ACTA NEUROBIOL. EXP. 1984, 44: 17-28

MOTOR ACTIVITY AND ALIMENTARY BEHAVIOR AFTER RADIO-FREQUENCY AND 6-OHDA LESIONS OF LATERAL HYPOTHALAMUS AND SUBSTANTIA NIGRA IN CATS

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Key words: far-lateral hypothalamus, substantia nigra, nigro-striatal system, alimentary behavior, motor activity, 6-OHDA, RF lesion, cat

Abstract. Effects of radio-frequency lesions or injections of 6-hydroxydopamine (6-OHDA) into far-lateral hypothalamus (FLH) and substantia nigra (SN) on feeding behavior and motor activity were studied in four groups of cats. Hypoactivity, aphagia and adipsia followed by gradual recovery of alimentary behavior were observed only after radio-frequency lesions of FLH (group I). 6-OHDA injections into FLH evoked only slight and transient disturbances in regulation of fluid intake (group II). Radio-frequency destructions of SN produced long-lasting drop in drinking (group III) while 6-OHDA injections into SN caused long-lasting fall in food consumption (group IV). In both groups with SN damages different pattern of alimentary behavior was accompanied by motor hyperactivity.

INTRODUCTION

Electrolytic lesions of the lateral hypothalamus (LH) produce in rats various short- and long-term deficits directly and indirectly related to the regulation of alimentary behavior (3, 26, 28, 29). These disturbances have been referred to as the lateral hypothalamic syndrome (29). In the past decade it was demonstrated that destruction of dopaminergic fibres

of nigro-striatal bundle (NSB) may reproduce almost all known behavioral and physiological symptoms of LH syndrome (23, 24, 26, 28, 31).

As in rats, lesions of LH in cats produce aphagia and adipsia (3, 34) followed by the same pattern of recovery of ingestion (34). Somnolence, catalepsy, hypokinesia and sensory neglect typical for early stages of LH syndrome are similar to those observed in rats (19, 34, 35).

However, the relationship between LH syndrome and the disturbances seen after destruction of nigro-striatal dopamine (DA) pathway have not been analyzed in cats. To answer these questions, we undertook an analysis of the deficits in alimentary behavior and motor activity following NSB damage. Destructions of nigro-striatal pathway were performed at two levels: the far-lateral hypothalamus (FLH) and the substantia nigra (SN). These places were lesioned either neurotoxically (6-hydroxydopamine) or by radio-frequency current (RF lesion).

MATERIAL AND METHOD

The experiments were carried out on 55 cats of both sexes weighing 2–3 kg. The animals were divided into four groups according to different localization and kind of lesions of NSB (Table I). The cats were allowed 1 h access to solid food (barley with boiled meat) and milk daily. After 1 h the food and fluid intake was measured.

TABLE I

Localization and type of lesions in particular groups of cats

Group	Type of lesion	*N*	male	female
I	FLH-RF	10	4	6
	FLH-sham	4	2	2
II	FLH-6-OHDA	10	5	5
	FLH-AA	4	2	2
III	SN-RF	9	5	4
	SN-sham	4	2	2
IV	SN-6-OHDA	10	5	5
	SN-AA	4	2	2

FLH, far-lateral hypothalamus; SN, substantia nigra; RF, radio-frequency lesions; 6-OHDA, injection of 6-hydroxydopamine — 10 μg/2 μl; AA, injection of ascorbic acid solution — 0.1%; *N*, number of animals.

Surgery. Bilateral lesions of FLH and SN were achieved by passing RF current or by injections of 6-hydroxydopamine hydrobromide (6-OHDA HBr, Sigma) according to stereotaxic coordinates earlier described (17). The RF current was applied for 15 s through stainless steel electrode 0.9 mm in diameter, insulated with teflon except for 0.5 mm at

the tip. In animals of the control groups (FLH-sham, SN-sham) the electrode was only guided into brain 1 mm deep above the site of real lesion.

6-OHDA was dissolved to concentration of 10 μg/2 μl (free base) in cooled to 4°C vehicle (0.1% solution of ascorbic acid in izotonic saline). 6-OHDA was always dissolved just before the injection. Cats of the control groups (FLH-AA, SN-AA) received 2 μl of vehicle solution. The solutions were administrated once, by Hamilton microsyringe. The rate of fluid administration was 1 μl/min. The canulae of microsyringe was removed 1 min after the injection.

Apparatus and procedure. Spontaneous motor activity was measured for 10 min daily, in 1 m square open field, area of which was divided into 100 equal squares. The activity units (au) were computed on electronic counter when the cats triggered the squares, moving in the experimental cage. The behavior of animals was observed on a TV set by means of TV closed circuit. Motor activity was always measured after 23 h of food deprivation. Following surgery, those cats that became aphagic and adipsic were maintained by placing small bits of food and instilling milk into their mouths. At the end of experiments each animal was sacrificed, its brain fixed in formalin and stained with cresyl violet (Nissl's method) for the purpose of histological verification of the destroyed area.

RESULTS

Histology. The localization of RF and 6-OHDA destructions were described in details previously (17). The localization of the damaged area allows us to consider that fibres or cellular elements of NSB were destroyed in each animal (Fig. 1 AB).

Alimentary behavior and motor activity. The ANOVA (Lindquist, mixed design, type I) (20) was used for statistical evaluation of data. The effect of days — A, effect of group — B, and interaction AB were analyzed. Further analysis was made with the use of Duncan's test (25). Because the effect of group was insignificant only the effect of A and AB factors were shown on the Figures. We did not find any significant changes in alimentary behavior and motor activity in the control groups. Hence, the Figures are showing only the patterns of disturbances in lesioned groups of cats.

Alimentary behavior. RF lesions of FLH (group I) evoked in all cats aphagia and adipsia lasting not more than one week (Fig. 2 II, III). During forced feeding animals manifested some sensorimotor impairments in "oral ingestive behavior": chewing, biting and swallowing were slow

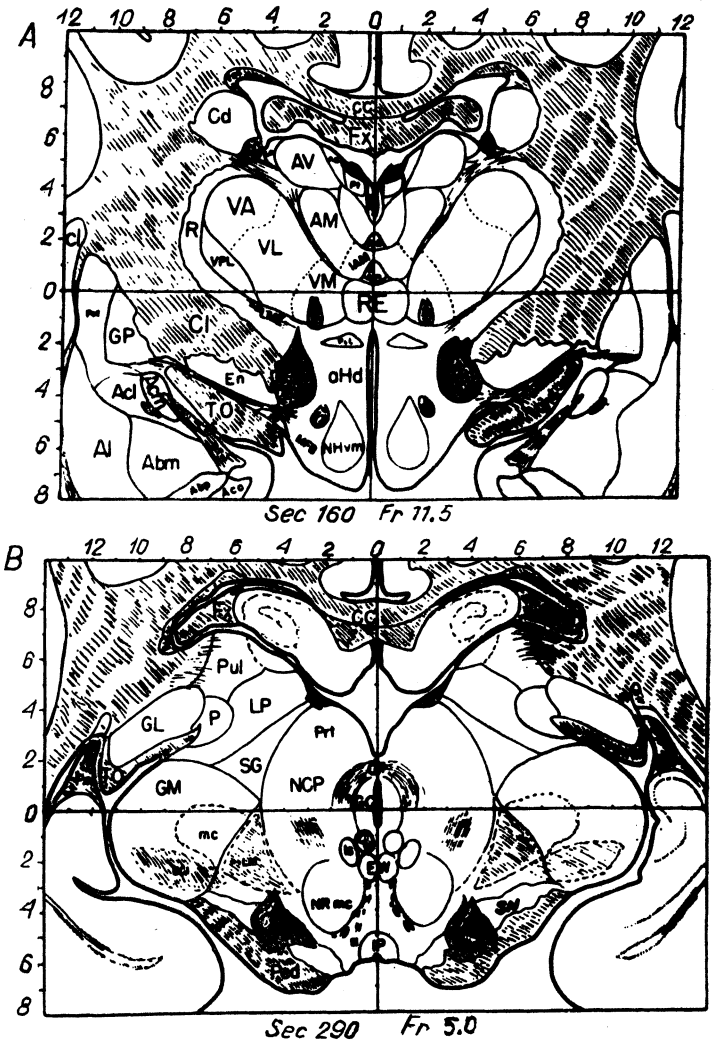

Fig. 1 *A–B*. *A*, reconstruction of representative RF (blackened area) and 6-OHDA (spotted area) destruction of far-lateral hypothalamus. *B*, reconstruction of representative RF (blackened area) and 6-OHDA (spotted area) lesion of substantia nigra.

and awkward. On the next days of recovery, food and milk intake gradually increased and reached the preoperative level at the end of experiments.

6-OHDA destructions of FLH (group II) did not cause statistically significant changes in food consumption (Fig. 3 II). The milk drinking was significantly reduced only between 1–3 postoperative day (Fig. 3 III).

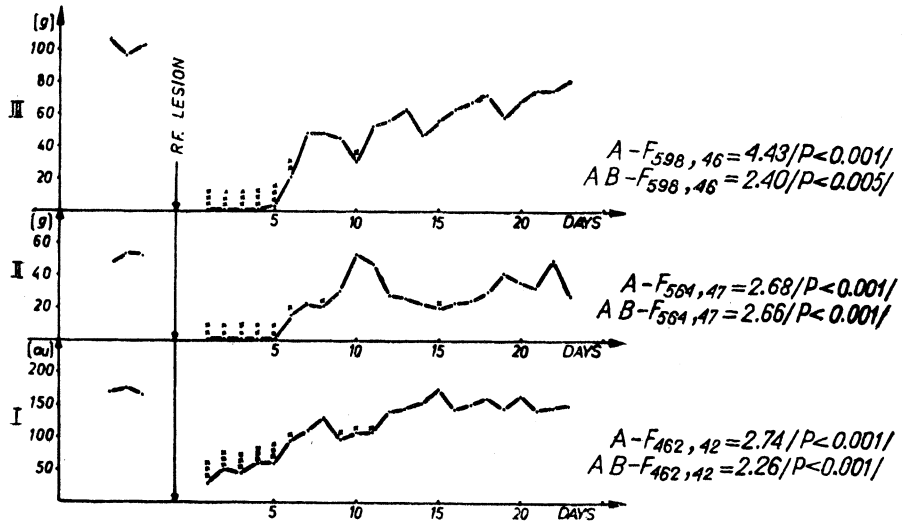

Fig. 2. Motor activity (I), solid food intake (II) and milk intake (III) in cats with RF lesions in far-lateral hypothalamic area (xxx — $P < 0.001$, xx — $P < 0.01$, x — $P < 0.05$ as compared to the last preoperative data, Duncan's test).

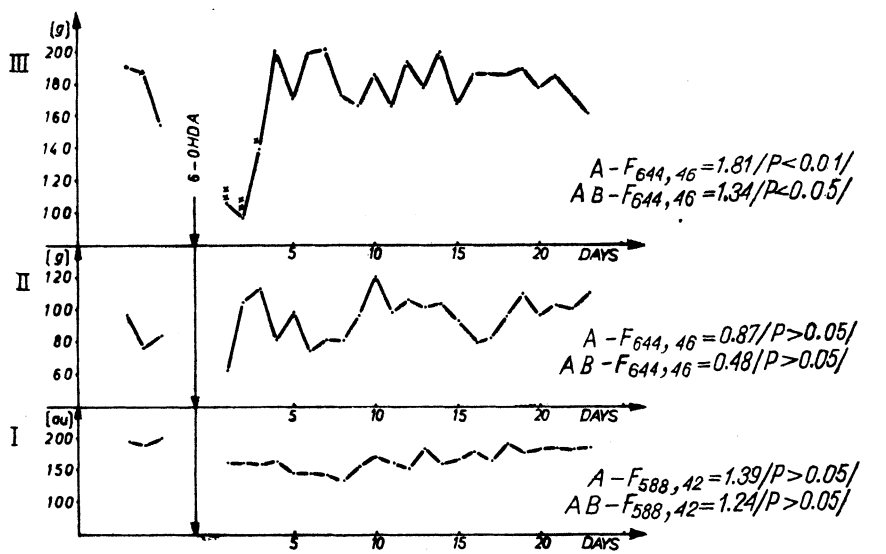

Fig. 3. Motor activity (I), solid food intake (II) and milk intake (III) in cats with 6-OHDA lesions in far-lateral hypothalamic area (xxx — $P < 0.001$, xx — $P < 0.01$, x — $P < 0.05$ as compared to the last preoperative data, Duncan's test).

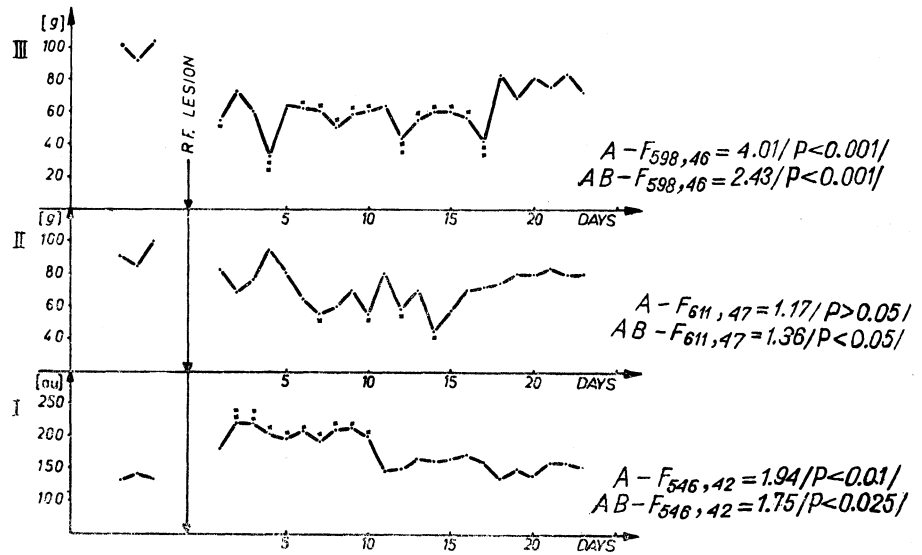

Fig. 4. Motor activity (I), solid food intake (II) and milk intake (III) in cats with RF lesions in substantia nigra (xx — $P < 0{,}01$, x — $P < 0.05$ as compared to the last preoperative data, Duncan's test).

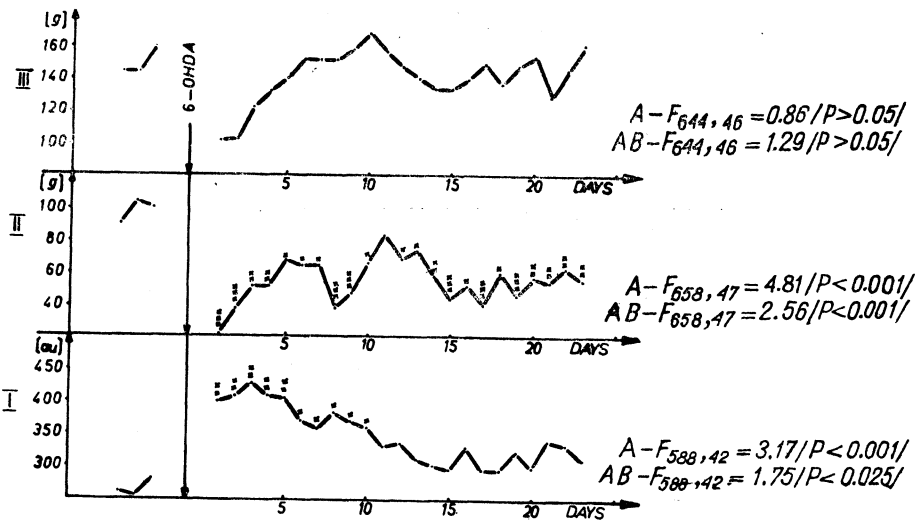

Fig. 5. Motor activity (I), solid food intake (II) and milk intake (III) in cats with 6-OHRA lesions in substantia nigra (xxx — $P < 0.001$, xx — $P < 0.01$, x — $P < 0.05$ as compared to the last preoperative data, Duncan's test).

RF damages of SN (group III) produced only long-lasting decrease in milk intake (Fig. 4 III) while 6-OHDA injections into the same area (group IV) evoked only long-lasting fall in food consumption (Fig. 5 II).

Motor activity. Deficits in alimentary behavior seen in animals of group I were accompanied by initial akinesia or hypokinesia (Fig. 2 I). As those cats were recovering from aphagia and adipsia, the motor activity gradually increased and after about two weeks reached the preoperative level.

6-OHDA injections into FLH (group II) did not evoke any disturbances in behavior of cats. The motor activity of those animals was unchanged (Fig. 3 I).

All cats with RF and 6-OHDA lesions in SN (group III and IV) manifested pronounced hyperactivity (Fig. 4 I and 5 I). Changes in motor activity in animals of both groups were independent of different patterns of disturbances in alimentary behavior.

DISCUSSION

Ingestive behavior. Aphagia and adipsia followed by gradual recovery of alimentary behavior were observed only after RF lesions in FLH. On the other hand, 6-OHDA injections into FLH evoked slight and transient disturbances in regulation of food and fluid intake. RF destructions of SN produced a long-lasting drop of milk drinking while 6-OHDA injections into SN caused a long-lasting fall in food consumption.

Disturbances in alimentary behavior in cats of group I are typical for LH syndrome. It is worth noting that even the most severe deficits in regulation of food and fluid intake observed in those cats were not as severe and long-lasting as described in cats and rats by other authors (3, 12, 29, 34). In our experiments cats were allowed an access to liquid and solid food (but not to dry, standard food and water) which in case of destructions evoking disturbances in "oral ingestive behavior" may be very significant. These results confirm the view that severity and duration of deficits in feeding behavior depend also on the experimental diet used (33).

Only after RF damages in FLH aphagia and adipsia were accompanied by some deficits in "oral ingestive behavior". Since, several other neural pathways lead through FLH area (16) and they may directly or indirectly (e.g., by the control of motor function) take part in regulation of ingestive behavior (22), it is likely that RF lesions as unspecific type of damage affected the function of these pathways.

In none of remaining groups was the full LH syndrome obtained and what is more, aphagia and adipsia (with exception of transient changes in group II) never appeared jointly (group III and IV). In light of Ungerstedt's (31) and Stricker and Zigmond's (28) hypothesis aphagia and adipsia as well as whole behavior of animals with LH lesions are the effect of decrease of endogenous activation as the result of destruction of fibres of NSB. The proper localization of RF and 6-OHDA lesions allows us to judge that NSB was damaged in all groups of cats. Therefore, according to the above mentioned hypothesis one should expect more severe disturbances in regulation of ingestive behavior. In the present experiments the intracranial method of 6-OHDA injection (without pretreatment with desmethylimipramine — DMI) was used. This technique according to other authors (4, 6, 9, 10, 15, 24, 36) appeared to be effective in evoking aphagia and adipsia in rats. However, the fact that 6-OHDA without pretreatment with DMI damages not only DA neurons but the other catecholaminergic (CA) systems as well, cannot be omitted (5, 21). The area of the lateral hypothalamus is penetrated by fibres of the ventral noradrenergic bundle (VNB) (30) and a selective destruction of this bundle produce hyperphagia and hyperdipsia (1, 2). It is very probable that the pattern of ingestive behavior in the cats of group II may be the result of lesion of two CA systems, opposing in relation to the control of alimentary behavior (NSB and VNB).

As compared to FLH, SN area is neurochemically more homogenous: approximately 90% of cells of zona compacta contains DA (14). In light of these data the results of group III and IV are difficult to explain. They suggest that in SN apart from DA neural elements (whose damage by 6-OHDA caused long-lasting drop in food intake) the neural substrate of the antagonistic functions must also exist. That may be why the unspecific RF lesions did not evoke any disturbances in eating. Results obtained in III and IV group indicate moreover that NSB does not control drinking behavior on the SN level. Chemical specificity of mechanisms counteracting changes in food consumption in cats of group III as well as the neurochemical substrate responsible for the control of drinking behavior in SN are unknown.

Motor activity. In their neurochemical model of LH syndrome Stricker and Zigmond (28) have recently proposed that NSB destruction is critical for behavioral arousal. Hence, they put forward a hypothesis that a general factor such as loss of endogenous activation is involved in etiology of LH syndrome i.e., disturbances in alimentary behavior as well as in somnolence, catalepsy, hypokinesia, sensory neglect. Above and previously described data (19) do not confirm the mentioned hypothesis: motor hypoactivity, somnolence, catalepsy and deficits in "oral

ingestive behavior" were seen only after RF damage of FLH. 6-OHDA injections to FLH did not change motor activity and both techniques of SN destruction used evoked motor hyperactivity. No changes in activity in cats of group II suggest that CA mechanisms of LH area are not directly involved in control of motor arousal. Motor hyperactivity observed in animals of both SN lesioned groups (group III and IV) indicates that damage of CA (mainly DA) substrate in SN evokes increase in motor arousal which is in agreement with results obtained in rats (11). The mechanism of hyperactivity in cats of III and IV group is not quite clear. Considering the reasons of motor arousal after lesions of the different neural areas (32) and the fact that SN is involved in midbrain reticular formation which mediates the regulation of motor function (27), the hyperactivity may be the result of specific arousal of motor system by compensatory mechanisms activated by lesions (8).

Motor function and ingestive behavior. Hypophagia and hypodipsia simultaneously with hypoactivity were observed only after RF lesions in FLH (group I). The effect of damage of DA elements of SN on motor activity was independent of their effect on fluid and food intake (group III and IV). It appears therefore that deficits in alimentary behavior obtained after FLH and SN destructions cannot be explained only on the basis of changes in general arousal level as it was suggested (28).

Another problem is the role of oral motor disturbances in evoking aphagia and adipsia. In the present paper we have confirmed the view (18, 22) that aphagia and adipsia may be the effect of motor failure produced by damage of neural systems which are involved in control of movements essential for eating and drinking. It does not mean, however, that aphagia and adipsia observed after NSB damage are always connected with motor disturbances: the latter were not observed in group III and IV while aphagia and adipsia appeared sporadically. Therefore, it seems that regulation of motor function and alimentary behavior may be realized quite independently. This view is confirmed by results obtained in rats (7, 13).

Lateral-hypothalamic syndrome and NSB in cats. Obtained results indicate that the fully expressed complex of disturbances called LH syndrome is evoked only by unspecific lesions in LH. These disturbances seem to be the effect of destruction of several neural elements of LH area. The present data confirm the fact that the dopaminergic NSB is essential for feeding (but not drinking) behavior in cats. One may doubt however, that this bundle is essential for LH syndrome of aphagia and adipsia in these animals.

I am very gratefull to Dr. P. Jastreboff and Mr. M. Sikora for the statistical evaluation of the results.

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Accepted 22 October 1983