Recovery of Weight Regulation Following Ablation of Frontal Cortex in Rats

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GLICK, S. D. AND S. GREENSTEIN. Recovery of weight regulation following ablation of frontal cortex in rats. PHYSIOL. BEHAV. 10(3)491-496, 1973.—Recovery of a postoperative weight loss following bilateral ablations of frontal cortex in rats was quicker when food pellets were scattered on the cage floor than when pellets were available only in attached food hoppers. Food deprivation prior to surgery facilitated recovery when food was scattered on the cage floor after surgery. Successive stage surgery also facilitated recovery. Despite and facilitative influences on recovery from the initial postoperative weight loss, all frontal rats showed a temporary weight loss 4-5 weeks after surgery if food previously available on the cage floor was removed (food remained in the hoppers). The results indicated that time per se after surgery and postoperative experience had different roles in recovery of function following brain damage.

Frontal cortex  Weight regulation

RATS subjected to bilateral ablation of frontal cortex lose up to 25% of their body weight within 3-4 days after surgery and regain this weight within the next 10 days [5]. Although residual long-term disturbances in weight regulation have been investigated [1, 2, 5, 9, 10] relatively little attention has been directed to the early postoperative changes following damage to frontal cortex. The aim of the present investigation was to determine what kind of deficit (e.g. motivational, motor) was responsible for the initial postoperative weight loss and what factors were involved in the subsequent recovery. An attempt was made to discern what aspects of the recovery involved time per se vs. experience after surgery. Both factors have been implicated in the recovery following lateral hypothalamic damage [4]. Comparisons were also made between rats receiving bilateral lesions simultaneously and rats receiving successively a unilateral lesion followed in two weeks by a lesion of the contralateral side.

GENERAL METHOD

Animals and Apparatus

The animals were naive female Sprague-Dawley albino rats approximately three months old at the beginning of each experiment and weighing between 220-280 g. Rats were housed in standard individual Wahman hanging cages (#LC-75/A) with attached food hoppers (#LC-303) and holders for water bottles. Purina laboratory chow (pellets only) was used throughout the study.

Surgery and Histology

All surgery was performed under methohexital anesthesia (Brevital, 40 mg/kg IP). A scalp incision was made along the midline of the head and subcutaneous tissue was deflected. With the use of a dental drill, bilateral burr holes, each 5 mm in dia. were made in the skull, 0.5 mm from the midline and 0.5 mm in front of the coronal suture. This procedure alone constituted the sham operation. Frontal cortex was removed by suction through a 20 guage needle under a dissecting microscope. Both sham and frontal operations were completed by closing the wound with 7 mm wound clips.

Following their use in an experiment, all rats were killed and perfused with 10% formalin. Their brains were removed and immersed in 10% formalin for at least one week before frozen sections (40 μ, stained with Luxol blue and cresyl)

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violet) were made and histological examination was conducted. In all cases, histological study showed symmetrical lesions with the major area of destruction confined to frontal cortex and without any damage to the olfactory system. Only rarely was subcortical white matter (corpus callosum) included in the lesion. The major area of cortex destroyed extended rostrally to the tips of the frontal pole and caudally to the genu of the corpus callosum. The lesions always included medial but not sulcal cortex, as described by Leonard [7]. Figure 1 shows representative sections of a typical frontal ablation.

FIG. 1. Representative anterior (a) and posterior (b) sections of a typical lesion.
EXPERIMENT 1

The first experiment was generated by an accidental observation that frontal rats lose less weight after surgery if food pellets are placed on the cage floor than if food is present only in the hopper attached to the cage. A similar observation has been noted by Lynch et al. [8]. This phenomenon was now more systematically studied.

Procedure

Three groups of frontal and three groups of sham rats (N=5–6 in each group) were weighed before and on each day of the first two weeks following surgery. Prior to surgery, food was available ad lib but only in the food hoppers. After surgery three pairs of frontal and sham groups were treated in different ways: (1) food present only in the food hoppers as before; (2) approximately 50–60 g of food scattered on the cage floor in addition to that in the food hopper, or, (3) approximately 200–220 g of food on the cage floor in addition to that in the food hopper. Water was always available from a standard bottle.

Results

Figure 2 shows the postoperative weight curves of frontal and sham rats treated in the three different ways. A two-way analysis of variance with lesion as one factor and days as the second factor was conducted in each case. Both main effects and the interaction were significant (p<0.05–0.01) for treatments (1) and (2). Only the main effect of days was significant (p<0.05) for treatment (3). Two other two-way analyses of variance were conducted for the frontal and sham rats separately; the two factors were days and treatment. Both main effects and the interaction were significant (p<0.05–0.01) for the frontal rats. The effect of days was significant (p<0.05) for the sham rats. Subsequent t tests confirmed that for frontal rats, recovery was quicker for treatment (3) than for treatment (2) and slowest for treatment (1).

FIG. 2. Recovery of body weight as a function of availability of food on the cage floor. See text for explanation.

Discussion

The results of this experiment indicated that the degree to which food is easily available determines how much weight frontal rats initially lose after surgery and how quickly this weight is regained. The specificity of these effects should be noted. Rats with posterior cortical lesions (5 mm in dia., placed 0.5 mm anterior and lateral to lambda) lose no weight after surgery and appear similar to sham controls under all conditions of food availability (Glick and Greenstein, unpublished observations). The present findings with frontal lesions appeared compatible with either a motor or motivational deficit. Accordingly, an attempt was next made to distinguish between these two interpretations.

EXPERIMENT 2

Procedure

Two groups of frontal and two groups of sham rats (N=5 in each group) were weighed before and on each day of the first two weeks following surgery. Prior to surgery, all rats were deprived of food for two days; prior to this deprivation period, food was available ad lib but only in the food hoppers. After surgery two pairs of frontal and sham groups were treated in different ways: (1) food present only in the food hoppers or (2) approximately 50–60 g of food scattered on the cage floor in addition to that in the food hopper. Water was always available.

Results

The postoperative weight curves of frontal and sham rats deprived of food prior to surgery are shown in Fig. 3. A two-way analysis of variance with lesion as one factor and days as the second factor was conducted for each of the two treatments. Both main effects and the interaction were significant (p<0.05–0.001) for treatment (1). Only the main effect of days was significant (p<0.05) for treatment (2).

FIG. 3. Effect of food deprivation prior to surgery on recovery.

Discussion

When allowed a small amount (50–60 g) of food on the cage floor, frontal rats showed no obvious disturbance in weight regulation only if deprived of food for two days prior to surgery (i.e. compare treatment (2) in Experiments 1 and 2). This finding is more consistent with a motivational than with a motor interpretation of changes in weight regulation.
induced by frontal cortical lesions. Food deprivation would appear to enhance the stimulus which elicits eating rather than ameliorate a difficulty in coordinating the movements necessary for eating per se. Another interpretation involving a motor deficit might attribute an important role to the hyperactivity frequently observed in frontal rats [3, 8, 9]. Recovery of weight might be facilitated by more food on the floor because of a necessarily higher probability of contact between rat and food. This interpretation also appears unlikely in view of the present finding that food deprivation facilitated recovery. Food deprivation has been shown to greatly enhance frontal hyperactivity [3]; if hyperactivity were the critical variable, food deprivation should have slowed rather than facilitated recovery. The persistent weight loss in frontal rats deprived of food prior to surgery but allowed to eat only from the food hoppers may indicate that the stimulus to eat was still not strong enough to induce frontal rats to work for their food. It should be noted that lower rates of bar pressing for food in rats with frontal cortical lesions have also been observed [3].

Besides illustrating the basic disturbance, the data of Experiments 1 and 2 have bearing on quite another issue. This relates to whether the recovery of weight regulation in frontal rats is dependent on time alone after surgery or the amount of postoperative experience. Stated more directly, is the eventual recovery of frontal rats allowed food only from the food hopper a function of postoperative experience obtaining food from the hopper or of processes solely dependent on time? The data thus far suggest that experience is of relatively little importance since food deprivation, which actually decreases the amount of consummatory experience immediately prior to surgery, somewhat ameliorates the intensity of the frontal deficit. This problem was next examined in more detail.

**EXPERIMENT 3**

**Procedure**

Two groups of frontal and two groups of sham rats (N=5 in each group) were weighed before and on each day of the first four weeks following surgery. Prior to surgery, food was available ad lib but only in the food hoppers. After surgery, two pairs of frontal and sham groups were treated in different ways: (1) food present only in the food hoppers for two weeks with added access to 200–220 g of food on the cage floor for the following week and finally access only to the food hopper for the last week or, (2) access to 200–220 g of food on the cage floor in addition to that in the food hopper for the first week, food removed from the floor for the second week, returned for the third week and finally removed for the fourth week. Water was always available.

**Results**

The postoperative weight curves for the four groups of rats are shown in Fig. 4. Two-way analyses of variance were conducted for the frontal and sham rats separately during each postoperative week. The two factors were always days and treatment. The main effect of days was significant (p<0.05–0.01) in each analysis. The main effect of treatment was significant (p<0.05) only during the first two postoperative weeks for the frontal rats; the interaction was also significant (p<0.05) only for these cases. Subsequent t tests showed the following significant (p<0.05) results: (a) with food present only in the food hoppers after surgery, frontal rats lost more weight in the first four postoperative days than other frontal rats lost in the four days following removal of food from the cage floor at one week after surgery; (b) complete recovery of this abnormal response to removal of food from the cage floor was not evident within three weeks after surgery; both groups of frontal rats lost weight for one day and regained this weight over the following four days.

**EXPERIMENT 4**

**Procedure**

Two groups of frontal and two groups of sham rats (N=4–6 in each group) were weighed before and on each day after surgery. Prior to surgery, food was available ad lib but only in the food hoppers. Four other groups of rats (N=5–6 in each group) received either unilateral frontal ablations or sham operations (two groups frontal two groups sham) two weeks prior to receiving the same surgery on the contralateral side. These latter groups were weighed before and on each day after the first stage of surgery. Prior
to the second stage of surgery, food was available ad lib but only in the food hoppers. After the completion of all surgery, four groups (one frontal and one sham group having simultaneous bilateral surgery and one frontal and one sham group having successive unilateral surgery) were treated in one way while the other four groups were treated in a different way: (1) approximately 50–60 g of food scattered on the cage floor in addition to that in the food hopper for two weeks or (2) food present only in the food hoppers for two weeks with added access to 200–220 g of food on the cage floor for the fifth week and finally returned for the sixth week. Water was always available.

Results

The postoperative weight curves for treatments (1) and (2) are shown separately in Fig. 5 and 6, respectively. The data of treatment (1) were analyzed in a three-way analysis of variance with lesion as one factor (frontal, sham), kind of surgery as the second factor (simultaneous or successive) and days as the third factor. All main effects, all two-way interactions and the three-way interaction were significant (p<0.05 in each case). Subsequent t tests showed that in contrast to rats with simultaneous bilateral frontal lesions, rats with successive stage bilateral frontal lesions lost only an insignificant amount of weight after the second stage of surgery; the weight curve of the latter frontal group was never significantly different from that of the appropriate sham group.

For the data of treatment (2), two-way analyses of variance were conducted for the frontal and sham rats separately during each of the four postoperative phases (i.e. no food on floor, food on floor, no food on floor, food on floor). The two factors were always days and kind of surgery (simultaneous-successive). The main effect of days was significant (p<0.05–0.01) in each analysis. The main effect of surgery was significant (p<0.05) only during the first phase (first two postoperative weeks) for the frontal rats; the interaction was also significant (p<0.05) only for this case. Subsequent t tests showed that although successive stage frontal rats lost less weight after the second stage of surgery than frontal rats with simultaneous bilateral lesions lost after surgery when food was available only from the food hopper, there was no difference between the weight losses of these two groups when food was removed from the floor during the fifth postoperative week. The later weight losses were both significant and comparable in extent to that observed during the fourth postoperative week in the previous experiment.

Discussion

The results of Experiment 4 further demonstrate the roles of time dependent and experience dependent processes in recovery phenomena. Successive state savings occurring soon after the second stage of surgery can largely be accounted for by processes occurring as a function of time per se during the interoperative interval. However, the persistent deficit of successive stage animals occurring several weeks after surgery apparently was compensated for by an adaptive process involving prolonged experience at obtaining food only from the hopper. The finding that successive stage animals had a persistent deficit indicates that the successive stage procedure facilitate the rate but not the asymptotic extent of recovery. The latter endpoint would seem to be a function only of lesion parameters [6].

REFERENCES


