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THE EFFECTS OF LATERAL HYPOTHALAMIC LESIONS ON FOOD INTAKE AND INSTRUMENTAL ALIMENTARY REFLEX IN DOGS

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Since Anand and Brobeck (1951) localized the "feeding center" in the lateral hypothalamus, the role of hypothalamic structures in alimentary mechanisms has been studied by many investigators (Teitelbaum and Stellar 1954, Miller 1957, Wyrwicka 1957, Chereshniev 1960, Morgane 1961a, Teitelbaum and Epstein 1962, Balińska 1963, Balińska and Brutkowski 1967, Wyrwicka 1967ab and others).

Most of the results concerning the lateral hypothalamic syndrome were obtained on rats, rabbits, cats, goats and monkeys, whereas few data were obtained on dogs. We purposefully chose the dogs as experimental subjects because they are very well known from the point of view of various conditioned reflex activities. In addition, their social relations with humans and lively emotional expression give one the opportunity for detecting even small changes in emotional behavior and motivation, caused by the operation, and make possible the undertaking of detailed studies on the various aspects of hypothalamic lesions.

The present paper is concerned with the effect of lateral hypothalamic lesions on food intake and instrumental alimentary reactions as well as on the general activity and emotional behavior of dogs.

MATERIAL AND METHODS

Experiments were performed on 20 male, adult, mongrel dogs weighing from 8—12 kg.

In the standard Pavlovian radiophonized CR chamber the instrumental alimentary conditioned reflex (CR) was established according to the Konorski and

Miller (1933) technique. As a conditioned stimulus a tone of 1000 c/sec was presented. The instrumental reaction consisted in putting the right foreleg on the food tray. The movement was immediately reinforced by the presentation of food (a small piece of bread mixed with minced boiled meat). Each experimental session consisted of 20 trials, with intertrial intervals of about 1 min. The dogs were trained to a criterion of 100% correct responses in the last 5 experimental sessions (100 trials).

Brain lesions were performed under Nembutal anaesthesia (35 mg/kg) by electrocoagulation. The electrodes were stainless steel needles 0.5 mm in diameter insulated by enamel except for 0.5 mm at the tip. Electrodes were placed stereotaxically and aimed at the lateral part of the hypothalamus, according to the coordinates based on the Atlas of Lim et al. (1960). The dogs were divided into two groups of ten dogs each. In the first group (LP) two points ($R_1 = 21.0$, $R_2 = 22.0$) were coagulated bilaterally by direct current 3 mA of one minute duration. In the second group (LM) only one point ($R = 21.5$) was coagulated bilaterally with the same parameters of current.

Animals were under observation from the first day after operation for 3—4 months. The dogs were tested twice during the period of aphagia on the 4th and 7th day after electrocoagulation. Regular testing sessions of the alimentary reactions were started when the dogs recovered from aphagia and were eating food from a bowl. If during five successive experimental sessions a dog did not show spontaneous recovery of the instrumental alimentary performance, it was retrained by passive movements. Food intake of all dogs was measured during 10 days before the operation, 20 days after the operation and then one month later.

After the experiments were accomplished, the dogs were sacrificed and their brains perfused with 10% formalin. Then the brains were embedded in paraffin and sectioned frontally at 20 μ. Every tenth section was stained by the Klüver or Nissl method alternately.

Anatomical verification

In all the dogs of the LP group the lesions were extensive, bilateral and symmetrical.

In eight dogs (LP 1—3, 5—8, 10) in the rostro-caudal plane the lesion destroyed the lateral hypothalamic area in the tuberal part of the hypothalamus and also reached the latero-posterior part of the hypothalamus damaging partially Forel's areas H_1 and H_2. In the ventro-lateral plane the lesion extended from the fornix region slightly beneath it and far laterally, damaging the infero-ventromedial part of the internal capsule. A typical lesion for this group is represented in Fig. 1 (dog LP 2). In dog LP 9 and LP 4 the lesion did not reach the posterior hypothalamus; moreover in dog LP 4 the fibers of the internal capsule were only unilaterally destroyed on the left side.

The anatomical examination of the brains of the dogs within the LM group showed that the lesions were small, bilateral and symmetrical. A typical lesion for this group is represented in Fig. 2 (dog LM 3).

In nine dogs (LM 1—5, 7—10) the lesions were localized within the lateral hypothalamus in the tuberal part slightly above the fornix and lateral from it.

In dog LM 6 the lesion was placed dorsally from the fornix.

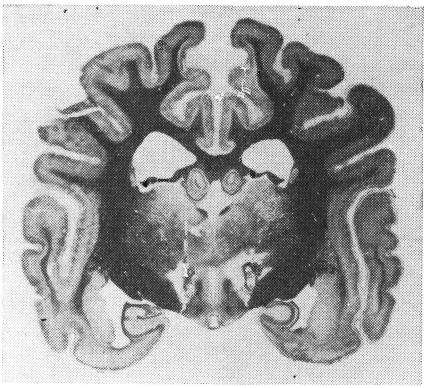

Fig. 1. Representative frontal section of the brain of dog LP 2 showing a typical extensive, bilateral, symmetrical lesion in the lateral and latero-posterior hypothalamus which resulted in aphagia and total disappearence of trained movements

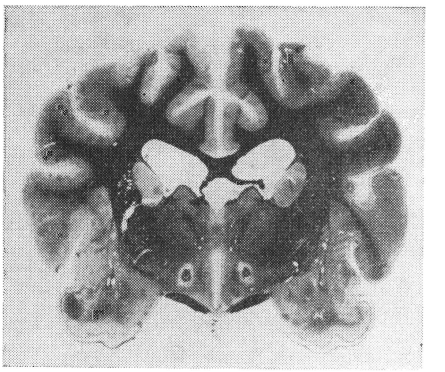

Fig. 2. Representative frontal section of the brain of dog LM 3 showing a typical small, bilateral, symmetrical lesions in the lateral hypothalamus resulting in hypophagia and temporal disturbance of trained movements

RESULTS

Group LP

Food intake. In all the dogs of this group aphagia and adipsia has been found; they were therefore kept alive by means of gastric tube feeding. In this period the dogs often vomited. Step by step spontaneous feeding capability was recovered in dogs LP 1, 3, 4, 5 and 8 within 12, 10, 16, 9, 11 days respectively; in dogs LP 2, 6, 7, 9 and 10 it was recovered within 2—6 days. Fig. 3A shows the mean amount of food intake in grams measured before and after the operation. At the beginning of the food intake recovery the dogs had to be encouraged to eat by putting small morsels into the mouth, drawing a bowl close to them, by serving more attractive food and so on. At the first attempts of spontaneous eating the movements of jaws and tongue were clumsy, the food was splashed around and the dogs often choked. The dogs preferred food prepared from milk, sugar, yolk, butter and vitamins, and they willingly drank milk. Raw meat and water were definitely rejected. After 2—3 weeks the preference for or aversion to any special food was no longer observed. The dogs had the ordinary diet but ate less than before the operation. In the period of hypophagia vomiting was often observed, usually appearing 15—20 min after eating. Sometimes the dogs licked and ate the vomited food and vomited again.

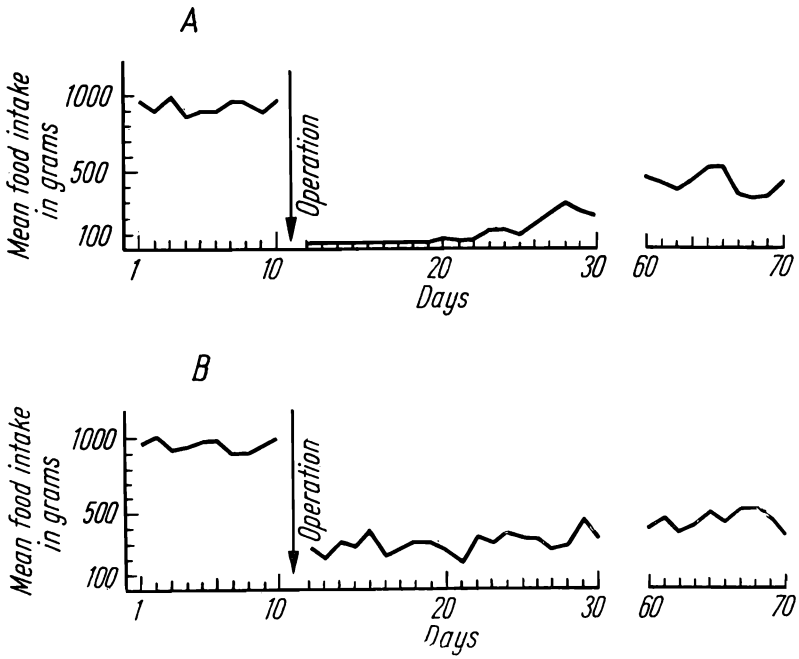

Fig. 3. Preoperative and postoperative food consumption in dogs with extensive (A) and small (B) lateral hypothalamic lesions. Ordinate: mean value of daily food intake for each group. Abscissa: time in days I, before the operation II, during 20 days after the operation III, one month later

General behavior. The general motor activity was lessened in all dogs; they walked slowly and looked sad and apathetic. It was very difficult to keep them clean, because they often lay down on the vomited food and excretions. For an hour or more they could stand motionless with one paw lifted, with the head and trunk twisted and without changing position. Such unnatural and strange cataleptic-like postures were observed only during the first weeks after the operation but no longer. Also we observed a negativism in our dogs, specially manifested during the attempts of carrying them out of the cage on the leash; they resisted vigorously and drew back.

The dogs lost their friendliness towards people, becoming indifferent to the experimenter; they did not listen to his orders, did not follow him spontaneously and so on. In spite of the apathy in some dogs we observed a defensive-aggressive attitude, which was usually manifested during a casual meeting with other dogs.

Conditioned reflex activity. In all dogs the instrumental reflexes were greatly impaired. During 5 succesive sessions they were completely

abolished and therefore they had to be retrained by the method of passive movements. In 6 dogs (LP 1, 2, 5, 7, 8, 10) the instrumental reflexes disappeared completely and in spite of a long retraining lasting about 4 months they could not be reestablished. In 4 dogs (LP 3, 4, 6, 9) the first correct reactions reappeared on the 18th, 23rd, 28th and 21st day after the beginning of the retraining, but the number of correct responses was low and these animals never reached criterion (Fig. 4A).

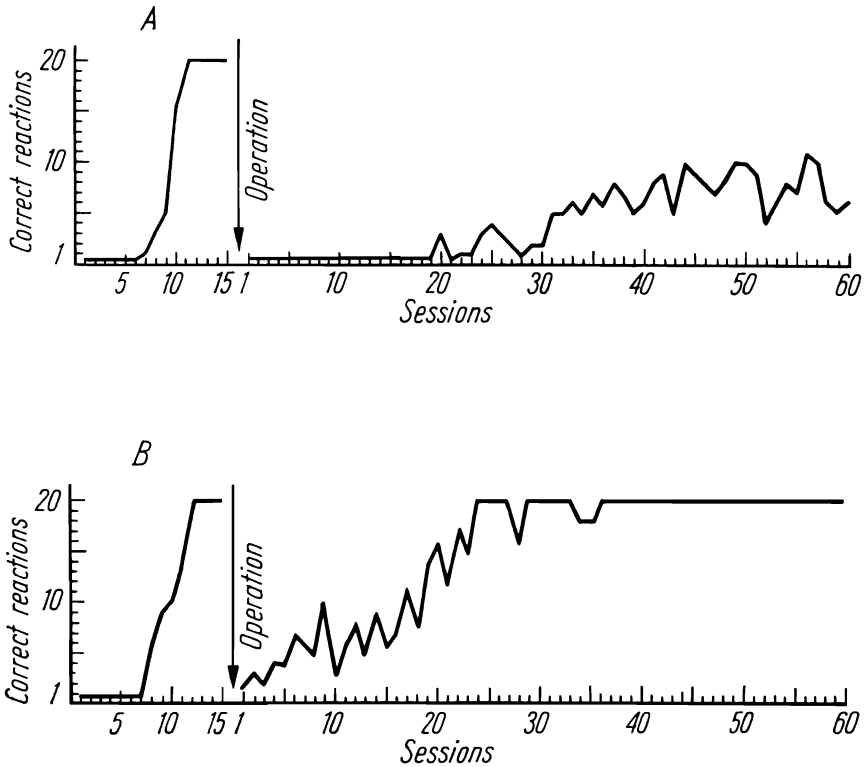

Fig. 4. The mean number of correct instrumental reactions in each group during initial training and postoperative retraining. A, group LP with extensive hypothalamic lesions; B, group LM with small lesions

Group LM

In all dogs after surgery hypophagia and adipsia was found, both lasting about 2 months. A preference for wet and sweet food was also observed. Vomiting occurred sporadically.

Immediately after the operation we observed a temporary diminution of general motor activity, though cataleptic-like postures and negativism

were not noted. In these dogs the instrumental reflex was only temporally disturbed. The proper reactions occurred on the 1st, 3rd and 4th days after the beginning of the experiments though at first the number of correct responses was low. The dogs often used the left paw instead of the right one. The number of correct responses oscillated markedly from day to day but after approximately 24 days of retraining the dogs reached criterion (Fig. 4B).

The difference between training and retraining in dogs from LP and LM groups is highly statistically significant ($p = 0.01$). In group LP and LM an analysis of variance was applied in order to compare the changes in food intake. The difference in food intake before and after the operation within these two groups and between them is statistically significant ($p = 0.01$). The amount of food intake gradually increased but did not reach normal level even after a month (Fig. 3AB).

DISCUSSION

Our results obtained in dogs with lateral hypothalamic lesions are basically consistent with the effects described by other authors on rats, cats, rabbits and monkeys, i.e. aphagia with subsequent hypophagia, adipsia, decrease of general motor activity and disturbances of the alimentary instrumental responses. Besides such generally known symptoms we observed persistent vomiting, deep apathy, cateleptic-like postures and permanent loss of the instrumental performance.

The most pronounced and multiform changes were observed in the group of dogs (LP) with large hypothalamic lesions, which involved also the posterior hypothalamus and destroyed fibers of the medial edge of the internal capsule.

In dogs with small, bilateral lesions placed in the lateral hypothalamus close to the fornix (group LM) all the symptoms were much less pronounced. In these cases total aphagia was never observed, hypophagia and adipsia lasted less long, vomiting occurred sporadically and a decrease of general motor activity was observed mostly in the first two weeks after the surgery. The disturbances of the instrumental reflexes were transient and all the dogs from this group could be retrained to a preoperative level of performance.

In comparison with data obtained after lesion of the lateral hypothalamus on various species by other investigators (Anand and Brobeck 1951, Teitelbaum and Stellar 1954, Wyrwicka 1957, 1967a, Morgane 1961a, Teitelbaum and Epstein 1962, Balińska 1963) the hypothalamic syndrome in dogs shows several differences. To begin with, in our dogs aphagia occurred only after extensive lesions and was transient, lasting sixteen

days at the longest. Moreover, as a result a small lesion only hypophagia was observed.

In the state of hypophagia a preference for wet and sweet food was observed, whereas a marked aversion for raw meat occurred. Food preference was described in rats by Teitelbaum and Epstein (1962). However, contrary to rats, our dogs were not eating much of this preferred food and never ate voraciously. Similarly to dogs described by Andersson and McCann (1956) our dogs willingly drank milk, but not water.

The occurrence of vomiting has not been described so far by other authors as a result of lesions of the lateral hypothalamus. Vomiting occurred in almost all dogs that underwent the operation, but in animals with large lesions this occurred more often and was more persistent than in animals with small lesions. Several authors indicate the existence of connections between the lateral hypothalamus and the vomiting centre, which according to Borison and Wang (1949), Wang and Borison (1950) is situated in the medulla oblongata in the neighbourhood of the fasciculus and nucleus solitarii and it embraces the dorso-lateral boundary of the lateral reticular formation. Vomiting may be the effect of an alteration in the motor activity of the stomach. As appears from the work of Glavcheva et al. (in preparation) the motor activity of the stomach is greatly disturbed after lesions of the lateral hypothalamus. The mechanism connected with the occurrence of vomiting is undoubtedly complicated and needs to be studied in detail.

One of the most fundamental symptoms of the lateral hypothalamic syndroms in dogs was the considerable disturbances of instrumental conditioned responses. In six dogs with extensive lesions there was a total loss of these responses, and in 14 dogs the instrumental reflexes were severely impaired for a long period of time. This agrees with the findings of Wyrwicka (1957) who was the first to find in lateral hypothalamic rabbits the loss of instrumental reflexes in the period of aphagia and hypophagia, followed by a slow recovery of the reflexes. In her other work Wyrwicka (1967a), as well as Balińska (1963) found after lateral hypothalamic lesions disturbances of reflexes in cats, rats and rabbits. In dogs, Chereshniev (1960) after extensive lesions mainly in the region of the posterior hypothalamus and corpora mammillaria observed a total loss of the motor alimentary conditioned reactions and in spite of long-lasting retraining they did not recover. According to Wyrwicka (1967b) a prolonged absence of the instrumental reactions after the animal's recovery of spontaneous eating may depend on long-lasting decrease of alimentary excitability and on the break of connections between the "feeding center" and the motor system.

Gladfelter and Brobeck (1962), Teitelbaum and Epstein (1962), Baillie

and Morrison (1963) and others found in aphagic rats a deficit of motor coordination of food and water intake as well as considerable decrease of locomotor activity. In our dogs we also observed a decrease of general activity, which in dogs with small lesions (LM) was only temporary but in dogs with large lesions of lateral and partly posterior hypothalamus (LP) these changes were very pronounced and long-lasting. In this latter group also other changes in behavior were noticed like apathy, lack of interest in the stimuli of surroundings, indifference toward humans, negativism and sometimes aggressive-defensive behavior. Most of the dogs from this group showed the cataleptic-like reactions and postures. Ranson and Ingram (1932), and others believe that the "cataleptic" postures occur after damage of the posterior hypothalamus. Also in our dogs the cataleptic-like postures most often were observed when the lesions extended caudally and involved the posterior hypothalamus. On the other hand, the whole hypothalamic syndrome was most pronounced if the lesions extended also laterally and invaded the medial edge of the internal capsule.

Several authors also stressed the importance of the extension of the hypothalamic lesions towards the internal capsule in producing the most severe syndrome of aphagia (Morgane 1961a, Gold 1967). This fact was interpreted as due to interruption of fibers of the motor system, both pyramidal and extrapyramidal (Morgane 1961b, Gold 1967) pointed out that the connections with globus pallidus (i.e. the pallidofugal tract) passing through this area are the most important in this respect. However in some of our cases the lesions might also disrupt the fibers connecting the hypothalamus with the dorso-medial amygdala.

Recently Fonberg (1966, 1968ab, 1969ab) observed in dogs a very similar syndrome as the result of the lesions of the dorso-medial part of amygdala: aphagia with subsequent long-lasting hypophagia, vomiting, decrease of general activity, aggressive-defensive behavior and disturbances of alimentary instrumental reflexes. The similarity of symptoms appearing after the lesions of lateral hypothalamus and the dorso-medial part of amygdala may point to the existence of a common motivational system, especially since direct anatomical connections between dorso-medial amygdala and lateral hypothalamus have been proved by Valverde (1965) using Nauta's method.

Konorski (1967) supposes that in the amygdala as well as in the hypothalamus there are two reciprocally connected centers controlling alimentary activity in animals, which the author calls the hunger drive and the hunger anti-drive center respectively. According to this author alimentary centers located in hypothalamus control the unconditioned re-

flexes, whereas centers in the amygdala mainly control corresponding conditioned reflexes.

Our findings indicate that the effect of the damage of the lateral hypothalamus is not only a temporal decline in food intake but the deficit appearing after those lesions is much more profound and general, since it concerns instrumental reflexes as well as the whole animal's motivation system causing deep changes in their behavior.

SUMMARY

Bilateral stereotaxic lesions of the lateral hypothalamus were performed on 20 dogs. They resulted in temporal aphagia and subsequent long-lasting hypophagia, adipsia, vomiting and impairment of the instrumental alimentary reflexes. Additionally, pronounced changes in general behavior were observed: apathy, decrease motor activity, negativism, cataleptic-like postures and loss of social relations with humans.

All these symptoms were much more pronounced in the group with large lesions of the lateral hypothalamus involving caudally the posterior hypothalamus and extending laterally toward the internal capsule, than in the group with smaller lesions restricted to the hypothalamic area lateral to the fornix.

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