Striato-pallidal influence on food intake, body weight and locomotor activity


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MS received 23 August 1976

ABSTRACT

The food and water intake, body weight, and locomotor activity (wheel runs) were studied before and after stereotaxic electrolytic lesions at different planes of caudate nuclei of adult male and female albino rats. Lesions of lateral preoptic area, medial forebrain bundle and marginal regions of globi pallidi led to aphagia and adipsia lasting for 8–38 days. Locomotor activity, however, remained normal and there was no motor deficit. There was significant increase in wheel running (100–450%) after tiny lesions in the anterior part of caudate nucleus (A 8–6) whereas marked drop (50–90%) in daily wheel running was observed with posterior lesions at A 7–6. Increase in body weight (30–35%) and food and water intake (15–20%) without any change in locomotor activity resulted after tiny symmetrical lesions involving caudate nucleus just above the globus pallidus (A 7–4). Lesions involving nucleus accumbens, medial preoptic area and ventromedio-marginal part of caudate nucleus, however led to 10–25% decrease in body weight in spite of 30–35% increase in food intake. The results suggest a differential striato-pallidal regulation of food and water intake, body weight and activity.

1. INTRODUCTION

Just as the hypothalamus has enjoyed its supremacy in the control of food and water intake over the years, the striatum has been known for its role in the regulation of motor functions. Recently the involvement of striato-pallidal structures in the regulation of food and water intake has been stressed.

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Morgane \(^1\) observed aphagia and adipsia in rats after lesioning of pallido-fugal fibres at the site of their origin. It has been reported that the caudate nucleus is essential for the appearance of feeding behaviour both in the decorticate cat and rat. \(^2\) Involvement of striato-pallidal fibres, in food intake has also been observed by Gold. \(^3\) In addition, one-stage or two-stage bilateral lesions of the pallidum have been shown to produce a transient aphagia and adipsia. \(^4\)

A conspicuous increase in the frequency and amplitude of electrical activity of the caudo-lateral part of the caudate nucleus just anterior to the anterior commissure was reported by Sharma \(^5\) after 4 minutes of intragastric glucose load in the freely moving rat. Insulin, by contrast led to some depression of the activity. Opposite effects were observed from rostro-medial portions of the caudate nucleus in that gastric glucose load decreased while insulin increased the electrical activity. Selective changes in the electrical activity of the caudate nucleus of unanaesthetized cats after gastric distension and intragastric infusion of glucose and/or sodium chloride, have also been reported. \(^6\) Rubinstein and Delgado, showed that the stimulation of structures in the head of the caudate nucleus in monkeys produced immediate stoppage of and inhibition in their normal interest in food intake. Drinking was also reported to be inhibited on such stimulation.

It is known that the state of hunger or satiety is linked in some way with general \(^8,9\) motor activity. Satiated animals tend to be lethargic and show decreased motor movements while hungry animals show an increased level of motor activity which may be manifested in wheel running, searching and other associated locomotor movements. Shirley, \(^10\) and Baumeister et al. \(^11\) reported that wheel running activity is sensitive to several types of appetitive motivation. Decreased motivation in any sphere involving the performance of locomotor acts has also been observed in VMH lesioned obese animals. \(^13\) However, no systematic studies on the involvement of the caudate nucleus in motor performance and food intake behaviour have been done. In the present series of experiments, an attempt has been made to study the effects of discrete electrolytic lesions of the striatum on food and water intake and its relationship to body weight and locomotor activity of the rat.

2. Materials and Methods

Thirty seven Holtzman adult albino rats (12 females and 25 males) form the basis of this study. Out of these, twenty-four rats (12 females and 12 males) were housed in individual running wheel activity cages with ad lib food and water readily available. Food and water intake, body weight, and wheel runs were charted every day. The other group of 13 male rats were
maintained on ad lib food and water in individual cages without running wheels. Daily records of food and water intake and body weights were kept. The rooms were kept on a 12-hour day-night cycle and at 70–75°F for all experiments.

After initial observations of 4–5 weeks, bilateral electrolytic lesions were made at different planes in the caudate nucleus of 29 rats. The coordinates used were A 7·5 mm to A 9·00 mm, R and L, 1·75 mm to 2·00 mm, and vertical −1·0 to +1·0 mm (Degroot).13 The lesions were produced by a direct current of 2 m amp passed through a 0·25 mm stainless steel electrode for 20 sec. The remaining eight rats served as controls. Three of these eight rats had sham operations. Food intake, water intake, body weight and wheel runs were recorded for 1–2 months postoperatively.

Animals which turned aphagic and/or adipsic were kept on oral glucose/saccharine, wet diet, liquid diet, doughnut, cookies or tube feeding. In a few rats intraperitoneal and/or subcutaneous Ringer lactate was also given when tube feeding led to diarrhoea and rectal bleeding. A few animals showed signs of marked decrease or increase in urinary output postoperatively, and twentyfour hour urine was collected in these animals and also in some control animals.

At the end of the study the animals were perfused with 0·9% saline followed by 10% formalin solution and the brains were taken out for histological examinations to confirm the site and extent of lesions.

3. RESULTS

The lesioned rats presented a variable picture with respect to food and water intake, changes in body weight, and locomotor activity, with the results largely depending on the site, nature, and extent of the lesions. Broadly, the rats can be divided into the following five categories showing particular manifestations: (i) aphagia and adipsia; (ii) increased locomotor activity with no change in food intake and body weight; (iii) decreased locomotor activity with no change in food intake and body weight; (iv) increased body weight with no change in locomotor activity; and (v) decreased body weight with increase in food intake. Sites of lesions in representative rats from each of these groups are diagrammed in figure 1.

(i) APHAGIA AND ADIPSIA.—

Eight of the rats had aphagia and adipsia lasting for 8–38 days. Four of these rats died after 10–14 days of aphagia and adipsia in spite of tube feeding. They showed a conspicuous loss of body weight (30–45%), the rate of loss showing virtually a constant slope till death. Their locomotor activity, however, remained normal except for the last 2–4 days before death, when it showed a marked decline. Informal but frequent neurological examination did not reveal any motor deficit.
Figure 1. Diagrammatic representation of brain sections at various co-ordinates. The sites of lesions are shown by hatched lines.

The responses observed in rat No. 7, representative of the recovered aphagic and adipsic rats, are shown in figure 2. As observed in other rats of this group, bilateral symmetrical lesions at A 7.4, involving lateral preoptic area, medial forebrain bundle and marginal region of globi palladi (figure 1; rat No. 7), produced marked aphagia and adipsia. Various choices of food to eat and drink, like glucose solution, bread soaked in milk, chocolate chip cookies, doughnut, etc. were offered without any success for 23 days. The glucose or liquid diet of Teitelbaum and Epstein was given by intragastric tube on alternate days for 10 days until the animal showed diarrhoea and frank blood per rectum. The intragastric feeding was stopped at this time and the animal was revived by intraperitoneal and subcutaneous lactate
Figure 1. Food and water intake and body weight before and after the lesions. X—X: bread-milk mixture.

Ringer solutions with 5% dextrose (Hartmann's solution: Travenol Lab. Inc. Morton Grove, Ill.) and the injection schedule continued for another 10-12 days. It was interesting to find that this animal which was reduced virtually to its skeleton and looked miserable became alert and active for several minutes after systemic lactate—Ringer injection but still would not make any attempt to eat or drink on its own. On the 24th day of aphagia, the animal started licking the milk from the dish containing bread soaked in milk. For the next 12-13 days, it consumed the liquid out of the milk-bread mixture but refused stock diet or water even when bread-milk mixture was withheld. It started eating stock diet on the 38th day and drank water from the 39th day onwards. Though food intake came back to the preoperative level within two weeks time, water intake remained at a substantially lower level. The weight curve showed some increase after the animal started eating and drinking but the weight barely reached the preoperative level after 70 days. Locomotor activity remained quite comparable to the control level during the first week after operation, then became variable and generally declined although it again reached normal levels coincident with the restart of stock diet and water intake.
Figure 3. Food intake shows periods of wet diet (X—X) and stock diet (O—O). On 20th day salt diet (O) was given. Body weight and water intake are also shown.

Another rat (rat No. 41) of this group had aphagia for 8 days but showed adipsia for 30 days (figure 3). This rat had slightly asymmetrical lesions occupying the lateral preoptic and marginal part of the globus pallidus on one side and part of the lateral and medial preoptic areas on the other side at the level of A 7.4 (figure 1; rat No. 41). After the period of aphagia, the animal started taking wet diet. Intake was significantly increased when the rat was kept on wet diet but was quite comparable to the preoperative values when kept on stock diet. The animal, however, refused to drink water or glucose solution or even milk when offered. On one of the days (20th) salt diet was also tried to see if salt would induce the rat to drink water but that too did not produce drinking (see figure 3). When the animal finally started drinking (30th day), its daily water intake rapidly rose to a level that was substantially higher than the preoperative level. This increase in water
intake was observed in spite of the larger amounts of wet diet taken by the animal. Concomitant with this increased water intake was a marked increase in urine output (figure 4). During the aphagic period body weight loss was about 30-40% and remained at this level for almost three weeks even though the animal started taking food in amounts quite comparable to or greater than the amounts it consumed preoperatively. Once the animal started drinking water (30th day) its body weight showed some increase but was still about 15% lower than the pre-operative weight after 55 days.

(ii) INCREASED LOCOMOTOR ACTIVITY WITH NO CHANGE IN FOOD INTAKE.— The four rats forming this group showed increased wheel running activity but little change in food intake (figure 5). The increase in locomotor activity ranged daily from 100% to about 450%, and this increase was manifest within 10 to 15 days of the operation. Rat No. 30, like other animals of this group had small and slightly asymmetrical lesions in the caudate nucleus at the level of A 8.6 (figure 1; rat No. 30). After a brief aphagic and adipsic period of 1-2 days, this animal started eating normal amounts of stock diet. Water intake showed a mild increase, and the day to day water intake variations increased, particularly after about four weeks. Not only did locomotor activity show a significant rise but its daily variations were also large.

(iii) DECREASED LOCOMOTOR ACTIVITY WITH NO CHANGE IN FOOD INTAKE— Five rats, showing small symmetrical lesions involving the caudate nuclei just above the anterior commissure, at the level of a A 7.6 (figure 1; rat No,
26), formed this group. The animals showed a marked drop in daily wheel running activity ranging from 50 to 90%. There was, however, no essential change observed in food and water intake or body weight (figure 6).

(iv) INCREASED BODY WEIGHT WITH NO CHANGE IN LOCOMOTOR ACTIVITY. — Two of the animals showed a 30–35% increase in body weight 3–4 weeks after receiving lesions and the body weight increases were maintained for the rest of the experiment. An increase of about 15–20% both in food and water intake was also observed during this interval. There was, however no change in locomotor activity. The lesions were typically tiny and symmetrical, involving the caudate nucleus just above the globus pallidus at A 7.4
Figure 6. Shows marked decrease in wheel turns without any change in body weight, food and water intake after the operation in rat No. 26.

(figure 1; rat No. 22). Figure 7, shows the results obtained in rat no. 22 of this group. The animal showed aphagia and adipsia for 3–4 days followed by a 40–42% increase in food intake and a 50–55% increase in water intake lasting for about a week. The food and water intake continued to be higher for the rest of the period although the magnitude of increase only ranged between 15–20%.

(v) DECREASED BODY WEIGHT WITH INCREASE IN FOOD INTAKE.—Three rats showed a 10–25% decrease in body weight in spite of a 30–35% increase in food intake. These animals had lesions at the level of A 8·6 that were rather medial as compared to group (ii) animals and involved part of
nucleus accumbens, medial preoptic areas and ventro-mediomarginal part of the caudate nucleus (figure 1; rat No. 45). Rat No. 45 is a typical animal of this group and its results are presented in figure 8. The animal showed aphagia for 2–3 days followed by a 35% increase in food intake both on dry and wet diets. Water intake showed a decrease on the days of wet diet though the total water intake was somewhat elevated (5-15%), the extra water being provided by the wet diet. In comparison to wet diet days, the water intake on dry diet days showed no change and was similar to preoperative ingestion levels. The body weight, which had initially shown a drop of about 22% during the period of aphagia, remained about 10% lower than the preoperative body weight even at the end of 50 days when the animal was taking 30–35% more food. The urine output also remained lower throughout this period (figure 4).
Aphagia and adipsia in group (i) animals was always an immediate postoperative phenomenon. The animals in which aphagia and adipsia lasted for 4–5 days only showed a decrease of 20–30% in body weight during this interval and recovered to their normal growth rate within two weeks. Of the 4 rats which died within 10-15 days of aphagia and adipsia, the weight loss was in the range of 32–45% in spite of tube feeding. Such a rate of weight loss is in confirmation of earlier studies by Morgane. Rat No. 7 which was aphagic and adipsic for almost 3 weeks did start drinking the milk out of the milk-bread mixture though it refused stock diet and remained adipsic to water for another 2 weeks. Its brain damage was restricted to medial segments of globi pallidi and preoptic areas. Morgane reported prolonged aphagia and adipsia after lesions of internal segments of globi pallidi but his rats which were supported on food
and fluid diets died or reverted to aphagia and adipsia after tube removal. The coordinates for his rats were at AP 5·6 and 6·0 as compared to the more anterior (AP 7·4) lesions of the present study. Though it became difficult to maintain aphagic and adipsic rat No. 7 on tube feeding because of gastro-intestinal stress, complete recovery resulted with frequent systemic injections of lactated Ringer solution. It is felt that maintenance of electrolyte balance by systemic routes must be maintained in such aphagic and adipsic animals. The recovery of these animals from stages of aphagia and adipsia through anorexia and hypodipsia to complete recovery can be compared, in many ways, to the recovery of feeding and drinking after lateral hypothalamic lesions, as shown by Teitelbaum and Epstein.\(^{14}\)

Rat No. 41 on the other hand, was aphagic and adipsic for 7 days but started taking wet diet on the 8th day, though it remained adipsic to water or other palatable solutions like glucose, saccharine or milk for another 3 weeks or so. This rat had asymmetric lesions. The preoptic area, medial forebrain bundle and a small lateral outer segment of the globus pallidus was destroyed on one side whereas the lesion on the other side was rather medial involving only the preoptic areas. Both the lateral hypothalamus (LHA) and the lateral preoptic area (LPO) have been shown to be involved in drinking behaviour. Almli and Weiss\(^{15}\) suggest an unexplained separation of appetitive and consummatory drinking behaviour following neural destruction of either of the two neural zones i.e., LHA and LPO. The postoperative polydipsia and polyuria of rat No. 41 towards the end might even suggest involvement of origins of hypothalamicohypophyseal pathways.

The bilateral destruction of lateral hypothalamic areas has been repeatedly shown to produce varying degrees of aphagia and/or adipsia.\(^{3,5,6,7}\) Teitelbaum and Epstein\(^{14}\) studied the lateral hypothalamic animal over an extended period of time and reported various phases of recovery in their aphagic animals. Based upon the evidences from the work on spreading cortical depression and the parallel between recovery and development, Teitelbaum\(^{18}\) suggested that the lateral hypothalamus is part of a highly encephalized system involved in the control of food and water intake. Morgane\(^{1}\) reported complete aphagia and adipsia of lateral hypothalamic lesioned animals after bilateral lesions in the internal segments of the globi pallidi and concluded that the lateral hypothalamic area, rather than being thought of as a 'feeding' or 'drinking centre', should instead be thought of as a coinfuence or merging area for many critical neuronal systems not only from the limbic and rhinencephalic forebrain area, but also from the globi pallidi. Ungerstedt\(^{19}\) reported an ascending nigro-neostriatal dopamine pathway passing through the far lateral hypothalamic region. Selective
destruction of this bundle by applying 6-hydroxydopamine to the substantia nigra produce aphagia and adipsia.20

**Changes in body weight with or without changes in food and water intake**

Both Brobeck *et al.* 21 and Kennedy22 reported hyperphagia and obesity following damage to V.M.H. But the obesity of these lesioned animals has been attributed to a significant increase in food intake by Brobeck *et al.* and to changes in the metabolic systems of the animal by Kennedy. Kennedy proposed that V.M.H. lesions disrupt the energy metabolism in such a way that the animal over-eats until a new but considerably higher level of balance between food intake and energy expenditure can be achieved. Recently Rabin and Smith23 and later Rabin24 have reported independence of food intake and obesity following V.M.H. lesions in the rat.

In the present study small bilateral ventral lesions involving caudate nuclei just above the globus pallidus produced a 30-35% increase in body weight but only a 15-20% increase in food intake and no change in locomotor activity, suggesting that this extra increase in weight may be a primary effect of the lesions which is not accounted for by hyperphagia. This differential functional aspect of caudate and associate forebrain structures becomes more challenging for further study especially when a 10-25% decrease in body weight is observed in spite of a 30-35% increase in food intake after bilateral involvement of the medial part of the nuclei accumbens, anterior commissure, medial preoptic areas and ventro-medio-marginal parts of the caudate nuclei. It may be mentioned here that these were male rats and they should have shown a rising growth curve had they been left unoperated. The decrease of 10-25% in body weight is only compared to the body weight recorded on the day of operation. This percentage decrease would be much more when compared to an extrapolated growth curve. Both groups (increased and decreased body weight) showed aphagia and/or adipsia for 3-4 days but one group with lesions of the posterior ventrolateral caudate only came back to its preoperative weight level in 7 days and showed a later increase in body weight whereas more medial and larger anterior paleo-striatal lesioned animals had a very slow increase in their body weight, remaining below the preoperative level even towards the end.

These observations clearly point out that though under normal circumstances an increase in food intake can be expected to increase the body weight, disruption of metabolic pathways may lead to opposite results, and one of the ways to disrupt such a metabolic sequence may be by damaging certain forebrain structures.
The caudate nucleus has been identified as a major source of inhibitory influence on motor functions, and lesions in the caudate nucleus increase motor activity. Both increases and decreases in locomotor activity without any change in food intake, water intake or body weight have been observed after damage to the caudate nucleus, the sites of lesions varied in their antero-posterior placements. Lesions of the ventral caudate at A 8.6 led to a 100 to 450% increase in activity, whereas lesions of the ventral caudate at A 7.6 produced a 50 to 90% decrease in locomotor activity. The functional heterogeneity of the dorsal and ventral aspects of the caudate nucleus has been stressed by various authors. Hull, Buchwald and Ling suggested that the caudate may be part of the cholinergic inhibitory system. Neill and Grossman however stressed a word of caution against the assigning of all behavioural inhibition to a single cholinergic system. They found that a blockade of cholinergic components of the dorsal caudate increased locomotor activity only in a novel environment but blockade of cholinergic components of the ventral caudate increased locomotor activity in both novel and familiar environments. Also, lesions of the ventral caudate led to inhibition of locomotor activity, just opposite to that observed in blocking of the cholinergic component, and may indicate the involvement of the non-cholinergic system as well. Neill and Grossman further suggested that this non-cholinergic component of the ventral caudate may be a part of the dopaminergic system. It is quite likely that the anterior lesions of the present study leading to increased activity might have involved the cholinergic system of Neill and Grossman and posterior lesions with decreased activity are a result of involvement of the non-cholinergic system.

Such a diversity of changes from aphagia and adipsia to isolated changes in locomotor activity or changes in body weight show that functionally the stratum is not one unit. Anatomically it consists of several nuclei traversed by important fiber bundles. Functionally it is the paleostriatum, which includes the putamen, globus pallidus, bed of striaternalis, and that part of the caudate which is related to striaternalis and nucleus accumbens, which seems to have a differential effect on regulation of food and water intake and maintenance of body weight. The changes in locomotor activity appear to be independent of food intake.

REFERENCES