Technical Papers

Obesity Following Unilateral Hypothalamic Lesions in Rats

Jean Mayer
Department of Nutrition, School of Public Health, Harvard University, Boston, Massachusetts

Russell J. Barrnett
Department of Anatomy, Harvard Medical School, Boston, Massachusetts

It is well known that electrolytic lesions involving the ventromedian nuclei of the hypothalamus result in hyperphagia and obesity (*1*). This report (*2*) deals with the production of obesity by unilateral hypothalamic lesions.

Female albino rats of the Wistar stock weighing 220 to 260 g were used in these experiments. The animals were housed in separate cages placed in a room with constant temperature and regular illumination. They were fed Purina Dog Chow and water *ad libitum*. Hypothalamic lesions were produced with the Krieg stereotaxic instrument (*3*) on animals anesthetized with ether. The lesions were placed unilaterally between planes 56 and 57 (as defined by Krieg) 1 mm to the right of the midline and 0.5 to 1.00 mm superior to the sphenoid bone. The current used was 1.5 or 2 ma for 30 sec.

At autopsy the rats were decapitated, and after removal of the lower jaw and the calvarium, the heads were fixed in neutral 10 percent formalin.

After 24 hr the brains were dissected free and were cut down to blocks extending from the optic chiasm to, and including, the mammillary bodies. The ventral portion of the thalamus was included in each block as well as the piriform cortex and the amygdaloid nucleus laterally. These blocks were refixed in formalin for 24 hr and washed in tap water overnight. After dehydration they were imbedded in paraffin. Serial sections cut at 10 μ were taken of the entire block and mounted on slides. The sections were stained with eosin and methylene blue.

Twenty-nine rats received unilateral lesions on the right side. A group of 30 rats of similar ages and weights were examined for normal weight gains. On the basis of their rate of weight gain, as well as of previous experience with this stock, it was considered that operated animals could be presumed hyperphagic if they either maintained a rate of daily weight gain greater than 0.5 g for an extended period (more than 100 days) or if they exhibited a rate of daily weight gain greater than 1 g during the first 20 days postoperatively. By these criterions 13 animals were rendered hyperphagic by the operation. Of particular interest are the few rats that exhibited very marked hyperphagia. Animal No. 3 gained 71 g in 63 days; animal No. 19, 93 g in 18 days; animal No. 23, 105 g in 108 days; animal No. 24, 70 g in 108 days; animal No. 27, 108 g in 64 days. Each animal, when killed, weighed in excess of 350 g. The brains of these rats were examined histologically to determine the site and extent of the lesions. These were described according to the nomenclature introduced by Krieg (*4*).

The lesions were large and were confined to the hypothalamic nuclei on the right side of the third ventricle, except in the case of animal No. 3 in which the midline and a small part of the left arcuate nucleus ventral to the third ventricle were also involved. Although identical coordinates and strength and time of current were used, there was some variation in the extent of the lesions. However, in all five animals the ventromedian nucleus, parts of the periventricular, lateral, and the arcuate nuclei were destroyed. In one case the ventral part of the dorsal median nucleus was also involved. In three cases the lateral extent of the lesions included the caudal portion of the supraoptic nucleus, the commissure of Gudden, the commissure of Meynert, and the subfornical fibers of the median forebrain bundle. Anteriorly the lesion in two cases involved the anterior nucleus but did not include the paraventricular and suprachiasmatic nuclei or the anterior part of the supraoptic nucleus. Caudally the lesions did not embrace the mammillary nuclei. It should be noted in particular that the lesion of animal No. 19, which gained 93 g in 18 days postoperatively, was completely confined to one side of the hypothalamus.

Although the animals just described were undoubtedly hyperphagic, their weight gains were generally less than those seen in 28 comparable animals of the same stock subjected to bilateral lesions at the same time (2 ma for 15 or 30 sec); 24 became transiently or permanently hyperphagic. Steady weight gains of 6 g/day or more were seen in eight animals. One animal maintained a rate of weight gain of 9 g/day for 13 days postoperatively. One hundred days postoperative seven animals exceeded 500 g. Five more reached weights between 400 and 500 g, and three more reached weights between 350 and 400 g.

The fact that some animals with large lesions restricted to one side of the hypothalamus became obese is of interest. It seems to establish the fact that the medial centers (ventromedian nuclei), the destruction of which causes hyperphagia, are not simply each one paired with a lateral feeding center (lateral hypothalamic area) as a brake on the facilitatory eating mechanism, as is suggested by some authors (*5*). Apparently lateral feeding centers have to be bilaterally destroyed in order that anorexia prevail (*6*), whereas unilateral medial lesions may cause hyperphagia. It is, of course, not impossible that a lesion of one side could functionally involve both sides by the destruction of crossing fibers. However, it seems much more likely that two centers, bilaterally disposed, both normally act to prevent hyperphagia. The removal of either one permits the development of about half the

obesity caused by the destruction of both. In accordance with this view is the observation that the excess weight gain over normal after successful unilateral lesions was about half of that observed in successful bilateral lesions. It must be noted that in the mouse, obesity follows bilateral but not unilateral destruction of the ventromedian nucleus (*7*).

References and Notes

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Evidence for Echolocation in the Rat

Mark R. Rosenzweig, Donald A. Riley, David Krech

Department of Psychology, University of California, Berkeley

We wish to present evidence that rats can guide themselves in a maze by auditory cues—probably the echoes of sounds they produce.

Ten blinded rats were trained on an elevated maze (Fig. 1). On each trial, either path *L* or path *R* was blocked 20 cm from its beginning by a 15- by 15-cm metal barrier *B*. Each path was blocked on half the trials in a random sequence. A response was counted incorrect if an animal placed all four feet on the blocked alley so that its vibrissae could touch the barrier. Upon reaching the goal, the rat was allowed to eat briefly before starting the next trial.

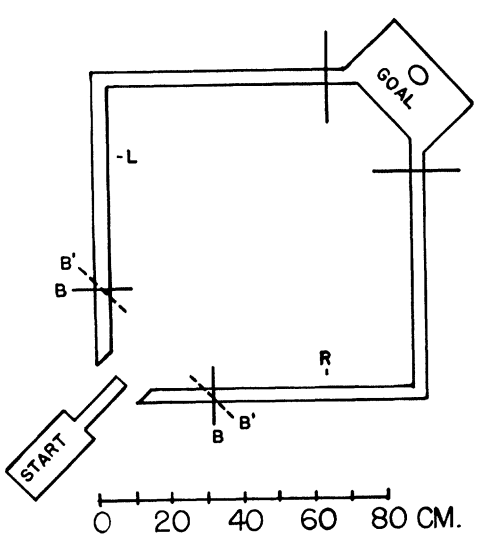

Fig. 1. Floor plan of the elevated maze used in the experiment.

The test situation was designed to prevent solution by nonauditory cues. Olfactory cues were excluded by the constant position of the food, and vibratory-tactile cues were excluded by suspending the barriers independently from the maze. Painting the barriers flat black did not alter the rats' behavior; this test thus excluded reflection of radiant energy as a cue. The orientation of the maze in the room was changed each day in order to vary possible extra-maze cues.

All the rats learned to select the correct path. Seven attained a level of 18 correct out of 20 successive trials. Two critical tests give positive evidence that the effective cue is auditory. (i) The angle of the barriers with respect to the pathways was changed from the usual 90° (*B* in Fig. 1) to 45° (*B'*). The performance of the six animals used in this test dropped to the chance level. Performance returned to normal when the barriers were again set at 90°. Presumably the performance deteriorated because sound was not reflected back to the rat but was reflected out to the side of the apparatus. (ii) Three of the animals were then tested with their ears occluded. Performance again dropped to chance.

Our initial hypothesis was that rats might guide themselves, as bats do, by the echoes of ultrasonic cries, since rats can hear sounds in the ultrasonic range (*1*) and can produce ultrasonic cries (*2*). Accordingly, we monitored their performance with a system consisting of a condenser microphone, amplifiers, and a cathode-ray oscilloscope (*3*). We were able to confirm the production of ultrasonic cries by the rats. However, these cries are given very rarely in the maze, and they do not seem to be related to maze performance.

The rat frequently does produce other sounds in the maze—it may sniff, sneeze, click its teeth, or scratch the floor, and even its footfalls are often audible to a nearby observer. On some trials the rat does not produce any sound that we can hear before making its choice, yet it performs correctly; this may indicate nothing more than our inability to hear all the noises that the rat does. Considering the present evidence, it seems likely that the rat, like the human being (*4*), can use the echoes of the incidental sounds that it produces in order to detect objects in its environment. This possibility should be considered in designing experimental situations in which the rat is to be used.

References and Notes

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