

may be factors in the mechanism by which mannitol prevents acute renal failure.

Summary. The hemodynamic response to rapid infusion of hypertonic mannitol was examined in 12 normotensive subjects. At osmolar clearances of 10 to 15 ml/min glomerular filtration rate was decreased in all, the maximal reduction ranging from 19.2 to 39.4%. The maximal reduction in effective renal blood flow was less than 10% in the majority of subjects. Extraction ratio for p-aminohippurate was unchanged in the 4 subjects in whom this measurement was made. The decrease in filtration rate which occurs during osmotic diuresis as induced by mannitol probably results, at least in part, from a reduction in net filtration pressure caused by increased tubular volume and hydrostatic pressure. It is recognized that changes in the interstitial pressure and renal vasomotor

activity may also participate in the renal response to hypertonic mannitol infusion.

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Role of Thalamic Gustatory Nucleus in Diet Selection by Normal and Parathyroidectomized Rats.* (32331)

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Until recently, studies on the role of taste in food and water consumption have been fraught with difficulty mainly because a complete elimination of gustatory functions was not technically feasible. Denervation of the taste buds by sectioning of the chordae tympani and IXth nerves was inadequate since in many animals these receptors are found not only on the tongue, but also on the palate and the pharynx(1). Surgical interruption of central gustatory pathways could not be done with certainty because anatomical descriptions of these pathways have been incomplete. An arrangement by which an animal can self-inject food directly into its stomach is novel and valuable(2), but it does not permit an evaluation of central gustatory mechanisms.

At present, destruction of gustatory func-

tions can be accomplished by electrocoagulation of a definite region in the rat thalamus. Behavioral tests indicate that, provided all gustatory neurons of this thalamic region are destroyed, the animals are unable to distinguish between tap water and a quinine hydrochloride solution of high concentration(3). Consequently, this technique for experimental disruption of the gustatory system was used to study the influence of the thalamic gustatory neurons on the selection of particular dietary items under conditions of normal physiological needs and under a heightened need for calcium after parathyroidectomy.

Materials and methods. Young male Sherman rats, weighing 234 ± 11 g (avg \pm S. E.), were housed individually in cages fitted with 7 calibrated Richter drinking bottles. Carbohydrates and proteins were made available in the form of dextrose and spray-dried egg whites; fats were offered in

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TABLE I. Self Selection of Dietary Substances During 10 Days Prior to Experimental Treatments.

Dietary items presented for self selection	Avg daily intake (ml or g /100 g B.wt)	S.E.*
Dry items		
d (+) dextrose, anhydrous	6.3	.4
Egg whites, spray dried	3.4	.2
Solutions		
Pure olive oil	1.8	.1
3% sodium chloride	3.4	.2
2% sodium dibasic phosphate	3.9	.3
2% calcium gluconate	5.2	.4
1% potassium chloride	4.6	.4
1% vitamin mixture	5.6	.5
Distilled water	3.6	.5

* Standard error of mean.

the form of pure olive oil, and salts were presented in solutions. The "Vitamin Diet Fortification Mixture" supplied by Nutritional Biochemicals Corp. was used to provide the necessary vitamins. These substances and distilled water were available continuously. The weight of each rat and the amount of each dietary item consumed were recorded at 48-hour intervals. It took approximately 2 weeks for the animals to stabilize their dietary selection. Thereafter they continued to ingest the particular substances in relatively fixed proportions. The average values of consumption for each substance for a 10-day period prior to experimental treatments are shown in Table I. The relatively small quantity of distilled water ingested reflects only a small fraction of total water intake since most items were offered as solutions.

Following the 10-day control period, the animals were divided into 2 groups: 1) parathyroidectomized (Ptx) and 2) unoperated controls. Ether anesthesia was used, and a low power dissecting microscope with a light beam coincident to the optical system aided the surgery. Since postoperative trauma influenced dietary selection, the first records following Ptx and thalamic lesions were disregarded. Twenty days later electrophysiologically monitored lesions were placed in two separate thalamic positions. These were to destroy the thalamic neurons for taste, or neurons for the thalamic relay of somesthesia from the animal's snout. Under Nembutal anesthesia small openings in the cra-

nium were produced bilaterally with a dental drill. A stainless steel electrode with a tip diameter of approximately 10 μ was oriented stereotactically through one and then the other opening to reach the particular thalamic sites. To insure a greater accuracy of localization, multiunit responses were recorded with tactile stimulation of the snout or the tongue according to a technique described previously(4). If responses were obtained with tactile stimulation of the tongue, the electrode was slightly reoriented to reach a more medial site. According to previous reports (5,6), thermal and gustatory neurons are found medial to those neurons which relay touch from the tongue. The exact positions

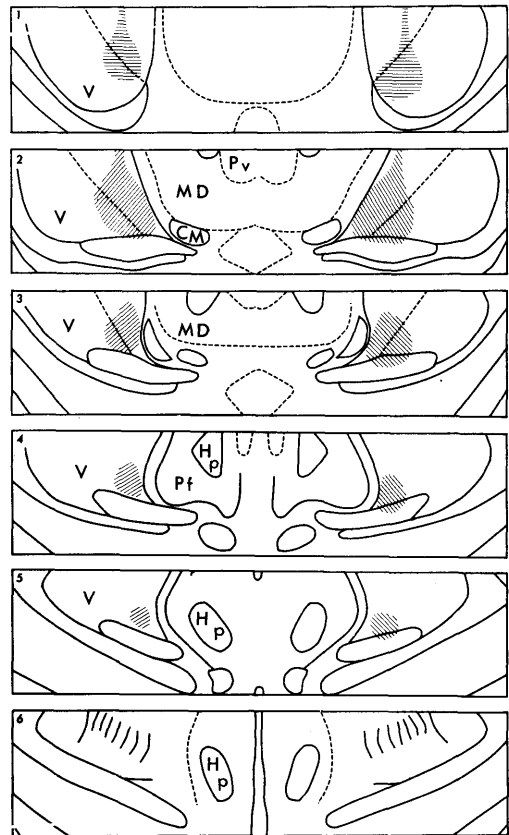


FIG. 1. Reconstruction of thalamic lesions which destroyed some neurons for somesthesia from the snout in one experimental animal. No. 1 to 6 on the diagrams indicate their anteroposterior sequence showing portions of the rat thalamus at 0.2 mm distances. CM, n. centrum medianum; Hp, tractus habenulointerpeduncularis; MD, n. medialis dorsalis; Pf, n. Parafascicularis; Pv, n. paraventricularis; V, n. ventralis posterior.

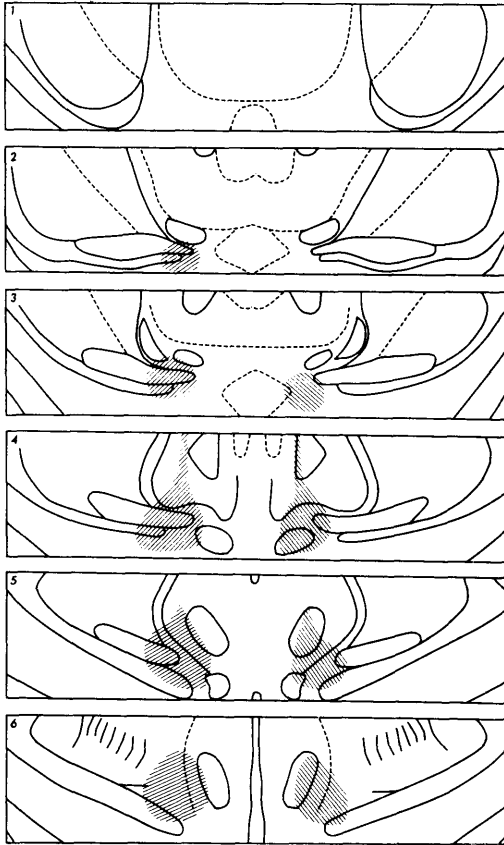


FIG. 2. Reconstruction of thalamic lesions which destroyed gustatory neurons on left side but spared most of them on right side.

of the lesions were ascertained post-experimentally by histological analyses of the brains, and representative examples of such analyses are presented in Fig. 1, 2, and 3. The extent to which these lesions destroyed the thalamic neurons for taste can be visualized by comparing Fig. 1, 2, and 3 with Fig. 4.

Results and discussion. Changes in the intake of calcium gluconate in relation to particular experimental treatments are shown in Fig. 5. To allow each animal to serve as his own control, the results are expressed as the change from control intake. In harmony with the results of previous work(7), the Ptx animals significantly increased their calcium intake (Table II). The latency of this response varied between 2 to 4 days post-operatively for 8 animals, while a latency of 6 to 10 days was exhibited in 4 rats. Body

weight of the Ptx animals was at a low point 3 days after surgery, but thereafter it began to rise at approximately the preoperative rate (Fig. 6).

Thalamic lesions depressed calcium intake of animals in all experimental groups, but the degree to which it was depressed depended greatly on the thalamic site of the lesions and the experimental treatment prior to brain surgery. Lesions which destroyed thalamic neurons for taste in Ptx animals were the most effective in bringing about a decrease in calcium intake. For 3 animals this amount of calcium consumption proved to be insufficient for maintaining life. They lost weight rapidly, and on the days indicated by arrows in Fig. 5 and 6, they died in tetany. At the time the second animal died, the third rat exhibiting severe tetany was given a subcutaneous injection of 2% calcium glu-

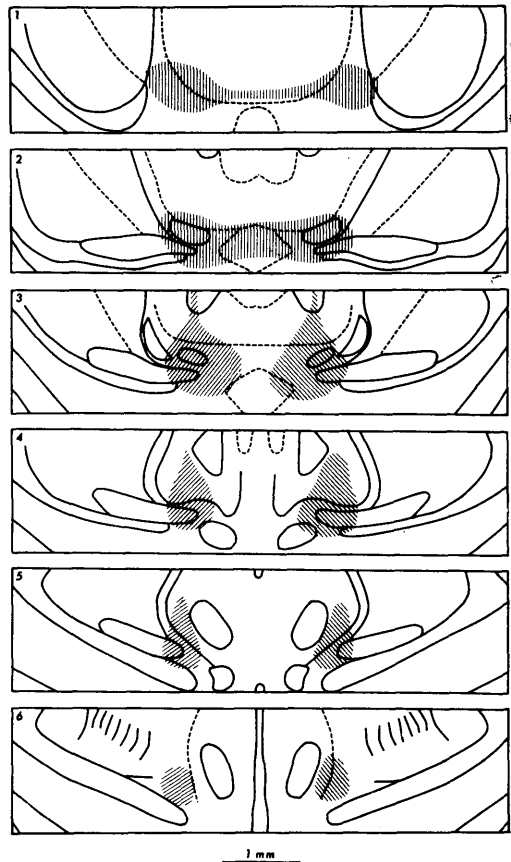
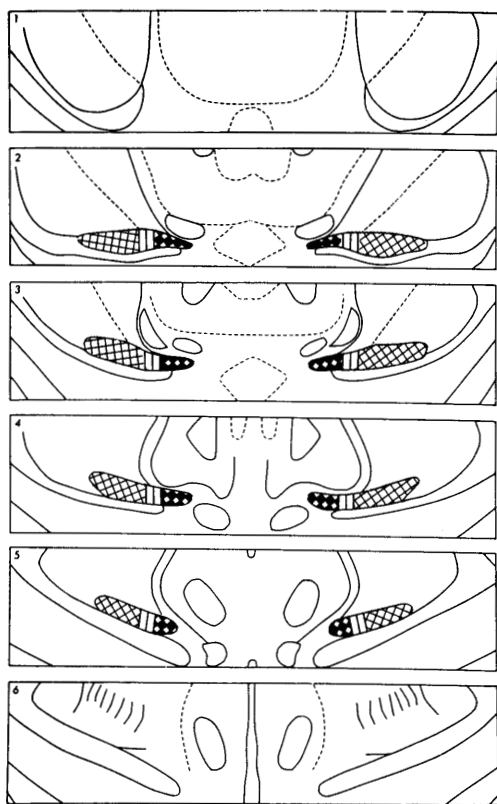


FIG. 3. Reconstruction of thalamic lesions which destroyed gustatory neurons bilaterally.



■ taste- ||| thermal- ⊞ tactile relays

FIG. 4. Location of thalamic neurons subserving 3 lingual modalities.

conate and on the next day an injection of parathormone (100 U.S.P. units Parathyroid Injection, Lilly). These treatments improved the condition of the animal and resulted in an increase in food and water intake and a rise in body weight. This improvement was short lived; when the treatment was discontinued, the animal died 6 days later in tetany. Previous studies in this laboratory have shown that the plasma calcium for young adult Sherman male rats fed Rockland Rat Ration is normally 11.7 mg% and it decreases to 7.3 mg% by the third day following Ptx. The time sequence of these changes in plasma calcium are in general accord with the behavioral changes noted in this study.

Not all animals of the Ptx group died in tetany. This was not completely unexpected since it is known that the susceptibility of rats to calcium deficiency varies greatly(8).

Moreover, calcium intake of the surviving Ptx animals after the destruction of the thalamic gustatory nucleus was significantly higher than the calcium intake of those Ptx animals which died. Perhaps this higher intake represented the learning of some animals to identify the solution by olfaction. It has been demonstrated that rats can learn to distinguish between a solution of quinine chloride and water by olfaction alone(3).

If thalamic lesions in Ptx animals did not destroy the gustatory nucleus completely (Fig. 2), calcium gluconate intake remained high. Apparently, those gustatory neurons which remained intact enabled the animals to identify the substance adequately. Therefore, Ptx animals with lesions, as illustrated in Fig. 1 and 2 were combined in a single group. For this group of animals calcium gluconate intake was significantly higher than for the Ptx animals with a complete destruction of the thalamic gustatory nucleus bilaterally (Table II). If this nucleus was destroyed in previously normal rats, the average value of their calcium consumption did not differ significantly from the corresponding preoperative value (Table II) but the variability of calcium intake increased. This was also the case with destruction of the gustatory nucleus in Ptx animals if the standard error of the mean was not calculated separately for animals divided in subgroups on the basis of survival time.

Although the experimental treatments influenced the consumption of calcium most, changes in the ingestion of other dietary items also occurred. After Ptx the intake of sodium dibasic phosphate and distilled water diminished, while the consumption of sodium chloride increased. The amount in which other substances were consumed did not change significantly. A diminution in the amount of phosphate ingestion following Ptx has been reported previously(7), and is probably related to an increased phosphate retention under hypoparathyroid conditions. The consumption of distilled water was dependent on the amount of fluids ingested with solutions. As the Ptx animals obtained a large quantity of water from the calcium gluconate solution, their consumption of distilled water

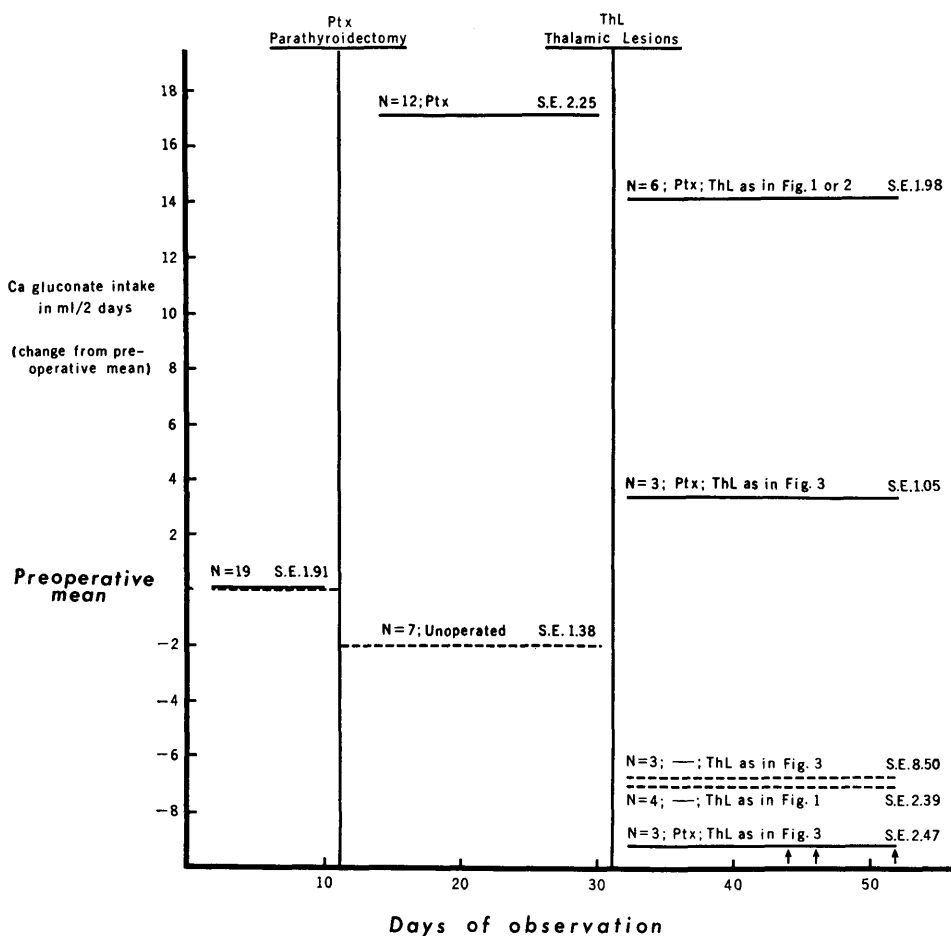


FIG. 5. Calcium gluconate intake before and after experimental treatments. Ptx, parathyroidectomy; ThL, thalamic lesions; S.E., standard error. Arrows indicate death of individual animals.

decreased. No explanation can be advanced for the increase in sodium chloride intake by Ptx animals.

Destruction of the thalamic gustatory nucleus in Ptx animals promptly decreased the high sodium chloride intake and slightly raised the consumption of phosphate and distilled water. If the gustatory nucleus in Ptx animals was spared, consumption of the dietary items did not change significantly from values obtained prior to brain surgery. Thalamic lesions destroying the gustatory nucleus in previously normal rats increased the variability in the amount of consumption of dietary items. No other effects were observed.

A totally unexpected finding was the one

dealing with the order of preference in which the dietary items were selected. During the preoperative period, although each animal selected particular substances in a definite quantity fairly regularly, individual differences as to the preference of certain dietary items were pronounced. Consequently, it was surprising to learn that Ptx promptly abolished such individual differences. The animals reorganized their order of preference with respect to the amount in which they consumed a particular substance and 8 of the 12 Ptx animals established an identical order of preference for the 4 salt solutions. Calcium gluconate was preferred most, then sodium chloride, potassium chloride, and sodium dibasic phosphate the least. Two ani-

TABLE II. Statistical Evaluation of Ca* Intake by Animals of the Experimental Groups.

Groups	Avg change from preoperative mean Ca intake (ml ± S.E./2 days)		P
Following preoperative period:			
Ptx	17.23 ± 2.25) 6.08†	<.01
Unoperated	-1.95 ± 1.38		
Following thalamic lesions:			
Ptx + ThL in snout region	13.97 ± 1.98) 3.56	<.01
Ptx + ThL in gustatory n. (S)	3.37 ± 1.05		
Ptx + ThL in gustatory n. (D)	-9.75 ± 2.47) 4.90	<.01
Ptx + ThL in snout region	13.97 ± 1.98) 6.74	<.01
Unoperated + ThL in snout region	-7.00 ± 2.39		
Unoperated + ThL in gustatory n.	-6.75 ± 8.50) .03	>.05
Ptx + ThL in gustatory n. (S)	3.37 ± 1.05) 1.18	>.05
Unoperated + ThL in gustatory n.	-6.75 ± 8.50		
Ptx + ThL in gustatory n. (D)	-9.75 ± 2.47) .34	>.05

Ptx (parathyroidectomized). ThL (thalamic lesion). Snout region (thalamic projection region for touch from the snout). S (animals survived until termination of experiment). D (animals died at the times shown in Fig. 5).

* 2% Ca gluconate solution.

† t values;) indicates values being compared.

mals had a single reversal between sodium and potassium chloride, and 2 other rats preferred potassium chloride more than calcium gluconate. Thalamic lesions destroying the gustatory nucleus interfered with this order of preference; it became scrambled, except for one animal who retained it. If the lesion did not destroy this nucleus, the order of preference established after Ptx was retained without exception.

In general, the results of this study indicate 1) that the gustatory system was essential for enabling the animal to satisfy its dietary needs optimally, and 2) that the day by day and animal to animal variations in dietary selection may not have reflected poor regulation of consumatory behavior but, on the contrary, an exquisite following of the everchanging, highly individual needs.

Deaths caused by insufficient ingestion of calcium by Ptx animals after destruction of the thalamic gustatory nucleus point to the importance of taste in dietary selection in a very vivid manner. However, death and survival should not be used for evaluation of the adequacy to which a dietary need is met; survival can indicate the minimal but not the optimal satisfaction of such a need. Apparently, the minimum dietary requirements could be met by healthy animals without participation of the gustatory sys-

tem but optimal satisfaction of a need as expressed by consumatory behavior of intact animals required an intact taste. This was evidenced by the fact that after lesions in the gustatory nucleus the intake of dietary items became quite variable and the animals were unable to retain the order of preference which they established after Ptx.

Summary. Young male Sherman rats were allowed to select individual components of their diet from 9 sources. After the selection of dietary items became relatively stable, a group of the animals was parathyroidectomized to intensify their need for one dietary component, calcium, while the rest of the animals served as unoperated controls. The role of thalamic gustatory neurons in mediating the response to dietary needs was then determined by destroying the thalamic gustatory nucleus in a certain number of the Ptx and the unoperated animals. Thalamic lesions which spared the gustatory neurons were also made to provide for adequate controls. If the thalamic lesions destroyed gustatory neurons in Ptx rats, the animals significantly reduced calcium intake. This reduction was sufficiently large to cause tetany and death in some of the animals. Changes in the consumption of sodium dibasic phosphate, sodium chloride, and distilled water also occurred. Destruction of the thalamic gustatory nu-

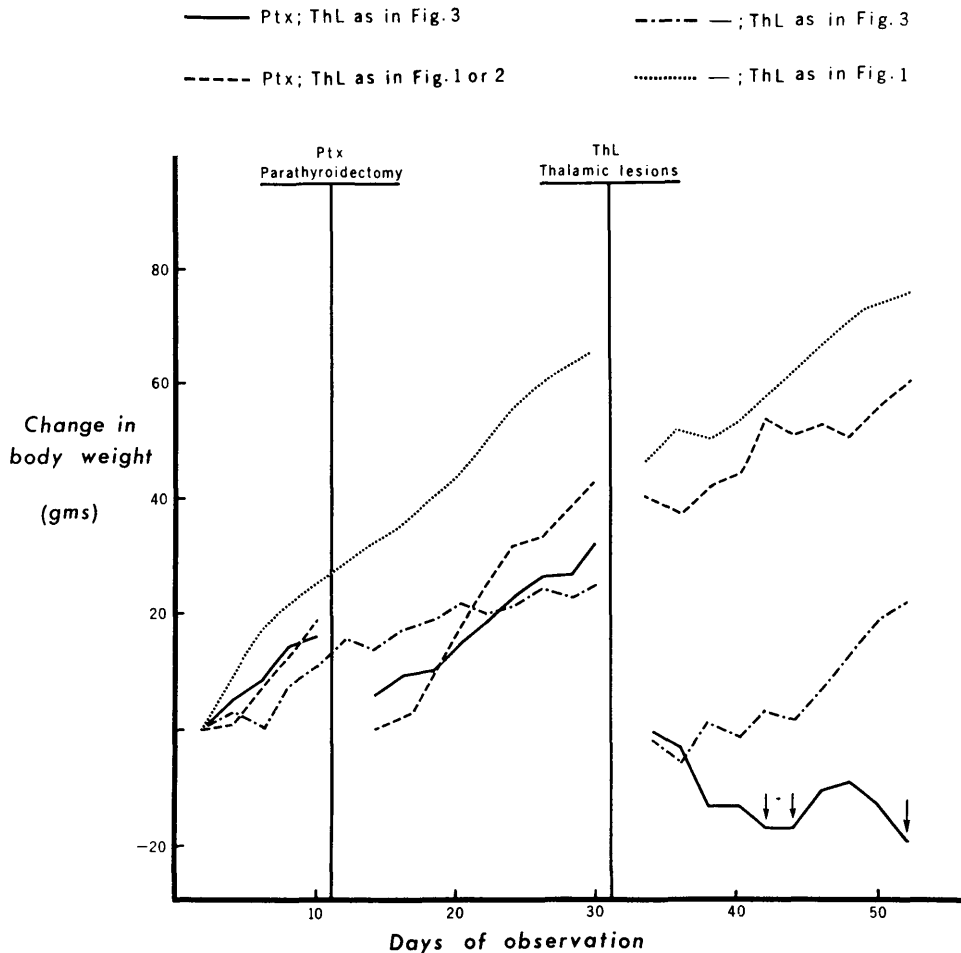


FIG. 6. Change in body weight as a function of time and experimental treatments. Arrows indicate death of individual animals.

cleus in previously normal rats did not diminish calcium intake significantly but the consumption of this item as well as other components of the diet became highly variable. These findings indicate that the gustatory system usually exerts a profound influence on the selection of diet not only under special circumstances but also in normal rats.

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