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Experimental Obesity in the Dog.

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During the past 5 years obesity in dogs frequently has been observed following operations on the hypophysis and hypothalamus. The operations, performed mostly through the oral approach, involved: (1) removal of the posterior lobe with or without removal of the pars distalis; (2) section of the fibers to the neurohypophysis with the immediate or subsequent removal of the adenohypophysis, the infundibular stem and the infundibular process; (3) removal of the neuro and adeno hypophysis at one sitting; (4) median transverse section of the posterior hypothalamus between the infundibular stem and mammillary bodies with or without removal of the posterior lobe and the pars distalis. The conclusions reported in this paper are based on observations made on 125 animals with a fairly equal distribution among the above classes.

The animals were kept in metabolism cages and 24-hour urine collections were made. They were fed measured limited amounts of dog chow and horse meat except when for experimental purposes unlimited but measured quantities were allowed. The dogs were kept for a period before operation to establish a constant weight and to determine the normal daily urine output. They then were subjected to operation and kept for periods of observation varying from 3 months to over a year. All but 6 of the animals have been sacrificed to obtain anatomical material to determine the lesions present in the hypophysis and in the hypothalamus. The brains were fixed *in situ* by irrigation through the carotid artery with formalin 1 to 10 after bleeding the animal. After further fixation the sella and its contents were separated from the hypothalamus. Both parts were then examined microscopically in serially cut 20-micron sections. Cresyl violet was used to stain the hypothalamic tissue, hematoxylin and eosin for the sella and its contents.

In this report are presented urine and weight charts (Fig. 1) and photomicrographs (Fig. 2) from 2 animals in each of which a lesion, caudal to the region of the paraventricular nuclei was made in the posterior hypothalamus. The pars distalis and posterior lobe

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also were removed in both, but the median eminence was not disturbed appreciably. These 2 dogs were chosen because of a critical difference in their lesions. In one, which became obese, the cells in the caudal portions of the paraventricular nuclei are absent (retrograde degeneration) in the animal which did not become obese the nucleus has its normal length. The shortening of the paraventricular nuclei in the obese dog is due to retrograde degeneration of the cells following the interruption of their axons by the posterior hypothalamic puncture. The puncture in the other dog did not sever these axons. The paraventricular nucleus gives rise to fibers going to the neural divisions of the hypophysis and to fibers which descend toward the brain stem.

Analysis of our entire material yielded evidence that obesity is dependent upon such a loss of cells in the caudal portion of the paraventricular nuclei. In addition a marked loss of cells in the supra optic nuclei appears to be a contributing factor in the development of maximal obesity. All the dogs in this series with marked diabetes insipidus became more obese than those partially diabetic but with a comparable degree of loss of cells from the caudal portion of the paraventricular nuclei alone. The degree of loss of cells of the supra optic nuclei is not critical in determining the degree of obesity. For instance, the degree of cell loss (87% estimated) in the supra optic nuclei of dog 0191 which did not become obese is somewhat greater than in dog 0190. The urine charts indicate that neither had significant diabetes insipidus but that the average percentage increase in urine output for dog 0191 was somewhat greater than for dog 0190. In 4 other dogs in which lesions were made in the hypothalamus between the stalk and the mammillary nuclei with a

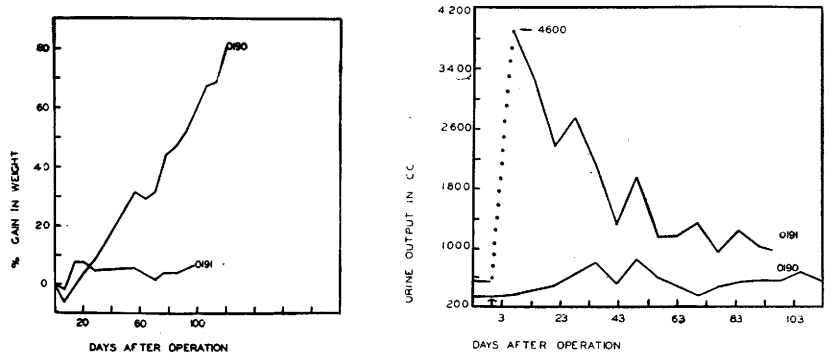

FIG. 1.

Plots of percentage increase in weight against time and of urine output in days after operation for dogs 0190 and 0191.

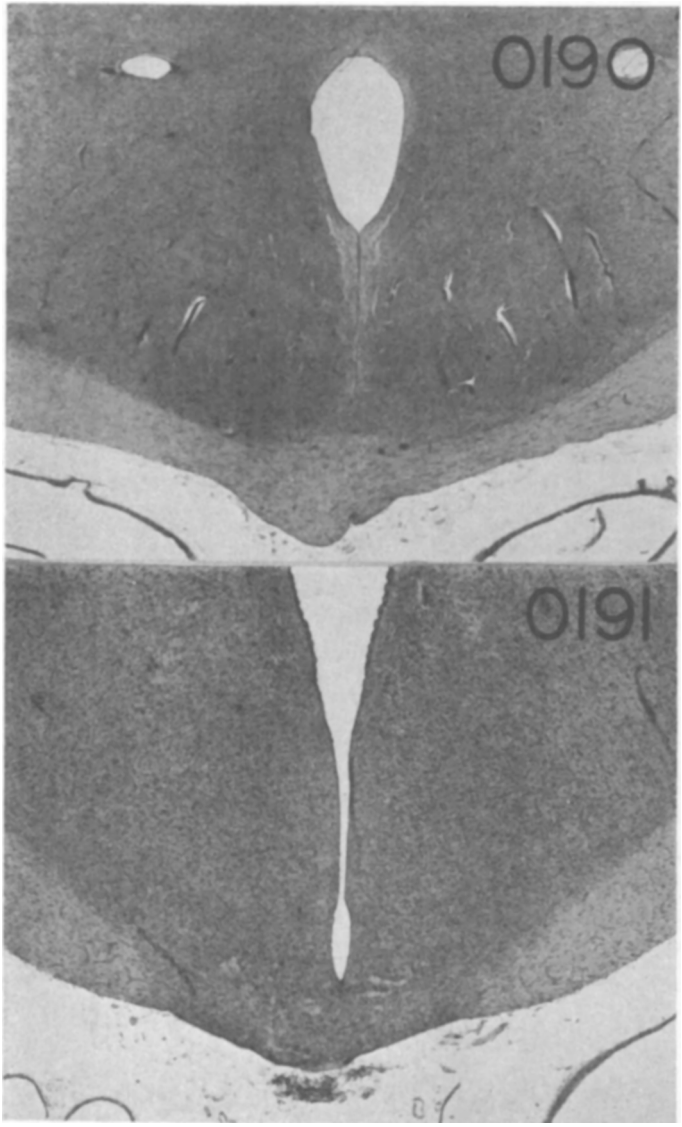

FIG. 2.

Photomicrographs, 12.5 diameters of frontal sections through the hypothalami of dogs 0190 and 0191. Note in dog 0190 the paraventricular nuclei have ended at a level still in the optic chiasma and more rostral than the section shown from dog 0191, caudal to the chiasma, in which the nuclei still are present.

resultant cell loss of considerable degree in the caudal portions of the paraventricular nuclei but with insufficient loss of cells from the supra optic nuclei to produce diabetes insipidus, the average weight

gain was 50% in 6 months. In other dogs with definite diabetes insipidus resulting from supra optic damage and with a comparable loss of cells in the caudal portions of the paraventricular nuclei the average weight gain has been 75 to 110%.

The conclusions drawn from an analysis of the entire material from which the above examples have been selected are: (1) Obesity in the dog results from partial destruction or retrograde degeneration of the paraventricular hypothalamic nuclei, particularly of their caudal portions. (2) Marked obesity results when destruction or denervation of the neurohypophysis and partial destruction of retrograde degeneration of the caudal paraventricular nuclei coexist. (3) Removal of the pars distalis in itself does not result in significant obesity (0 to 20%). The presence of the pars distalis in animals with partial destruction or degeneration of the supra optic and paraventricular nuclei is favorable to the development of marked adiposity. (4) The results suggest that a lack or marked lessening of the secretion of the neurohypophysis may aid in fat storage in the presence of a diminution in the number of cells of the caudal portion of the paraventricular nuclei.

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Body Fluid Changes in Neurogenic Hypertension and Total Paravertebral Sympathectomy.

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This is a report of changes which have been observed in the blood volume, plasma volume, hematocrit and red blood cell count under various conditions of vascular tension resulting from operative interference with vasomotor nerve supply. These studies have been made on normal dogs, dogs made hypertensive by resection of both carotid sinuses, both aortic depressor nerve pathways, and one or the other vagus, and dogs made hypotensive by total paravertebral sympathectomy. Two hypertensive dogs have been subjected to total paravertebral sympathectomy and 2 sympathectomized dogs to the procedure used for production of hypertension and the subsequent changes noted.

Plasma volume was measured by the use of disappearance curves of the blue dye, T-1824. Blood volume was estimated from the plasma