FEEDING RESPONSES ELICITED BY THE ELECTRICAL STIMULATION OF LATERAL HYPOTHALAMUS IN THE CAT: THE EFFECTS OF METHAMPHETAMINE

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In stimulating to the lateral hypothalamic area (HL) electrically, eating responses which bound to stimulation directly were obtained in 15 out of 98 cats. These animals discriminated between edible and inedible objects. Successive behavioral changes were observed in varying the parameters (voltage or frequency) of stimulation. The loci eliciting the above responses lay in the external part of HL at the level of the ventromedial hypothalamus (Hvm). Diffuse area in HL commonly produced sniffing responses.

Low-voltage fast activity appeared in Hvm lead selectively when the cat was eager to get food after 24 hr starvation.

Methamphetamine (2.0 mg/kg i.v.) elevated the threshold of stimulus intensity during 15-30 min after injection.

It has been demonstrated mainly through injury techniques that the hypothalamus plays an important role for the regulation of feeding behaviors. Lesions of ventromedial hypothalamus (Hvm) result in hyperphagia and obesity, while lesions of lateral hypothalamus (HL) result in the opposite effects, i.e., aphagia and shorter survival time compared to the intact rat deprived of food and water (Anand & Brobeck 1951; Stevenson & Montemro 1963).

Delgado and Anand (1953) observed that the amount of daily food consumption was markedly increased after long duration stimulation to HL. As to the feeding responses induced immediately after the onset of stimulation, Brügger (1943) obtained an impressive symptom in cats. The animals, however, mouthed both edible and inedible objects, and sometimes it would outlast the stimulation for periods up to twenty minutes. Miller (1960) has conducted a series of experiments to determine whether similar eating elicited by electrical stimulation to hypothalamus of satiated rats is a specific gnawing reflex or has all of the properties of normal hunger. Furthermore, Morgane (1961) concluded that the “feeding center” consists of two anatomical portions, and that the mid-lateral and perifornical portion of the lateral hypothalamus contain hunger motivational system, important in food drive, and that the far lateral mechanism is the more basic feeding system, and is mostly dependent on activation of pallidofugal fiber trajectories having primary influences perhaps on neuro-metabolic regulation.

The purpose of the present study is to confirm the loci of feeding responses induced by the stimulation of hypothalamus in cat and to inquire the effects of methamphetamine on these responses.

Brobeck et al. (1956) have already pointed out that amphetamine derivatives increased the frequency and amplitude of the recorded activity of medial hypothalamus. The relation between the electrical activity of HL and Hvm is reported to be reciprocal (Oomura et al. 1964). It might be expected that methamphetamine inhibits the hypothalamic feeding
responses or elevates the threshold of electrical stimulations concerned.

Method

Ninety-eight male cats have been used in this study.

Operation was performed under pentobarbital anesthesia. Bi-polar electrodes, made of two 0.25 mm diameter stainless steel wires and insulated except for the tips, were implanted with the aid of a stereotaxic instrument into HL (two in each adimal). The electrodes were fixed to the cranium with dental cement. The electrode ends were soldered to the connectors. Penicillin 100,000 U, was injected to prevent infection.

After two weeks postoperative period, each animal was put in a plastic observation cage, 60 cm diameter, 60 cm high. Then, the freely moving cat was stimulated through these implanted electrodes. Parameters of stimulation were frequency, 100 per sec; pulse duration, 1 msec; duration of stimulation, 5-10 sec; and interval between stimulations, 15-30 min. The stimulus intensity was gradually increased until the threshold of responses concerned was reached. Animal takes food (boiled fish and rice) in a small vessel set in the cage at any time. Hypothalamic responses were observed repeatedly once or twice a week. During the stimulation periods, the observers stood in full sight of the animal to write the behavioral patterns in detail. The amount of daily food consumption was measured.

Methamphetamine, 2.0 mg/kg was injected intravenously.

At the end of experiment, the animals were sacrificed. The brain was perfused and fixed with 10 per cent formalin. Serially section at 40 μ with every fifth section stained with thionine for determination of the location of the electrode tips.

Results

As Hess (1956) and other investigators have already mentioned, we also observed various behavioral patterns such as fear-like behaviors, rage reactions, somatomotor responses, urination, pupillilatation, etc., in stimulating the various portions of hypothalamus in cat. In addition to these, we obtained two types of feeding responses, i.e., one was sniffing and the other, eating.

A. Behavioral observations

1) Sniffing

This response has been the most common reaction elicited by HL stimulation. In general, the animal sniffed something on the floor with the contralateral circling movement. Meeting with food, the animal stopped moving, and sniffed it carefully, and again walked contralaterally. In some cats the responses were accompanied by head turning towards contralateral site of the stimulated point without locomotion. Other cat dashed to approach to the food immediately after the onset of the stimulation and sniffed it. All these responses would not be led to the eating. On increasing the stimulus intensity the movement became more rapid and the animal seemed to be frightened, and mewed with long and low voice after the offset of the stimulation. The points eliciting the above responses were dotted in a rather diffuse zone of HL. Location of all electrode points were summerized in Fig. 2.

2) Eating

Fifteen points were found to be effective for eliciting the eating responses (Fig. 2). Fig. 1 shows the typical eating responses. Soon after the onset of the stimulation at certain intensity, the cat approached the food vessel with sniffing (Fig. 1-B) and ate fish energetically (Fig. 1-C, D, E). This responses would cease immediately upon shutting off the current (Fig. 1-F). At this time for several seconds, the cat showed the freezing posture like "arrest reactions" (Hunter & Jasper 1949). Even if the cat had its mouth full of food, it would not chew or swallow it.

Wecker stimulation gave no apparent
responses. When the voltage was gradually increased, the successive changes of responses could be observed. The animal began to be aware of the stimulation, and then looked up contralaterally and sniffed something. On increasing the stimulus intensity the responses became more violent, and the cat could not discriminate between edible and inedible objects, i.e., the cat bit the food vessel, too. The range of appropriate stimulus intensity was 1.8–5.5 v. in this experiment.

The stimulation with the frequencies of 1–8 per sec, pulse duration 10 msec produced no overt behaviors, and at the stimulation with 20–40 per sec, 5–3 msec, the animal became aware of it and began to sniff or to search around, but would not take food at all. The stimulation with 60–100 per sec, 1.0 msec produced the eating responses.

All fifteen cats have a capacity to discriminate between food and inedible substances such as paper or cloth. Presented with only some pieces of paper, the animal searched something around in the cage, and would not bite them. They would not drink water either. When dish was put far and water near from the animal, they selected fish, though they approached...
Feeding Responses Elicited by the Electrical Stimulation

B. EEG

EEG was taken when the cat was deprived food and water for 24–32 hr, from the electrodes in HL and Hvm to which stimulation elicited eating and rage responses. When the food was put outside the cage (the cat was eager to get food), high-voltage irregular waves and 4–8 per sec bursts appeared in Hvm lead, whereas low-voltage fast activity was recorded from HL lead. On the contrary, we could not see the differences in the wave form of both leads in general consciousness levels, i.e., in awake state low-voltage fast waves were taken from both two leads, and these patterns were replaced by high-voltage slow waves in the deep sleeping state (Fig. 3).

C. The Effects of Methamphetamine

Methamphetamine 2.0 mg/kg i.v. was administered to six cats that showed the hypothalamic feeding responses.

The electrical stimulations were given 30, 15, 0 min before and 15, 30, 60, 120, 180, —min after injection of drug. The stimulus intensity was raised by 0.2 v. step until it reached the threshold for eating response. The experiments were repeated

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ATTENTICN TO FOOD

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Fig. 3. Recordings from lateral hypothalamus (HL) and ventromedial hypothalamus (Hvm) in 24 hr deprived condition. High-voltage slow activity, 4–8 c/sec bursts appeared in Hvm lead selectively when the animal was eager to get food.
Fig. 4. Typical curves showing the effects of methamphetamine (2.0 mg/kg i.v.) on the thresholds of stimulus intensity.

2–5 times in each cat. Fig. 4 represents three typical curves showing the time course of the effects of drug. Methamphetamine elevated the stimulus threshold up to 0.2–0.4 v. during 15–30 min after injection in all cases. The recovery to control level was observed during 60–120 min after injection.

DISCUSSION

It is well known that the lesions of Hvm result in hyperphagia and obesity in rat (Hetherington & Ranson, 1942), cat (Anand et al., 1955) and monkey (Hamilton & Brobeck, 1964). Delgado and Anand (1953) have reported that the stimulation of HL produced an increase of daily food intake which may be as high as 1,000 per cent with respect to the control level. It is conceivable in these cases that the responses suggest the participation of some neurohumoral mechanism. But the hypothalamic responses in this study bound to the stimulation directly, i.e., eating was elicited by the onset and ceased by offset of stimulation, and we did not observe the after-effects of stimulation such as the increase of daily food consumption. Thus it may not be proper that the above explanation should be applied to our results. Perhaps the electrical stimulation produced gnawing or eating responses associated with hunger motivation as Miller (1960) have described, for our cats ate or chewed only food and did not care about the inedible objects.

In Miller’s experiment using the rat, the points are clustered along a line running between the mammillothalamic tract and the fornix. But the loci in this study lay in the external part of the lateral hypothalamus at the level of the ventromedial hypothalamus. These are overlapped with that of Delgado’s experiment. What caused the different results? Is the parameter of stimulation crucial factor? But in stimulating with the frequencies of 60 per sec, pulse duration of 0.2–0.5 msec like Delgado et al., we observed the eating responses. It seemed that the area eliciting the feeding responses are very limited.

Anand et al. (1955) have reported that hypoglycaemia decreased the activity of “satiety” centers and occasionally slightly increased the activity of the “feeding centers”, and that hyperglycaemia produced opposite changes. Our findings in respect to EEG are consistent with these results.

Sharma (1961) mentioned that the gastric distention led to production of high voltage irregular waves and occasional spikes selectively in the region of the satiety center, and the gastric hunger contraction did not change the electrical activity of either feeding and satiety center. Hockman (1964) have recently reported that in either 23 or 48 hours deprived condition, the recorded activity presented a pattern of low-voltage fast activity, whereas in the ad libitum condition, these patterns were replaced by high-voltage slow wave patterns. These two studies differ from ours in two important respects; a) they recorded the electrical activity of hypothalamus in the awakening state, and did not refer to the changes of EEG in sleeping state or in increased hunger motivation when the animal was eager to get food. We would fail to observe the differences of the electrical changes of between HL and Hvm, recording only in the awakening state. b) It is uncertain that the electrical activities were taken really from feeding and satiety...
centers as they expected, for they did not observe the behaviors induced by the electrical stimulation to the same electrodes from which EEG were taken.

Methamphetamine elevated the threshold up to 0.2–0.4 v. (11–22 per cent) during 15–30 min after injection, or in other words, this drug has inhibiting effects on the hypothalamic eating responses to some extent. Duration time is comparatively short. This is in line with the results reported by Nakajima et al. (1964) who investigated the effects of methamphetamine on the changes of brain temperature. It is well known that methamphetamine has an appetite-depressing effect. We found that this drug inhibits as well the centrally elicited feeding responses as the normal feeding behaviors. According to Brobeck et al. (1956), amphetamine derivative increases the electrical activity in Hvm. It might be expected that methamphetamine affects in the same manner.

References

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