels of the nervous system Each of the forebrain feeding mechanisms that we have activated has been conceived as the diencephalic component of a longitudinal system which extends caudally to the hindbrain With regard to electrically elicited feeding, Waldbillig [38] has mapped effective brain loci along the path of the medial forebrain bundle, caudal to the level of the ventral tegmental area of Tsai Dopamine-containing neurons appear to mediate this goal-directed feeding response to EBS at these brain sites [26 28] Electrical stimulation of more posterior brain sites in the dorsal pontine tegmentum which are devoid of DA-containing neurons has been found to elicit a more reflexive feeding response which occurs even in the absence of an appropriate goal object [4,23] Dopamine-containing fibers in the LH also appear to mediate the rewarding effects of EBS (e g , [27]) Lateral hypothalamic EBS may induce feeding by enhancing the rewarding effects of food and/or food-related stimuli

With regard to neurochemical systems eliciting feeding behavior, Leibowitz [18] and Leibowitz and Brown [20] studying noradrenergic drugs, and Gold *et al* [13] investigating wire knife cuts, have suggested that the PVN is the rostral focal point of a longitudinal neural circuit involved in feeding Leibowitz has found the PVN to be the most effective site for elicited feeding after NE injection with the entire periventricular zone of the diencephalon exhibiting a moderate degree of sensitivity Furthermore, Leibowitz and Brown have recently identified ascending catecholamine projections in the dorsal midbrain tegmentum which appear to innervate specific noradrenergic receptors in the PVN mediating feeding The work of Gold suggests that cells in the PVN or a region just ventral and rostro-caudally coextensive with the PVN send descending projections through the lateral hypothalamus and into the midbrain The precise path of these fibers, and their target areas have not as yet been delineated These fibers may include, but do solely consist of those mediating the eating response to central NE

injection Future investigation may reveal a possible interaction of the systems mediating EBS- and NE-elicited feeding at brain levels caudal to the diencephalon

The role of each of these feeding systems in naturally occurring behavior remains elusive The metabolic and/or environmental signals which trigger these systems are not well understood However, the vagus nerve is an important efferent link through which both central NE and EBS appear to influence behavior Subdiaphragmatic vagotomy has been shown to abolish both NE- and EBS-elicited eating [1, 29, 32] Moreover, evidence exists suggesting that medial hypothalamic NE injection and lateral hypothalamic electrical stimulation act similarly to influence a variety of digestive processes For example, both have been shown to increase pancreatic release of insulin [10,34] In light of the fact that NE may exert its influence on feeding by inhibiting neuronal firing in the medial hypothalamus [3], it is noteworthy that electrical stimulation of the medial hypothalamus causes a decrease in insulin release [12] Similarly, lateral hypothalamic EBS increases gastric motility [2], gastric release of pepsin [25], and blood flow to the gut [2], while medial hypothalamic EBS causes a decrease in the magnitude of these digestive events Autonomic nervous system activation during naturally occurring feeding is partially understood Further knowledge as to how the brain feeding systems studied here interact with the autonomic nervous processes is likely to shed light on the functional role of these brain systems in naturally occurring behavior

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