Facilitation of survival following lateral hypothalamic damage by prior food and water deprivation*

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Rats with bilateral lateral hypothalamic lesions lose weight at a slower rate and survive longer if deprived of food and water for 2 days prior to surgery. This effect appears to be a function of the duration of food and water deprivation preceding surgery rather than of the preoperative level of body weight.

Powley & Keesey (1970) recently proposed that lateral hypothalamic lesions lower the set-point for weight regulation. They attributed changes in feeding behavior following such lesions to an attempt by the animal to regulate its body weight at the new set-point. Starvation of rats prior to lesioning the lateral hypothalamus shortened the duration of postoperative aphagia and anorexia. The present experiment was designed to further investigate the effect of preoperative starvation on early postoperative changes in lateral hypothalamic rats. Lateral hypothalamic lesions enhance catabolic processes (Morrison, 1968), resulting in quicker death than would follow from continuous food and water deprivation of normal rats. On a simplistic basis of enhanced postoperative stress and fatigue, it would be expected that food and water deprivation prior to lesioning the lateral hypothalamus would impair postoperative survival if such rats were not given special postoperative care (i.e., tube feeding, very palatable foods, etc.). As shown in the present experiment, however, lateral hypothalamic rats allowed access to only dry food and water lose weight at a slower rate and live longer if deprived of food and water for 2 days prior to surgery. Moreover, in contrast to Powley & Keesey (1970), this effect appears to depend upon the duration of food and water deprivation preceding surgery rather than on the preoperative level of body weight.

SUBJECTS

The Ss were naive female albino (Sprague-Dawley) rats weighing 220-280 g.

SURGERY

All surgery was conducted under methohexital anesthesia. A Kopf stereotaxic instrument was used for lesion placement (according to atlas of Pellegrino & Cushman, 1967). Electrodes were made of stainless steel wire insulated with Formvar except for 0.25 mm at the tips. Lesions in the lateral hypothalamus were made with a direct anodal current of 2 mA for 30 sec. Coordinates were 0.8-1.0 mm anterior to bregma, 2.5 mm lateral to midline, and 2.0 mm from the base of the skull. Sham surgery was identical except that no current was passed.

PROCEDURE

Three groups of five rats each received bilateral lateral hypothalamic lesions. One of these groups was allowed ad lib access to food and water preoperatively. The second group was deprived of both food and water for 2 days prior to surgery. The third group of lateral hypothalamic rats was deprived of both food and water for 5 days beginning 6 days before surgery and allowed ad lib food and water for the last preoperative day. Two groups of three rats each received sham surgery. One sham group was allowed ad lib food and water both pre- and postoperatively. The other sham group was deprived of both food and water postoperatively until death. All rats were weighed preoperatively and on each postoperative day. If not deprived, Purina Lab Chow (pellets only) were always present on the floor of each rat's cage. No special postoperative procedures (i.e., tube feeding, access to very palatable foods, etc.) for maintaining rats were conducted. Rats were killed (death considered imminent) when a righting response and locomotion could not be elicited by a tail pinch.

RESULTS

Histology

Two or three rats of each lateral hypothalamic group were allowed to die before being killed. Rats considered "imminently dead" were killed so that adequate perfusion with Formalin and more accurate histology could be performed. Brains were sectioned at 40 microns and lesions were mapped on photocopies of the Pellegrino & Cushman (1967) atlas. This report includes only rats with bilaterally symmetrical lesions in the far-lateral (Morgane, 1961) hypothalamus. Occasional damage to the medial internal capsule and ventral subthalamus was also noted. The

Table 1
Mean Weight Changes (Percent of Preoperative Weight) Following Lateral Hypothalamic Lesions

	Groups*				
	LH	LH-D	LH-DS	S	S-D
	Weight (Grams) 6 Days Before Surgery				
	209	254	258	212	215
	Preoperative Weight				
	229	226	228	234	235
	Percent Change—Days After Surgery				
1	87.7	93.5**	88.1	99.2	92.9
2	81.3	89.5**	81.6	101.8	87.6
3	75.4	85.0**	75.9	103.8	83.6
4	70.8	81.2**	71.6	105.6	80.0
5	65.8	77.1**	66.3	108.1	76.9
6		73.3**	61.9	110.0	74.1
7		69.7**		111.3	71.6
8		66.6**		111.2	68.8
9				111.8	66.1
10				114.1	63.3
	Mean Duration of Survival (Days)				
	7.4	10.1†	7.8	—	13.8

*LH = lateral hypothalamus; LH-D = LH deprived of food and water 2 days prior to surgery; LH-DS = LH deprived for 5 days, then allowed ad lib food and water 1 day prior to surgery; S = sham; S-D = sham deprived of food and water after surgery.

**Significantly greater than LH and LH-DS at $p < .01$ but not significantly different from S-D at $p > .1$ (t tests).

†Significantly greater than LH and LH-DS at $p < .01$; if 2 days of preoperative deprivation included, not significantly different from S-D at $p > .1$ (t tests).

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extent of lesions in the three lateral hypothalamic groups was very similar. Four rats (not previously mentioned) had asymmetrical lesions and were excluded.

Weight Data

All lateral hypothalamic rats were continuously aphagic and adipsic following surgery and died. However, the rate of weight loss and time of death differed among the three lateral hypothalamic groups. As shown in Table 1, lateral hypothalamic rats deprived of food and water for 2 days prior to surgery lost weight at a slower rate and lived longer than did the other two groups, between which there were no significant differences. Only the preoperatively deprived lateral hypothalamic group survived nearly as long as the sham group deprived of food and water postoperatively.

DISCUSSION

Far-lateral coordinates were purposely chosen to insure that otherwise untreated lateral hypothalamic rats would be certain to die of starvation (Ellison, Sorenson, & Jacobs, 1970; Balagura, Wilcox, & Coscina, 1969). Food and water deprivation prior to surgery clearly enhanced survival following lateral hypothalamic lesions. It is important to note that level of body weight alone was not a determinant of postoperative weight changes. Rats deprived of food and water for 5 days and then allowed ad lib food and water intake for 1 day prior to surgery had approximately the same decrement in body weight at surgery as rats deprived of food and water for 2 days prior to surgery. Yet the former group did not survive any longer than usual. This result is inconsistent with the weight regulation model of Powley & Keesey (1970) if reduced catabolism and facilitated recovery are functions of the same process. Although spontaneous eating and drinking with recovery did not occur in the present experiment, a direct relationship between enhancement of recovery and reduction of catabolism has previously been implicated (Morrison, 1968).

Why prior food and water deprivation should prolong lateral hypothalamic survival is certainly a perplexing question. Consistent with a supersensitivity model (Sharpless, 1964) recently suggested to account for lateral hypothalamic recovery (Glick, Greenstein, & Zimmerberg, in press), food and water deprivation might partially deplete the hypothalamus of norepinephrine, resulting in supersensitivity of hypothalamic neurons prior to surgery. Supersensitivity of remaining neurons would then mediate facilitated recovery and/or enhanced survival. Although there is no direct evidence that food and water deprivation depletes the hypothalamus of norepinpehrine, other findings support such a possibility: (1) food and water deprivation enhance electrical activity of the lateral hypothalamus (Hockman, 1964; Steiner, 1962); (2) norepinephrine is a probable transmitter in the hypothalamus concerned with the regulation of food and water intake (Leibowitz, 1971); (3) amphetamines having anorexic effects can partially deplete the brain of catechol amines (Brodie, Cho, & Gessa, 1970; (4) the anorexic effect of injecting amphetamine directly into the hypothalamus increases with increasing food deprivation prior to testing (Booth, 1968); and (5) lateral hypothalamic lesions reduce brain levels of norepinephrine (Zigmond, Chalmers, Simpson, & Wurtman, 1971). Although this depletion and supersensitivity model is entirely speculative at this time, further research should be aimed at correlating neurochemical findings with particular recovery phenomena.

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