INFORMATION TO USERS

This was produced from a copy of a document sent to us for microfilming. While the most advanced technological means to photograph and reproduce this document have been used, the quality is heavily dependent upon the quality of the material submitted.

The following explanation of techniques is provided to help you understand markings or notations which may appear on this reproduction.

1. The sign or "target" for pages apparently lacking from the document photographed is "Missing Page(s)". If it was possible to obtain the missing page(s) or section, they are spliced into the film along with adjacent pages. This may have necessitated cutting through an image and duplicating adjacent pages to assure you of complete continuity.
2. When an image on the film is obliterated with a round black mark it is an indication that the film inspector noticed either blurred copy because of movement during exposure, or duplicate copy. Unless we meant to delete copyrighted materials that should not have been filmed, you will find a good image of the page in the adjacent frame.
3. When a map, drawing or chart, etc., is part of the material being photographed the photographer has followed a definite method in "sectioning" the material. It is customary to begin filming at the upper left hand corner of a large sheet and to continue from left to right in equal sections with small overlaps. If necessary, sectioning is continued again—beginning below the first row and continuing on until complete.
4. For any illustrations that cannot be reproduced satisfactorily by xerography, photographic prints can be purchased at additional cost and tipped into your xerographic copy. Requests can be made to our Dissertations Customer Services Department.
5. Some pages in any document may have indistinct print. In all cases we have filmed the best available copy.

University
Microfilms
International

300 N. ZEEB ROAD, ANN ARBOR, MI 48106
18 BEDFORD ROW, LONDON WC1R 4EJ, ENGLAND

8103937

JACQUIN, MARK FRANCIS

PERIPHERAL OROSENSORY MECHANISMS: CONTRIBUTIONS TO THE NEURAL CONTROL OF INGESTIVE BEHAVIOR IN THE RAT

City University of New York PH.D. 1980

University
Microfilms
International 300 N. Zeeb Road, Ann Arbor, MI 48106

PERIPHERAL OROSENSORY MECHANISMS: CONTRIBUTIONS TO THE NEURAL CONTROL OF INGESTIVE BEHAVIOR IN THE RAT

by

MARK F. JACQUIN

A dissertation submitted to the Graduate Faculty
in Psychology in partial fulfillment of the
requirements for the degree of Doctor of Philosophy,
The City University of New York.

1980

This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

4/22/80
date

H P. Zeigler
Chairman of Examining Committee

7/23/80
date

Martin L Hoffman
Executive Officer

Dr. Anthony Sclafani
Dr. Joseph Griswold
Dr. Maria Miller
Dr. Carl Pfaffmann
Supervisory Committee

The City University of New York

Abstract

PERIPHERAL OROSENSORY MECHANISMS: CONTRIBUTIONS TO THE NEURAL CONTROL OF INGESTIVE BEHAVIOR IN THE RAT

by

Mark F. Jacquin

Adviser: Professor H. Philip Zeigler

The purpose of this report is to clarify the respective roles of trigeminal orosensory and gustatory inputs in the neural control of ingestive behavior in the rat. Detailed behavioral analyses were therefore carried out in rats subjected to peripheral trigeminal orosensory or gustatory nerve sections.

Trigeminal orosensory deafferentation produces behavioral and morphological changes whose magnitude varies with the number of orosensory nerves sectioned. This procedure: (1) affects the general condition of the mouth. Bite malocclusions, in combination with a reduction in the rat's typical gnawing behavior, result in incisor overgrowth and abrasions of the palate, lower lip, and tongue. (2) By removing an afferent limb of oromotor reflexes, deafferentation disrupts the sequential organization of consummatory behaviors (biting and licking), and subsequently reduces the efficiency of feeding and drinking. The extent of these disruptions depends largely on the modality and locus of the stimulus presented. Biting is elicited by intraoral tactile or extraoral noxious stimuli, while perioral stimuli rarely elicit biting. Licking is elicited only by intraoral gustatory and/or tactile stimuli. Deafferented rats, therefore, develop alternative modes of feeding and drinking. (3) Correlated with decreased efficiency is a reduced responsiveness to food and water. (4) Deafferentation results in a profound reduction in food intake whose magnitude and persistence is a function of the texture, and possibly the size and/or taste, of the available diets; and (5) a similar reduction in water intake. Though the initial periods of adipsia are not that striking, intake remains low for prolonged periods. (6) Responsiveness and feeding efficiency always predicted solid food intake. (7) When semi-liquid foods are available, deafferented rats resume sufficient intake to regulate body weight at reduced levels. Control procedures suggest that chronically reduced weight is a direct effect of decreased intake. (8) Normal food and water intake eventually returns, though lack of compensatory overingestion deters rapid body weight gains. (9) The "recovered" rat exhibits impaired sensitivity to QHCl solutions, reduced food intake while water deprived, and periodic relapses into earlier stages of recovery. (10) Preliminary studies suggest that recovery is due to regeneration of sectioned nerves, sprouting from intact nerves, and behavioral compensation.

Changes in oral morphology, possible abnormal or painful sensations in the oral region, impaired sensitivity to taste stimuli, and the consequences of severe feeding inefficiency are not individually sufficient to account for the severe and persistent intake deficits following trigeminal deafferentation.

Gustatory deafferentation doesn't produce oral abrasions or incisor overgrowth, nor does it impair orientation to sensory stimuli. Both the components and sequencing of ingestive responses appear normal. Deafferentation does, however, impair responsiveness to food, resulting in a significant reduction in food intake whose magnitude and persistence is a function of the taste of the available diets. Water intake also remains low for prolonged periods. Consequently, body weight is regulated below control levels. Evidence is presented in support of the conclusion that gustatory deafferentation effects are a direct result of taste impairment.

The symptomatology produced by gustatory deafferentation is quantitatively and qualitatively different than that produced by trigeminal deafferentation, suggesting a reevaluation of the relative importance of these two sensory systems in intake control in the rat.

Possible contributions of orosensory mechanisms to intake control are discussed in the context of oromotor reflexology, responsiveness to food and water, nutrient discrimination, body weight "set point", intake facilitation and inhibition, reinforcement, incentive, food conditioning, and general "activation".

The present findings suggest that we have seriously underestimated the significance of orosensory contributions to the quantitative control of hunger and thirst; i.e. these data point to the utility of a sensorimotor-reflex analysis in understanding motivated behavior. The mechanisms responsible for ingestive behavior may be isomorphic with the sensorimotor processes involved.

Dedication

This dissertation is gratefully dedicated to the late Peter Nikolic who provided unending motivation and expertise in collecting the majority of the data reported here. Science has finally provided for Peter's immortality.

And to Carol Woodbury who, perhaps, suffered most through the tenure of this project. Her love will never be forgotten. If only she could realize that my professional commitment was because of her and not in spite of her.

And to my mother and father who continue to grow with me. I hope they realize how important their emotional support was towards the completion of this, and many other, endeavors.

And to Professor Jerry Wodinsky who made it all seem so exciting and worthwhile. A more sincere professional I've never met.

Acknowledgements

I would like to express my heart-felt appreciation to the following people for their generous help towards the completion of this dissertation:

First, and foremost, to the distinguished members of my thesis committee. Dr. Phil Zeigler, my major professor, provided a never-tiring inspiration and standard of conceptual, experimental, and editorial excellence unmatched in the field. For without his help the thesis would've been completed a helluva lot sooner; admittedly, though, in a lot shoddier a fashion (Zeigler, 1976, 1977, 1978, 1979, 1980, personal communication). Drs. Tony Sclafani, Joe Griswold, and Maria Miller provided many insightful suggestions on the design, data analyses, and writing of the thesis. I thank them for their patience and emotional support at every agonizing step along the way. I'm also honored that Dr. Carl Pfaffmann, who initiated the type of thinking advanced in this thesis, was able to serve as an outside reader. Drs. Robert L. Thompson and Cheryl Harding did not serve on the committee, but might as well have. Their contributions were too numerous to mention here.

Drs. Don Webster and Maria Miller instructed me in the fine art of animal surgery. Only when attempting the types of denervation performed here does one come to appreciate their technical expertise. Dr. Martin Wild taught me the horseradish peroxidase technique and the beauty of anatomy. Agnes Reilly's contributions were innumerable, though she must be especially commended for doing <u>all</u> of my histology in a patient and professional manner, and for graciously helping with

animal care, data collection, and data analyses. More importantly, her listening ear made it possible for me to survive those moments only she can appreciate.

Actually, I had very little to do with carrying out the experiments reported here. Miriam Johnson provided 50 or so American Museum of Natural History volunteers that painstakingly performed animal care, some surgery, data collection, data analyses, and psychotherapy for the boss. Their reliability, honesty, and organizational skills allowed me to live a somewhat normal life over the last four years. I would especially like to thank Ursula Olazabal and David Riva who have remained with me since day 1. They enlightened me as to the potential in youth and the joy of teaching. The following volunteers also deserve special mention in view of their substantive contributions: Harry Atoynatan, Tom Balati, Marc Brilliant, Christine Chang, Francine Friedman, Oliver Fultz, Maureen Horrigan, Bob Kluberdanz, Carolyn Logan, Carolyn Lupfer, Kim Marks, Kim Marsulas, Allison Merow, Poisson Ng, Gus Pandazis, Claire Schacter, Barbara Schloss, Beatrice Segal, Betty Silver, Celeste Walicki, and Patrick Witt. I hope they learned as much from me as I learned from them.

Pat Levitt did a beautiful job on the figures and tables. She didn't get rich in the process, but I tried. Pat Brunauer and Bob Stollberg also fit in somewhere, I just can't figure out where. True friends are hard to find.

Speaking of which, the following people shared the graduate school experience with me and lended helpful suggestions and critical listening ears to my many theoretical ramblings: Dr. Richard Levine, Dr. Joe DeSantis, Dr. David Lewkowicz, Dr. John Mirenda, Gordon

Beckhorn, Roger Harris, Susan Herrick, David Crockett, Brent LaMon, Kevin Sheridan, and last, but surely not least, Brad Klein. It wouldn't have been the same without them.

Finally, Donna Day Tozer put the whole process in proper perspective for me. She also taught me the genuine essence of orosensation.

Table of Contents

TABLES

FIGURES

Fig. 11	Effects of varying degrees of trigeminal deafferentation upon the efficiency of the consummatory response of eating solid food. Two measures of efficiency reflect: (A) the mean (solid food intake / solid food removed from the dish), and (B) 1 / mean(crumbs/solid food intake). In both cases, the higher the ratio the greater the efficiency. Only those five day blocks where total crumbs or total intake was greater than 1g were entered into the group mean. On those few occasions where greater than 1g of crumbs were observed with no intake, that day was arbitrarily assigned the value one.
Fig. 12	Effects of varying degrees of trigeminal deafferentation upon responsiveness to solid foods (rat chow pellets, dry and moist cat chow). Responsiveness was determined by the amount of solid food removed from a 375ml heavy glass dish. SE's are indicated by vertical lines.
Fig. 13	Effects of varying degrees of trigeminal deafferentation upon the duration of aphagia (i.e. days to first intake of greater than 1g of food) for each of the diet types when presented concurrently ("cafeteria diet"). The occurrence of aphagic days subsequent to non-aphagic days was not a reliable phenomenon and is therefore not included in these data. (Complete deaff., N=10; "lingual intact", N=7; "alveolar only", N=6; unilateral deaff., N=3; sham surgery, N=8; infraorbital, N=5; ethmoid, N=2; teeth clipping, N=2.)
Fig. 14	Effects of trigeminal deafferentation, sparing the lingual nerves, upon food and water intake and body weight in a representative rat offered the cafeteria diet (30g rat chow mash offered on alternate days). Only those instances of greater than 1g intake are shown. ▼ indicates those days when the incisors were clipped.
Fig. 15	Effects of partial trigeminal deafferentation ("alveolar only") upon food and water intake and body weight in a representative rat offered the cafeteria diet. ▼ indicates teeth clipping and △ indicates 24 hour food deprivation.
Fig. 16	Effects of trigeminal deafferentation upon food intake and body weight when rats were offered either ad-lib rat chow pellets, ad-lib rat chow mash, ad-lib pablum, or the cafeteria diet. The first three groups served only in the single-choice condition. * indicates that preoperative data was not available for this group; these points were taken from three other rats.
Fig. 17	Effects of trigeminal deafferentation upon body weight, solid food intake, and water intake. Body weight is plotted as a percentage of the ad-lib value, i.e. the last weight taken before surgery. Sample sizes for different behavioral measures are separately indicated.

Fig. 18 Relationships between solid food intake, responsiveness, and efficiency in three trigeminal deafferented groups. Sample sizes are as in previous intake, responsiveness, and efficiency figures (figures 17, 12, and 13). The mean preoperative value is based upon 10 days.

Fig. 19 Effects of trigeminal deafferentation upon body weight in the cafeteria diet condition. Sample sizes as in Figure 13.

Fig. 20 Effects of trigeminal deafferentation ("complete" and "lingual intact") upon long-term regulation of body weight in four representative rats. Body weight is plotted as a five day mean percentage of the ad-lib weight. For each trigeminal rat, a yoked control rat, given the same types and amounts of food, is also plotted. The point at which the trigeminal rat began eating measureable amounts of rat chow pellets is approximately the point where the yoked rat was given ad-lib access to rat chow pellets ("unyoked"). From this point, divergent slopes represent a significant effect. Note that one rat did not exhibit a significant retardation in weight gain. "Day 0 BW" refers to each rat's actual weight at surgery.

Fig. 21 Effects of trigeminal deafferentation upon quinine aversion thresholds in four "recovered" rats (#78-13 and 17 are "comlete", #78-15 and 44 are "lingual intact"). Postoperative aversion thresholds were determined by a combined two-bottle preference and tracking procedure, i.e. the rat's two day relative QHCl intake determined the molarity available for the next two days. Less than 25% relative QHCl intake is defined as detection. Note that #78-17 was not tested preop. Molarity is plotted on a logarithmic axis for ease of presentation.

Fig. 22 The oropharyngeal taste bud distribution in the rat (from I. Miller, 1977, p.181). NID = nasoincisor duct, GS = taste stripe at the border of the hard and soft palate, PPF = soft palate.

Fig. 23 Surgical approach to the hypoglossal, glossopharyngeal, and pharyngeal branch of vagus nerves (from Richter, 1956, p.613).

Fig. 24 Effects of gustatory deafferentation upon quinine aversion thresholds in four representative rats. Only the descending method of limits was used in originally bracketing pre- and postop thresholds, followed by continuous tracking.

Fig. 25 Effects of gustatory deafferentation upon the efficiency of the consummatory response of eating solid food (rat chow pellets, dry and moist cat chow).

GENERAL INTRODUCTION

It is now widely accepted that "sensory stimulation, per se, together with its ensuing central neural events" is "a prime determinant in the chain of events culminating in acceptance behavior, reinforcement, and hedonic effect" (Pfaffmann, 1960). This conclusion is based upon a substantial body of data on the role of oropharyngeal inputs (taste, tactile, thermal, smell) in the arousal of hunger and thirst and the regulation of body weight. Studies using laboratory animals (especially the rat) have shown that orosensory stimuli act: (1) in nutrient discrimination and preference; (2) when incentives are required to elicit ingestion, i.e. expectancy of reward; (3) as potent reinforcers of operant behavior; (4) in controlling motor output patterns; and (5) in the initiation, maintenance, and termination of ingestive behaviors. Various research strategies have been employed in documenting these conclusions:

A. Orosensory Adulteration Studies (Palatability) - Many authors have discussed the "desirable" or "undesirable" sensations resulting from oropharyngeal, primarily gustatory, stimulation (Pfaffmann, 1960; Teitelbaum, 1964; Epstein, 1967; Young, 1967; Cabanac, et al., 1968; Wyrwicka, 1969; Brightman, 1977). By manipulating the stimulus properties of food, many investigators have shown that the qualitative and quantitative aspects of food can dictate incentive value and reinforcement, and subsequently, food preference. It is in the context of preference that most authors speak of palatability; defined as the acceptance of food and the amount eaten as determined by the stimulus properties of the diet. Most of the data point to orosensory factors as the prime control mechanism for palatability. For example, LeMagnen (1971) has shown that the rate of eating within a meal is different for two differently flavored foods, and that the initial speed and the differences between the ascending and descending parts of the curve can account for the greater intake of a corn-oil flavored food. In another experiment, LeMagnen (1956) trained rats to eat, in a two hour daily meal, a diet alternatively adulterated by four odorous chemicals. The four adulterated forms of the diet were successively presented for 30 minute periods and rats overate by 270% over their prior intake. Moreover, intake in the second 30 minute presentation resembled that of a rat which had not eaten in the preceding period. The sensory specificity of this effect has been demonstrated by Schulz and Lawrence (1958). Using a sucrose reinforcement for maze learning, satiated rats were found to learn the maze if they were satiated by the stock diet, while rats satiated by the sucrose solution did not perform. Many others have documented this shift in relative palatability as a result of prefeeding (e.g. Young, 1940).

The role of taste in absolute palatability was further investigated by Peck (1978) and Kratz and Levitsky (1979). Stock diets adulterated with a high fat substance or sucrose resulted in long-term increases in food intake and obesity. These rats overate as much and gained weight as rapidly as rats recovering from food deprivation. Interestingly, Peck found these obese rats to defend their increased body weight by eating more in the cold, less when force-fed by gavage, and more to restore weight after food deprivation. Kratz and Levitsky obtained obesity only in those rats where sucrose was mixed in with the stock diet and not when they were allowed a choice. The self-selectors maintained normal body weights. These findings are of interest in light of Teitelbaum's (1955) original report that caloric regulation is maintained at a normal level when the food was sweetened by mixing it with dextrose. Teitelbaum's data were often cited as evidence against an oropharyngeal component to long-term quantitative regulation of intake (Teitelbaum and Epstein, 1963). On the other side of the coin, Peck found that food adulterated with bitter quinine sulphate resulted in lower body weights maintained over periods of months in proportion to the percentage of quinine added. This finding substantiates Levitsky's (1970) original finding but again contradicts Teitelbaum and Epstein's (1962) results where rats continued to regulate caloric intake up to 1.25% quinine hydrochloride adulteration. Once again, the Teitelbaum and Epstein work is often cited as evidence against an oropharyngeal role in intake, since direct manipulation of the taste of the diet did not affect caloric intake at all.

The precise nature of the orosensory stimuli that control palatability is currently unclear. The examples provided above point to taste as _the_ relevant factor; however, the largely unexamined olfactory and somatosensory properties of food must offer unlimited sensory-specific responses of palatability (see Mook, 1974, on viscosity; and Allen, et al., 1972, on odor). What might also be important in palatability is the effort required for ingestion (see Morrison, 1968, on the greater energy expended to eat a rat chow pellet as opposed to lapping liquid food). Mode of presentation also appears to play a crucial role in dictating the importance of orosensory stimuli in palatability. For example, saccharin is largely preferred in a two-choice test, yet results from one-choice tests yields decreased intake (via decreased meal size) despite causing an initially high rate of intake. Positive hedonic stimulation, or sweetness, though preferred qualitatively, is not preferred quantitatively, resulting in shorter meals (Gentile, 1968). These discrepancies between data obtained using one-choice vs. two-choice tests (absolute vs. relative palatability) have been attributed to the greater role of post-ingestional effects in one-choice test behavior; e.g. the failure of animals to overeat preferred glucose has been interpreted as evidence for some kind of caloric regulation (Mook, 1963; Gentile, 1968). The common assumption is that the hedonic response, as measured by the two-choice preference test _is the_ response to the taste stimulus being presented. However, this assumption does not take into account the possibility that different tests of palatability sample different kinds of taste input effects. Gentile has hypothesized that animals ingest to a point of maximum gustatory stimulation, where satiety occurs; thus they have to eat less of an intense stimulus to acquire this set level of stimulation. A similar receptor-action hypothesis comes from Contreras (1977) in explaining the sodium-deficient rat's preference for salt water: satiety of drinking requires a critical number of NaCl-driven impulses in the chorda tympani nerve. More time and more drinking would be required for the taste nerve of a sodium deprived rat to accumulate this critical total number of impulses; therefore, time spent drinking should decrease with increased salt concentration, since impulse frequency increases with concentration.

An interesting theoretical formulation on palatability is provided by Mook (1974). Based on the finding that rats nearly always preferred saccharin-sweetened water to plain water, while rarely preferred saccharin-sweetened liquid food to bland food, Mook hypothesized that sweetness identifies a fluid as food in the informational sense. Thus, if other such cues are already present, sweetness is redundant and is ignored, and no legitimate distinction should be made between the "sensory" and the "motivating" properties of taste.

All of these examples indicate that orosensory inputs are crucial in allowing for diet discrimination, preference, incentive, and reinforcement. However, the relative contributions of gustation, somatosensation, and olfaction, as well as the nature of their interactions with mode of presentation, postingestional consequences, energy expenditure, level of deprivation, and informational processes has yet to be determined.

B. Metabolic Depletion and Meal Pattern Analyses - It is thought that, in the ad-libitum condition, meal size (maintenance and termination) is determined by orosensory and/or gastric inputs, while meal frequency (initiation) is determined by the level of caloric depletion (LeMagnen, 1971). This conclusion is based upon the following relationships: (1) amount ingested in a meal is uncorrelated to the length of intervals preceding these meals, and (2) meal size and the intervals following these meals are positively correlated (LeMagnen and Tallon, 1963, 1966; LeMagnen, 1969; LeMagnen and Devos, 1970; Balagura and Coscina, 1968; Thomas and Mayer, 1968; Snowdon, 1969, 1970).

Other lines of evidence suggest that the control mechanism responsible for determining meal size is not influenced by the diet's caloric level and the immediate caloric requirement. Janowitz, et al. (1949) showed that intravenous glucose infusion of 100% of the dog's daily caloric requirement six hours preceding a meal, did not affect the amount ingested in that meal. Also in dogs, intragastric intubation of the total daily ration six hours before (Janowitz and Hollander, 1955) or four hours after (Share, et al., 1952) the scheduled daily 45 minute food availability, did not affect the amount ingested in the single meal. Only after 150-175% of the daily caloric requirement is intubated does oral intake cease. Rats placed on diluted diets (cellulose) are incapable of making the immediate caloric adjustment in a single two hour presentation of food (Jacobs and Sharma, 1969); while the addition of a greasy mineral uncaloric fat or quinine results in drastic increases or decreases of intake irrespective of the energy balance obtained (Hamilton, 1964; Levitsky, 1970).

The above should not be taken to mean that rats have difficulty regulating their caloric requirement. The point is that increases or decreases in daily intake in response to adulteration or caloric infusion are accomplished through a rapid change in meal frequency, rather than meal size. Thus, it is thought by many that meal maintenance and termination are controlled by orogastric factors while meal initiation is regulated by caloric requirements.

C. <u>Caloric Adulteration Studies</u> - Miller (1979) has recently shown that trigeminal orosensory inputs play a role in the normal compensatory overeating response to caloric dilution. This suggests that trigeminal inputs play a role in the long-term quantitative regulation of food intake. Historically, however, the animal's ability to regulate caloric intake over a wide range of caloric adulterations (Janowitz and Grossman, 1949; Adolph, 1947; Teitelbaum, 1955; Teitelbaum and Epstein, 1962; Snowdon, 1969) or stomach preloadings (Thomas and Mayer, 1968) was taken to mean that oropharyngeal sensations are not involved (Teitelbaum and Epstein, 1963). As pointed out by LeMagnen (1971), however, long-term regulation cannot act independent of short-term control mechanisms. Tolerance, or compensatory hyperphagia, does not preclude the necessity of oral inputs in the long-term regulation of ingestive behavior.

D. Orosensory Conditioning Studies - Within various learning paradigms many workers have demonstrated a critical role of orosensory stimulation in food preference, the short-term patterning of feeding, and reinforcement. LeMagnen (1969) and Booth (1972) were able to show that orosensory stimuli can act as conditioned stimuli to elicit the feeding response. The systemic caloric action of intraperitoneal injection of glucose can act as a positive or negative reinforcer for orosensory elicited conditioned responses. Extinction ensues without caloric reinforcement. These authors concluded that with a specific food type, caloric excesses or deficits within a meal act to reduce or increase, respectively, the palatability and the size of a meal, through an "oral metering" mechanism. Thus, oral conditioning operates on meal size, but not on daily intake. The enormous literature on conditioned taste aversions and specific hungers (see Rozin and Kalat, 1971) attests to the importance of orosensory cues in conditioning via postabsorptive consequences, such as vitamin deficiency and nausea. It is widely agreed that oral conditioning of aversions allows animals to select foods suited to their metabolic requirements. In fact, Contreras (1977) has reported a change in chorda tympani unit firing patterns to salt in sodium deficient rats. Oral stimuli have also been shown to be effective reinforcers for maintaining lever pressing reinforced by intragastric infusion of food (Snowdon, 1969). Others (Sheffield and Roby, 1950; Guttman, 1953; Schlosberg and Pratt, 1956) have documented the powerful reinforcing properties of orosensation in the performance of maze running and lever pressing.

E. Sham Ingestion Studies - By creating an esophageal fistula through which ingested substances are immediately lost, preventing any change in fluid or energy balance, oropharyngeal contributions to feeding and drinking termination have been documented. In fact, Blass and Hall (1976) set the stage for this dissertation: "To the extent that peripheral controls are important in behavior termination, it would hardly be surprising if they were likewise important in behavior initiation" (p.372).

1. sham drinking - In their search for nonhydrational controls of drinking, Bellows (1939) and later Towbin (1949), in the dog, found sham drinking to be proportional to normal drinking, suggesting an oropharyngeal control mechanism. Recently, an elegant series of experiments by Blass and Hall (1976) pinpointed the relative contributions of oropharyngeal, combined oropharyngeal and gastric, and postabsorptive stimuli to drinking termination in the rat. Their original finding, and the basis for subsequent sham drinking studies, was that rats drinking to a specific level of overhydration following deprivation were behaviorally distinguishable from rats brought to this level by forced intubation. The intubated rats drank an additional 3.5 milliliters. That it was only 3.5 indicates the strong control exerted by cellular hydration; however, in that intubation did not suffice to eliminate further drinking, peripheral events associated with drinking must be given serious consideration. Their subsequent sham drinking experiments provide fourfold evidence for an oropharyngeal factor: (1) rate of sham drinking and volume sham drunk were directly related to deprivation length; (2) the ratio of approximately four between the amount drunk by sham as opposed to normal drinking held across a variety of conditions; (3) both sham and normal intake increased markedly when isotonic saline was the ingested fluid; and (4) alleviating the cellular, but not the extracellular def-

icit, reduced both forms of drinking. Their interpretation of the fourfold sham excessive intake is particularly insightful: "A physiological state (here, cellular overhydration) becomes especially meaningful within its behavioral context. Neither behavioral nor physiological events alone are sufficient to fully account for the 'permanence' of drinking termination. The necessary and sufficient relationship for its endurance is that both behavioral and physiological changes must be closely related temporally. When this temporal linkage is not honored, and physiological changes occur outside of the behavioral context, control is forfeited, causing behavioral excess ... Thus, when physiological alterations are uncoupled from their naturally occurring antecedent behaviors, equilibrium is lost" (p.367).

Additional support for an oropharyngeal metering comes from the sham drinking study by Waldbillig and Lynch (1979). Sham intake increased from five times that of normal drinking on the first two hour open fistula test to ten times that of normal on subsequent tests. More importantly, close examination of the drinking patterns revealed that the first fistula opening did not alter the position of the first pause in intake suggesting that the early portion of the drinking sequence is under the control of conditioned oroesophageal stimuli while the later phases of the sequence are controlled by stimuli arising from the alimentary canal and/or blood.

2. <u>sham feeding</u> - Miller and Kessen (1952), after demonstrating that the satiating effect of food by mouth is greater than food by stomach intubation alone, pointed out that sham feeding can have a satiating effect, be it a transient one. Sham feeding in dogs can also produce temporary satiety (Janowitz and Grossman, 1949b), but as in the rat,

meal frequency and meal duration are greatly increased. Later work by Young, et al. (1974) confirmed the notion that full satiety requires both that the material reach the stomach and be absorbed and that it stimulate oropharyngeal receptors. When the fistulas were opened for the first time, rats sham-fed uninterrupted during the entire test period of two or 7.5 hours. Thus, oropharyngeal sensations acting alone did not elicit satiety, casting doubt on LeMagnen's (1971) hypothesis that postingestive satiety mechanisms act solely as unconditioned stimuli for a learned oral control of feeding.

Mook's (1963) work with esophagastomized animals provides one of the clearest cases arguing for a stimulatory role of gustation in intake. Without the action of postingestive factors, glucose intake rose concomitantly with increases in concentration well into the higher ranges that would normally produce a decline in normal intake of glucose. Similarly, when procedures for limiting intake were used, such as short-term preference tests, the number of licks elicited was greatest for sucrose, next greatest for fructose, and still less for glucose, at equimolar concentrations (Davis, et al., 1975). In fact, the shape of the intake functions parallels the electrophysiological measures of taste afferent discharge to the same sugars (Hagstrom and Pfaffmann, 1959). The major thrust, however, of Mook's work with the "electronic esophagus" showed that the causes of solution drinking are complex and must include events occurring beyond oropharyngeal stimulation.

F. <u>Combined Intragastric Self-Feeding (or Self-Drinking) and Operant Conditioning Procedures</u> - A substantial body of data from studies using intragastric self-ingestion has been interpreted as indicating that when the rat is not faced with the problems of detection and discrimination and when the deprivation conditions are minimal, the quantitative control of intake is achieved in the absence of oropharyngeal sensations.

Originally developed by Epstein (1960), the procedure was designed to study the regulation of food and water intake in the absence of all oropharyngeal sensations, particularly taste, smell, and the consummatory acts of chewing and swallowing, by training the rat to press a lever to inject water or a liquid diet directly into its own stomach. Epstein first reported that rats exhibited normal daily water intake and compensated for the increased water loss of diabetes insipidus. Soon after, Epstein and Teitelbaum (1962) reported that rats regulated their daily food intake and body weight for periods of 13 to 44 days, continuing the normal slow weight gain. Compensatory responding was even shown following changes in diet concentration, individual stomach load size, and the number of presses required for a single load. In addition, the transition from oral to intragastric ingestion was made without any apparent difficulty. These data led Epstein (1967) to conclude that "oropharyngeal sensations are not essential for the arousal of hunger and thirst, for the satiation of both, for the control of the frequency and size of meals, and for the control of the total amount of food or water ingested daily for prolonged periods of time. Nor are they essential for the control of intake in the face of challenges such as dilution of the food or the threat of dehydration posed by the polyuria of diabetes insipidus" (p.211).

The technique of intragastric self-feeding has been criticized on methodological grounds by Holman (1969); the problems raised concerning load size, nasopharyngeal detection of the temperature of the food, visceral taste sensations, and actual performance of consummatory oral behaviors have yet to be satisfactorily resolved. Holman found that rats lever press for intragastric injection of a liquid diet only when very large load sizes are used, and only when oral stimulation from a weak saccharin solution, temperature changes in the nasopharynx, or self-produced chewing and licking movements accompanied injection of the food, and did not press for the oral stimuli or intragastric injection alone. It was also shown that intragastric administration of food enhances the effectiveness of oral stimulation but has no sustaining effect by itself on lever pressing.

Subsequent work from Epstein's laboratory (Snowdon, 1969) implies that the early intragastric-operant experiments underestimated the importance of oropharyngeal sensations in "motivating and sustaining feeding behavior at optimal levels" (p.98). Snowdon demonstrated that in the absence of food-elicited oropharyngeal sensations: (1) lever pressing for intragastric feeding extinguished rapidly; (2) rats could be retrained using an oral supplement; (3) subsequent intragastric food intake was reduced to about 75% of oral feeding levels; (4) lever pressing was brief and not sustained; (5) intragastric meals were smaller than oral ones; and (6) species-typical consummatory behaviors (biting, chewing, licking) directed at the lever often accompanied intragastric infusion of food. Similarly, Miller, et al. (1957) have shown that food and water are not as effective reinforcers if they do not pass through the oropharynx. In the water deprived rat, water ingested by mouth resulted in a greater diminution of subsequent water intake and water-reinforced lever pressing than did the same amount of water given through a gastric fistula. They also demonstrated the same phenomenon with enriched milk.

Epstein (1960), and later Kissileff (1973), have reported self-intragastric drinking in rats, yet the nasopharyngeal catheter was again used and is subject to all of the above criticisms. Kissileff's data is particularly interesting in that the response to intraperitoneal administration of hypertonic saline was less than adequate. Of three animals injected, only one responded by pressing the lever for intragastric water within six hours and consumption was only 50% as compared to a subsequent test when drinking by mouth. Similarly, relatively stable lever pressing for water rapidly extinguishes when the water which had been given partly for oral consumption is administered entirely by intravenous injection (Corbit, 1965).

Nicolaidis and Rowland (1974, 1977) were able to train rats to press a lever to obtain, through intravenous administration, all of their daily fluid requirements. However, within two to three days, the intravenous intakes had stabilized at about 50% of the oral intake of control rats. As Rowland (1977) points out: "These experiments were founded in the notion that the physiological competence to detect dehydration exists: it has thus been demonstrated that rats will perform self-intravenous rehydration. However, the performance is clearly quite different from that observed in orally drinking rats: all of the rats are dehydrated to some degree. By subtractive analysis, we might infer that oral and gastric sensory levels add to the systemic signals and sustain a higher level of motivation to drink" (p.264).

I believe the self-injection procedures do not provide data on the role of oral sensations in feeding and drinking because they involve the decoupling rather than the elimination of oral sensations. Oakley (1965) has argued that the intragastric technique is an illogical way of isolating the role of oropharyngeal sensations in that it only bypasses the consummatory responses. The procedure not only eliminates the species-typical consummatory behavior, but also substitutes a learned operant response (lever pressing). While the neural mechanisms controlling food intake and food-reinforced operant responding may be related, it is unlikely that they are identical (Zeigler, 1975b). For all of the above methodological and conceptual reasons, care must be taken in interpreting these data.

AIMS OF THE STUDY

The above-described experiments have all contributed to our current understanding of the critical role played by orosensory inputs in the initiation, maintenance, and termination of ingestive behaviors, food preference, nutrient discrimination, reinforcement, and the incentive value of food and water. However, these types of experiments have not provided the following specific information regarding the control of species-typical ingestive behavior: (1) the relative contributions of trigeminal orosensory, gustatory, and olfactory stimuli to responsiveness to food and water, and consequently the initiation of ingestion; (2) the relative contributions of each of the orosenses to the patterning of motor output, i.e. the consummatory responses; and (3) the relative contributions of peripheral vs. central orosensory pathways to the neural control of ingestive behavior.

An alternative procedure for the study of ingestive behavior, which addresses itself to all of the above questions, is to begin peripherally, i.e. with the consummatory behaviors themselves, elucidating their sensory control, and identifying the afferent and efferent structures which mediate the movement patterns involved (e.g. Doty and

Bosma, 1956; Kupferman, 1974; Zweers, 1974; Weijs and Dantuma, 1975; Zeigler, 1976). In the hands of neurobiologists the study of sensorimotor mechanisms has been a productive approach not merely to the study of ingestive behavior (Dethier, 1967), but as a fundamental strategy for the study of the central nervous system (Sherrington, 1906; Herrick, 1905; Lashley, 1938). Therefore, the fundamental aim of this dissertation is to clarify the role of trigeminal orosensory and gustatory inputs in the neural control of ingestive behavior in the rat. Towards this end detailed behavioral analyses were carried out in rats subjected to peripheral trigeminal orosensory or gustatory nerve sections.

Additional considerations dictated this peripheral strategy: (1) The strict centralist approach, namely the analysis of hypothalamic lesion effects, has proven to be an unproductive strategy for dissecting out specific neural subsystems related to hunger and thirst (Epstein, 1971; Zeigler, 1976). Unfortunately, the major thrust of the study of ingestive behavior has been expended on a neurology that <u>might</u> control a specific behavioral sequence, without a proper understanding of what's being controlled or regulated. Recourse to only central neural events, without due consideration of the peripheral controls which guide and orient behavior, and their interactions, is destined to yield an incomplete understanding of feeding and drinking (Morgane, 1969; Blass and Hall, 1976). (2) There is the formidable problem of making bilateral lesions of central representations of oral structures massive enough to produce substantial deficits in ingestive behavior, but discrete enough to avoid unacceptable damage to adjacent structures which may also play a role in such behavior, such as the major catecholamine systems (Stricker and Zigmond, 1976). By contrast, deafferentation studies, because their findings are so unambiguously related to a specific denervation procedure, can help define an array of behavioral deficits related specifically to trigeminal or gustatory structures. (3) Taken together with Zeigler's (1976) studies of deafferentation in the pigeon, similar studies in the rat promise to provide important comparative data on the contributions of trigeminal mechanisms in two vertebrate species which seem, superficially, so different in the morphology of their oral regions and in the stimulus control of their ingestive behavior. (4) Studies of peripheral mechanisms are necessary to provide a foundation for future research on the effects of central orosensory lesions. Also, it seems likely that the relation between the orosensory and hypothalamic systems would be better understood against a background of data on the roles of orosensory and oromotor structures at the most peripheral levels.

The studies to be described here were made possible by the development of surgical procedures for the selective denervation of the oral region which permit section of individual trigeminal orosensory or gustatory branches. Minor modifications of these procedures have permitted selective section of the trigeminal motor root, of the hypoglossal nerve, and of the ethmoid and infraorbital branches of the maxillary nerve. The development of these procedures has made possible for the first time a direct assessment of the differential contribution of sensory (somatosensory, chemosensory) and motor (jaw musculature, tongue musculature) systems innervating the oropharyngeal regions to ingestive behavior in the rat. However, this dissertation will focus only on the orosensory contributions, using oromotor denervation as a control procedure where applicable.

Orosensory deafferentation effects were evaluated in the following measures: food and water intake, body weight-regulation, feeding and drinking efficiency, responsiveness to food and water, sensorimotor-reflex functioning, quinine aversion, food preferences, and the organization of the consummatory responses for food and water intake. I have also explored the relation of sensory or motor deficits to the sensory properties of the diet by using an array of diets varying in texture, taste, and ease of oral manipulation. Perhaps the most difficult task was the design of control procedures to isolate pure effects of deafferentation on such hard-to-pin-down matters as responsiveness to food and water and body weight regulation. My hope is that, at long last, some light may be shed on the neurosensory control of hunger and thirst, a forever controversial and deceptively elusive issue.

EXPERIMENT 1

SELECTIVE TRIGEMINAL DEAFFERENTATION IN THE RAT: EFFECTS UPON FOOD AND WATER INTAKE, WEIGHT REGULATION, AND SENSORIMOTOR FUNCTION

INTRODUCTION

By contrast with the voluminous literature on the anatomy and physiology of the vertebrate trigeminal system (see Sessle and Hannan, 1976; Dubner, et al., 1978), there have been relatively few neurobehavioral studies of trigeminal orosensory function.

A. Prior Deafferentation Studies - The following attempts have been made to achieve complete surgical denervation or local anesthetization of orosomatosensation in studying the control of food and water intake:

Cannon(1918), arguing in favor of a "dry mouth" theory of water intake, cited the finding by Valenti (1910) that applying cocaine to the back of the mouth and upper esophagus in the water deprived dog prevented drinking. Adolph, et al. (1954) later reported that rats with mouths cocainized to the point of insensitivity to pain drank water in proportion to body-water deficits created by deprivation.

The earliest surgical denervation study (Bellows and VanWagenen, 1939) compared the effects upon water intake of selective section of the trigeminal, gustatory, and olfactory nerves and has been unjustifiably used to support the notion that oropharyngeal sensations do not contribute to the quantitative control of ingestive behavior (Teitelbaum and Epstein, 1963; Epstein, 1967). Bellows and VanWagenen observed the voluntary intake of water in three groups of dogs: (1) bilateral section of the glossopharyngeal and chorda tympani nerves in an attempt to eliminate gustation, (2) bilateral section of the root of the trigeminal nerves in an attempt to eliminate orosomatosensation, and (3) resection of the olfactory tracts. It was deduced that these procedures did not abolish the "urge to drink". Unfortunately, their experiments were unsystematic. With regard to their trigeminal deafferentation procedure, (1) both motor and sensory roots were sectioned producing "stiffness" in the masticatory muscles; (2) a six week interval was allowed between the unilateral and bilateral condition which is sufficient time for neural reorganization; and (3) smaller daily water intakes were, in fact, reported for both the trigeminal and olfactory groups, yet this was attributed to "enforced fasting". The present experiment represents, in part, an attempt at replicating the original Bellows and VanWagenen trigeminal work under more carefully controlled conditions. Their olfactory deafferentation data stands uncontested. In fact, Richter (1956) reported no effect on body weight regulation following olfactory bulbectomy in rats. LaRue and LeMagnen (1967) subsequently showed that olfactory bulbectomy did not alter the 24 hour intake of rats fed ad-lib on a familiar diet.

Zeigler and his collaborators have, over the past decade, systematically studied the role of trigeminal afferents in the ingestive behavior of the pigeon. The pigeon has proven to be a superb preparation since taste and smell play a minimal role in the sensory control of feeding, and the location of the trigeminal nerve permits deafferentation of the oral region without disrupting either motor or proprioceptive function. Zeigler, Miller, and Levine (1975) and Zeigler (1975a) found that trigeminal deafferentation produced no effect upon drinking, yet a disruption of feeding behavior qualitatively and quantitatively similar to the deficits encountered after lesions of central trigeminal structures (Zeigler and Karten, 1973a,b). Bilateral section of the mandibular, maxillary, and ophthalmic branches produced periods of aphagia ranging from one to eight weeks, followed by an equally prolonged period of hypophagia. The magnitude of these deficits was proportional to the number of nerve branches sectioned bilaterally. Even after their food intake had returned to its preoperative level, these deafferented birds failed to show the degree of compensatory overeating appropriate to their state of body weight loss. There was also a striking reduction in the efficiency of feeding, apparently mediated by impairments in grasping and mandibulation. Monitoring of feeding responses in the home cage under ad-libitum conditions provided clear evidence for an additional effect upon responsiveness to food; during the period of post-operative aphagia the number of daily pecking responses was drastically reduced. The nature of the deficit was more precisely defined in a recent study of feeding behavior patterns in deprived and deafferented pigeons (Miller, 1978a; Miller, Zeigler, and Miller, 1978). Miller's analysis indicates that the ingestion rates of deafferented birds are comparable to that of normal birds so that their reduced intake is not simply due to a disruption of the consummatory response. However, her studies showed that although deprived and deafferented birds show many similarities in their feeding patterns, these patterns lead to very different outcomes with respect to long-term food intake: compensatory overeating and weight gain in deprived birds, undereating and a reduced body weight in the deafferented birds. Deprived birds respond to a weight loss by increasing the size of the first few bouts in each feeding period while simultaneously sustaining the remainder of their daily feeding activity at normal levels. The result is a net increase in food intake and a rapid recovery of body weight. Deafferented birds also cvereat in the first hour but fail to maintain normal levels of feeding during the rest of the day. The result is an insufficient increase or a net decrease in food intake and a retardation in the rate of body weight gain.

In addition, Zeigler (1975b) found that trigeminal deafferentation had no direct effect upon food-reinforced key pecking. Its most obvious and immediate effect was to significantly reduce responses to food presented in the magazine during the reinforcement interval. Thus, there was a gradual decline in key pecking which resembled that seen during extinction. With continued testing there was a gradual increase in the number of feeding responses per reinforcement in some of the birds. With the resumption in measureable food intake, key pecking rapidly regained its preoperative levels. Taken in conjunction with the home cage pattern data, these findings indicate that the reduced intake of deafferented birds does not simply reflect either an inability to perform the pecking response or a reduction in the efficiency of eating.

Zeigler (1977) has attempted to explain these findings in terms of a "tonic hypothesis" (e.g. Pfaffmann, 1961), suggesting that trigeminal afferents, in addition to their informational (phasic) functions, also have a tonic function in modulating the excitability of central neural mechanisms underlying patterns of neural activity or behavior, in the pigeon.

Subsequent studies have extended these findings to the rat. Marwine and Zeigler (1975) produced trigeminal denervation by electrolytic lesions of the trigeminal sensory root and Gasserian ganglion. By varying the placement and extent of the lesions, they were able to produce a continuum of effects upon ingestive behavior varying from prolonged aphagia to varying degrees of hypophagia and hypodipsia and a significant retardation of body weight gain. Figure 1 (from Zeigler, 1976, p.369) shows the effects on food and water intake and body weight produced by a typical ganglion lesion.

Insert Figure 1 here

The reduced food intake of these deafferented rats appears to reflect, in part, a disruption of the sensorimotor control of their consummatory behavior toward rat chow pellets. Some of the animals were able to pick up the pellets in their jaws but were unable to shave food off the pellet surface. In addition to their reduced efficiency, deafferentation resulted in a reduced responsiveness to food and water. This was evident not only in their increased latency to feed and reduced contact time with food, but also in the fact that intake appeared to vary with the size, texture, and taste characteristics of the diet. However, interpretation of the findings was complicated by the fact that the lesion often produced damage to the trigeminal motor root. Thus, the lesion technique used for denervation does not appear to be suited for separating out sensory vs. motor contributions to the observed deficits, nor for controlling the somatotopic locus and magnitude of deafferentation.

Miller (1977) recently developed a technique for trigeminal deafferentation in the rat which avoids these problems and parallels in its specificity the method used with the pigeon. The procedure spares vibrissae innervation, leaves gustatory afferents largely intact, and does not disrupt proprioceptive afferents or efferents to the masticatory musculature. Employing intraoral and infraorbital approaches, Miller has sectioned the superior alveolar, inferior alveolar, lingual, and palatine nerves in different combinations to produce varying degrees and types of trigeminal orosensory deafferentation. The animals were offered an array of foods varying in size, taste, and texture; from semi-liquid pablum to rat chow pellets. As in the pigeon (Zeigler, 1975a), the disruptive effects of such a procedure are related to its extent and peripheral distribution. Complete deafferentation of both the upper and lower parts of the mouth, including the tongue, was followed by adipsia and aphagia persisting for a minimum of five weeks, at which time some animals showed rather abrupt recovery of intake and body weight. Neurological testing indicated that the aphagic and adipsic trigeminal rat was able to bite, chew, and swallow; yet "impairment in coordination of the consummatory act was suggested by a reduction in ingestion rate and inappropriate oral behavior in biting tests and during exploration of the food" (Miller, 1977). While the efficiency of their ingestive behavior was reduced, this could not account for their reduced intake, since the frequency of approach to food was also markedly reduced.

Some data on the effects of deafferentation are provided by a recent study on the sensory control of bite force in the rat (Daunton, 1977), In order to distinguish the roles of tactile and proprioceptive inputs, Daunton compared the effects of lesions of the trigeminal mesencephalic nucleus to the effects of local anesthetization (Novocain) of the rostral portion of the buccal cavity. It was found that cutaneous receptors from these areas is necessary for the discriminative control of bite force, while proprioceptive input from the jaw is not. It is also clear from an examination of her data that anesthetization reduced the probability of emission of a bite, of any force, for intraoral delivery of water reinforcement. These data suggest that cutaneous deafferentation of the oral cavity produced a deficit in operant responding without producing an impairment in the ability to emit a forceful biting response.

B. Peripheral Trigeminal Mechanisms and the Morphology of Ingestive Behavior in the Rat - As Wayner (1974) has noted, "Quantity consumed, the most remotely related dependent variable in terms of behavior, has received the greatest attention and can provide only limited information concerning the basic processes involved. Greater attention must be focused on the process of ingestion itself and the stimuli which are involved in the elicitation of these separate muscular activities" (p.857). The paucity of neurobehavioral studies of trigeminal orosensory function is therefore surprising, since several lines of evidence suggest that trigeminal inputs must play a dominant role in the control of ingestive behavior in the most commonly used laboratory animal, the albino rat.

Even cursory observations of eating and drinking in the rat make it clear that the food or water source is explored tactually and that somatosensory input is used to guide grasping, mandibulation, licking, and mastication. The typical ingestive sequence elicited by rat chow pellets or other relatively large particulate food objects involves, first, contact with the snout region followed by grasping of the object with the incisors. The object is then transferred to the forepaws where feeding consists of nibbling at the object held in the forepaws, and, in the case of large rat chow pellets, the incisors are used to shave off small bites from the pellet surface. Movements of the tongue and molar teeth are involved, successively, in mandibulating and masticating the food prior to swallowing (Weijs and Dantuma, 1975; Hiiemae and Ardran, 1968). Similarly, the tongue plays a critical role in ingestion via licking, not only of liquids, but of semi-liquid diets like wet mash. Hulse's studies of the rat's licking behavior have shown that burst size and interburst lick rate are directly proportional to drop size and unrelated to its gustatory dimensions. These and other findings have led him to conclude that the licking response in the rat is controlled largely by the tactile properties of the drop (Hulse and Suter, 1968, 1970). An important role for thermal stimuli in the control of drinking is suggested by studies of licking behavior elicited by air streams or cool metal surfaces (Mendelson and Chillag, 1970; Oatley and Dickinson, 1970). Kissileff (1973) has also concluded that somatosensory stimuli play an important role in the acquisition of intragastric self-injection behavior for water. Thus, the process of ingestion, whether for food or water, involves a continuous flow of trigeminally monitored input from the oral region.

Inputs from the trigeminal system, like those from other portions of the somatosensory systems "are designed to enable the organism to detect, localize, select, categorize, discriminate, and abstract aspects of the mechanosensory environment. Organized movement requires somatic sensory information" (Welker, 1973, p.253). Providing such information for the snout, there exists three general groups of trigeminal sensory functions: (1) exploration of the external environment via touch, temperature, and pain receptors, (2) characterization of objects within the mouth, and (3) sensory modulation of the organized flow of efferent impulses generating patterns of movement in the orofacial musculature.

Perhaps the most striking feature of the rat's trigeminal system is the extent of its development at both peripheral and central levels, rivaled only by the magnitude of the olfactory system. Figure 2 (from Greene, 1935, p.139) presents lateral and ventral views of the rat brain showing the location and relative size of the major cranial nerves.

Insert Figure 2 Here

The trigeminal ganglion (Gasserian) is continuous caudally with the trigeminal sensory root and rostrally with the three divisions of the trigeminal nerve (ophthalmic, maxillary, mandibular). The ophthalmic and maxillary cell bodies and fibers are combined to form a single mass occupying the more antero-medial portions of the ganglion. They continue rostrally as a massive fused structure containing ophthalmic afferents innervating the orbital and periorbital regions and maxillary afferents from the vibrissae, rhinarium, upper lip, and the dorsal half of the buccal cavity. The maxillary branch receives three major nerves responsible for innervating the upper buccal cavity: (1) the anterior superior alveolar from the upper incisors and upper rostral gums; (2) the sphenopalatine from the palate and cheeks; and (3) the posterior superior alveolar from the upper molars, upper caudal gums, and cheeks. The mandibular division forms the posterolateral portions of the ganglion emerging as a distinct branch through the foramen ovale. Its major nerve branches carry somatosensory input from the lower lip, lower teeth, gums, and floor of the mouth via the inferior alveolar nerve, and from the tongue via the lingual nerve (Darian-Smith, 1973; see Figure 3, from Miller, 1977, for a schematic diagram of the distribution of these five nerves).

Insert Figure 3 Here

Figure 4 (from Gregg and Dixon, 1973, p.494) illustrates the somatotopic organization of orofacial structures within the rat's trigeminal ganglion. Data on the divisional localization within the ganglion was based on the analysis of chromatolytic changes in ganglion cell groups following resection of specific peripheral nerve branches. The nature of somatotopic organization at the ganglion level is of interest because the differential representation of certain regions, e.g. the oral cavity and snout, presumably reflects their functional significance for the rat.

Insert Figure 4 Here

In the rat, mastication is accomplished by the incisors and molars of the lower jaw as they move in relation to the fixed incisors, molars, and palatal ridges of the upper mouth (Hiiemae and Ardran, 1968). Six different muscles are directly involved in mandibular (jaw) movement: the masseter, temporal, digastric, medial and lateral pterygoids, and the zygomaticomandibularis. Specific motions can be attributed to each jaw muscle. The masseters, together with the temporals, the zygomaticomandibularis, and the medial pterygoid muscles close (adduct) the jaw. The digastric and lateral pterygoid muscles are responsible for jaw opening (abduction). The masseter and pterygoid also play a role in protrusion of the lower jaw. The digastric and zygomaticomandibularis control jaw retraction. In sequence, these movements combine to produce grasping, chewing, grinding, and mandibulation (Weijs and Dantuma, 1975;

Halpern, 1977).

With one exception the mammalian jaw muscles receive their innervation via the motor branches of the trigeminal mandibular division, the sole exception being the posterior belly of the digastric muscle, which is usually innervated by the efferent branch of the facial nerve. Also important in mastication is the mylohyoid muscle, a jaw-related muscle which raises the floor of the mouth and moves the hyoid bone anteriorly. The trigeminal motor root, which innervates all of the above muscles (except the posterior digastric), originates in the brainstem motor nucleus of the trigeminal nerve.

Both the intrinsic and extrinsic tongue muscles of the rat are innervated by branches of the hypoglossal nerve, originating in the brainstem hypoglossal nucleus. Electrical stimulation of hypoglossal branches in the cat results in specific tongue movements or specific changes in shape, while multiple stimulation results in complex movement patterns (Abd-el-malek, 1939). Except for the sternohyoid and omohyoid muscles of the tongue, all tongue muscle innervation occurs via the ascending ramus of the hypoglossal nerve. The above two receive their innervation via the descending ramus (Greene, 1935).

Like other movements, appropriate tongue and jaw movement requires sensory feedback. The modulation and integration of orofacial motor patterns is best described as a "sensorimotor" function since it requires not only mechanosensory inputs from the orofacial skin, teeth, and mucosa, but also proprioceptive inputs from the muscles of mastication. In most mobile appendages such feedback is provided by mechanoreceptors in the joint capsule, tendon organs in the tendons, and muscle spindles in the muscle. The jaw is richly supplied by Golgi tendon organs, muscle spindles, and by receptors located in the temperomandibular joint. The cell bodies of Golgi tendon organs are located in the trigeminal ganglion and their axons (Group lb fibers) are carried centrally within the trigeminal sensory root. Muscle spindles, innervated by Group la fibers, have their cell bodies in the trigeminal mesencephalic nucleus (Mes. V) to which they project via the trigeminal motor root (Alvarado-Mallart, et al., 1975; McIntyre, 1951). The temperomandibular joint afferent pathways are not clearly understood at present.

Thus, the anatomical organization of the trigeminal proprioceptive, somatosensory, and motor nuclei (Mes. V, Pr V, Motor V) provide the functional basis for a variety of reflex mechanisms critical for the sensorimotor control of ingestive behavior. Cells of Mes. V give off collaterals to homonymous motoneurons of Motor V such that the spindle afferents and the motoneuron collaterals together constitute a two-neuron, monosynaptic reflex arc (Szentagothai, 1948). Figure 5 (from Zeigler, 1981) schematically describes the anatomical distribution of the trigeminal system and clearly shows how this simple reflex is controlled. This arrangement provides the feedback loops involved in the classical muscle stretch reflexes. It also permits various jaw muscle groups to interact with each other, via interneurons, to produce patterns of excitation and inhibition involving the masticatory muscles, which are analagous to those produced at spinal levels for limb musculature. Furthermore, Mes. V neurons also send collaterals to the hypoglossal motor nuclei of the same side. Since projections from Mes. V to both trigeminal and hypoglossal motor nuclei are bilateral, this organization provides a basis for the continuous integration of jaw and tongue movements during mastication in mammals (Kawamura, 1964; Darian-Smith, 1973; Sessle and Hannam, 1976).

Insert Figure 5 Here

Very little neurobehavioral work has been done on the role of these inputs in orofacial motor patterns. Goodwin and Luschei (1974), Luschei and Goodwin (1974), and Daunton (1977) reported no significant change in mastication following interruption of spindle input via Mes. V lesions in monkeys and rats. Chewing rates, chewing patterns, and oral manipulation of food showed no permanent changes after large bilateral lesions. Thus, spindle input is not necessary for the performance of ingestive behavior, though this does not preclude the importance of other movement-produced feedback. Jerge (1963) and Eisenman, et al. (1963) have obtained recordings from various trigeminal brainstem nuclei, other than Mes. V, indicating that other responses do occur to jaw position and to direction of movement. Movement-produced sensory feedback is therefore available from sources traveling afferent routes other than the trigeminal motor root.

It is becoming increasingly clear that somatosensory input is intricately involved in _all_ purposive movement (Taub, et al., 1977; Twitchell, 1954; Welker, 1973; Zeigler, et al., 1975; Dubner, et al., 1978; MacDonnell and Flynn, 1966; Zlatin, 1972; Schaerer, et al., 1966; Smith, 1972), leading me to hypothesize that orosomatosensory deafferentation would reduce both the efficiency of and the propensity for ingestive behavior in the rat.

The present work will extend Miller's (1977) observations and provide the neuronal and behavioral specificity not available in the original electrolytic lesion procedures of the Gasserian ganglion used by

Marwine and Zeigler (1975).

Possible deficits involved in the reduction of food and water intake will be evaluated, such as: (1) sensorimotor dysfunction, (2) heightened sensitivity to the sensory properties of the food, (3) general decreased responsiveness to food, (4) impaired feeding efficiency, and deficits in response to the challenge of food and water deprivation and long-term body weight loss. Taste sensitivity will also be evaluated using a two bottle quinine aversion series.

METHODS

A. Subjects and Housing

Male albino rats (Rattus norvegicus), 90-150 days old and weighing 200-450g, were obtained from a commercial supplier (Rockland Farms, Rockland, New York). They were housed individually in either large pigeon cages (45cm long X 39cm wide X 33cm high) or large rat cages (24 X 41 X 18) in a colony room which also contained pigeons during the first half of the experiment. The room was heavily trafficked during the day and cigarette smoke from adjoining rooms could often be detected. A 14:10 light/dark cycle was in effect and room temperature was controlled at 25 ± 4° C. All rats were allowed at least one week adaptation to the laboratory, given continuous access to Purina rat chow pellets and Tetracycline adulterated water (40 parts powder : 1000 parts tap water, by volume), and left undisturbed except for daily weighing and cage maintenance. Spilled food was accessible to the animal since deotized animal cageboard (Upjohn Co.) was placed flush under the grid floor of the cage.

B. Surgical Procedures

Rats were tranquilized with 0.3cc Taractan, i.p. (chlorprothixene, Roche Laboratories, 3.75mg), and anesthetized 15 minutes later by 0.05cc/150g body weight Vetalar, i.m. (Ketamine Hydrochloride, Parke Davis, 5mg/150g body weight). Supplemental doses of Vetalar (0.05cc) were given as needed.

1. Experimental groups - The neck and scalp were shaved and the rats placed in a Kopf stereotaxic head holder. Care was taken to insert the ear bars gently to minimize damage to the chorda tympani

nerve. Surgery was carried out with the aid of a Zeiss operation microscope (10X - 25X).

a. mandibular nerves - Deafferentation of the lower portions of the oral region was accomplished by section of the inferior alveolar and lingual nerves. A large midline incision was made in the neck, the two submaxillary glands were retracted, and the digastric and masseter muscles were gently teased apart to reveal the external jugular vein. Separation of the jugular from the rostrally retracted masseter exposed the chorda tympani, auriculotemporal, mylohyoid, inferior alveolar, and lingual nerves as they appear moving rostrally. Muscle retraction was gentle so as not to impede respiration. Superficial fascia was teased away and the inferior alveolar and lingual nerves were individually hooked and sectioned with microscissors as they exit from under the pterygoid plate. The lingual section was therefore proximal to its junction with the chorda tympani (see Figure 3). Tension in these two nerves caused them to spring apart after sectioning and no attempt was made to remove part of the cut ends. Figure 6 (from Richter, 1956) illustrates the ventral surgical approach.

Insert Figure 6 Here

b. maxillary nerves - Deafferentation of upper portions of the oral region was accomplished by intraorbital section of the anterior and posterior superior alveolar and sphenopalatine nerves. Figure 7 (from Gregg, 1973) illustrates the approximate positions of these three nerves as they merge with the main ophthalmic-maxillary nerve trunk.

Insert Figure 7 Here

Following a midline scalp incision and retraction of the skin, gentle retraction of the orbital contents from the skull with a dental spatula allowed easy access to the infraorbital nerve. Two thin glass probes were then used to laterally retract the infraorbital nerve, exposing the anterior superior alveolar in the rostral pole of the infraorbital canal and the posterior superior alveolar in the caudal pole, with the sphenopalatine lying between. Care was taken not to excessively stretch the ethmoid nerve, though minimal retraction was necessary to gain access to caudal portions of the infraorbital canal. All three orosensory nerves were gently hooked and sectioned with a microscalpel as they exit their respective foramena. Because the nerves are under tension, sectioning them produced separation of their cut ends. Thrombin and Gelfoam were used to control bleeding, which was heavy in this highly vascularized region.

All incisions were closed with silk sutures following liberal application of Neosporin powder. Combiotic (0.4cc) was also administered, i.m., to prevent postoperative infection. Rats were then placed in their home cages to recover.

In all but three rats, bilateral sections were performed in a single stage procedure, regardless of the number or types of branches sectioned. These three first sustained sham surgery, which was followed, two-three weeks later, by unilateral and bilateral deafferentation in two stages, with 14, 26, and 88 day intervals separating the latter stages.

A schematic diagram of the rat's head, in the sagittal plane, is presented in Figure 3 (from Miller, 1977) to show the approximate point of section of the five trigeminal nerve branches and their areas of innervation. The regions deafferented by the combined procedures are the inferior and superior molars and incisors, floor of the mouth, gums, lower lip, anterior portion of the tongue, palate, and cheeks. This is shown schematically in Figure 8. Note that all proprioceptive and motor nerves are spared as well as the major sources of taste afference via the chorda tympani, glossopharyngeal, and vagus nerves.

Insert Figure 8 Here

2. Control groups - Four types of surgical controls were prepared:

a. sham surgery - To control for muscle damage, bleeding, and the general malaise produced by surgery alone, rats were anesthetized and mandibular and maxillary orosensory branches were exposed but not sectioned.

b. infraorbital nerve sections - To evaluate the differential contribution of nonorosensory trigeminal inputs to ingestion, the infraorbital branch of the trigeminal nerve was bilaterally sectioned caudal to the infraorbital foraman. This removed cutaneous sensations from the upper lip, rhinarium, vibrissae, and facial pads.

c. ethmoid nerve sections - To control for inadvertent damage in the intraorbital approach, the ethmoid branch of the trigeminal nerve was bilaterally sectioned as it exits the ethmoid foraman. This removed intranasal cutaneous sensations.

d. teeth clipping - To evaluate the effects of periodic teeth clipping, which was necessary to control incisor overgrowth in many deafferented animals, a group of normal rats were subjected to clipping of the upper and lower incisors, twice weekly, over a three week period. During teeth clipping the rat was wrapped in a towel, the mouth opened, and the incisors grasped and shattered with surgical rongeurs. This usually resulted in a clean break, however, the incisors occasionally shattered down to the gums. Rats serving in the sensorimotor-reflex testing were subjected to periodic filing with a small dental burr under mild ether anesthesia. Teeth were kept moist during filing to prevent tooth pulp destruction.

In an attempt to clarify the neural basis for recovery of function, trigeminal nerve sections were carried out in previously deafferented rats (trigeminal orosensory). Bilateral resection of all three maxillary orosensory nerves was carried out in two "recovered" deafferented rats, while bilateral resection of both mandibular orosensory nerves was done in three other "recovered" rats. Three more received bilateral section of the infraorbital nerve. In addition, to determine whether taste nerves were responsible for recovery of function, two "recovered" trigeminal rats sustained bilateral sections of the chorda tympani, glossopharyngeal, and pharyngeal branch of the vagus nerves (see Experiment 2 for surgical procedures).

C. Histology and Post-Mortem Analyses

Verification of the central projections of sectioned nerves is one way to ensure proper identification of those nerves believed to innervate trigeminal orosensory fields. This was accomplished using a histochemical retrograde marker. Plugs of Gelfoam, saturated with 40% horseradish peroxidase (HRP: Boehringer-Mannheim) were bilaterally applied to the proximal cut ends of the inferior alveolar and lingual nerves in one rat and to the anterior superior alveolar and sphenopalatine nerves in another. After one hour, the plugs were removed. The animals were sacrificed after 48 hours with an overdose of Ketamine Hydrochloride and perfused through an internal carotid with 300ml of 2% dextran in saline followed by 500ml of fixative. The perfusate was a cold solution of 4% glutaraldehyde, 5% sucrose, and 1.2% $CaCl_2$ (4mM) in 0.1M Tris-HCl buffer, pH 7.6. The brains and Gasserian ganglia (with the trigeminal motor root attached) were removed separately. Special care was taken with removal of the main trigeminal nerve trunk, from its attachment at the pons to the peripheral branching of the mandibular and ophthalmic-maxillary nerves. Dura was gently teased away and all tissues were refrigerated overnight in the fixative with 10% sucrose added.

Serial coronal sections were taken from one each of the two sets of ganglia and the other two ganglia were sectioned horizontally on a freezing microtome. All tissue was collected in 0.1M phosphate buffer at pH 7.4, and then incubated for 15 minutes in Hanker-Yates reagent, H_2O_2, and 0.1M Tris-HCl at pH 7.6. Following three rinses in the buffer, the sections were mounted onto chrome-alum coated slides and air dried. Alternate sections were lightly counterstained with cresyl violet.

Regions of uptake were compared to those areas in the ganglion described by Gregg and Dixon (1973) as containing cell bodies for fibers innervating oral and perioral areas.

Post-mortem analyses were performed at two distinct postoperative periods to evaluate the possibility of regeneration and to verify the completeness and accuracy of the nerve sections. Six rats were perfused one week after surgery, while another six were perfused between weeks 4-16 postoperatively. Notes were made on the appearance of the original operative areas. In addition, twelve rats were examined after maximum behavioral recovery while being prepared for resectioning of regenerating nerves.

D. Condition of Oral Structures

Incisor length was measured at weekly intervals, from the midpoint of the incisor-gum junction, as well as the length filed of each incisor. After deafferentation, structural changes in the oral-perioral region were evaluated by trained raters. Rating scales were used for the tongue (1=normal, 2=mild abrasions, 3=severe abrasions, 4=tip bitten off), and for the palate and lower lip (1=normal, 2=mild abrasions, 3=severe abrasions).

E. Behavioral Procedures

1. Sensorimotor-reflex testing - Many of the measures used in the present study, for analyzing sensorimotor deficits in rats, were modelled on those described by Marshall and Teitelbaum (1974). Special attention was paid to oromotor responses. Two types of data were recorded: (1) the occurrence and coordination of biting, licking, and swallowing in response to stimuli which normally evoke such behaviors, and (2) responsiveness to proprioceptive, olfactory, auditory, visual, and extraoral tactile stimulation.

a. oral responses to stimulation - Deafferentation effects upon biting, licking, and swallowing were evaluated by four testing procedures, two of which involved responses to somatosensory and gustatory stimulation of the oral region, while two involved the elicitation of oral responses by noxious stimuli applied to other parts of the body. (1) While hand-held, chocolate Nutriment was placed on the tongue with an eyedropper and the occurrence of mouth opening, lapping movements, and swallowing was recorded in one trial. (2) While hand-held, the blunt end of a Q-Tip was gently placed inside the mouth between the tongue and palate in the right, left, and center positions. Three trials were run at each position and the occurrence of mouth opening, biting, or lapping was noted. This allowed for evaluation of the ability of intraoral tactile stimulation to elicit mouth opening and lapping reflexes, as opposed to Nutriment which also has gustatory properties. (3) Noxious stimulation of the paw and tail was used both to evaluate the rat's ability to respond to such stimulation in a directed fashion and to measure the probability of eliciting biting by extraoral stimuli. Each forepaw was mildly pinched with a large hemostat, three times in random sequence, and the occurrence of head turning towards the stimulus, mouth contact with the hemostat, mouth opening, and biting were recorded. (4) The biting sequence elicited by tail pinch was tested by mildly pinching the tail three separate times with a hemostat and noting whether head turning, mouth contact, mouth opening, or biting occurred, and whether it was directed at either the hemostat or a Q-Tip placed in front of the rat's snout. For the paw and tail pinch tests, qualitative observations were made on the latency to bite, bite force, and the strength of the pinch required to elicit the various components of the sequence. In addition, home cage observations were made on the rat's willingness to bite a Q-Tip rapidly presented to the snout area.

b. extraoral responses to stimulation - Limb use was evaluated by placing the rat in a small cage and turning it over on all six sides. The percentage of appropriate hanging and repositioning responses were noted for each side. A cotton swab soaked in ammonia was placed once to both the right and left of the animal's flank to check orientation to olfactory stimuli, in the home cage. The percentage of appropriate turning and sniffing responses were scored. Vibrissae functioning was also evaluated in the home cage by noting a turning response to displacement of the vibrissae with a Q-Tip, initially presented outside of the visual field. Three trials were randomly performed on each side. The occurrence of periodic whisking behavior was also frequently checked. The corneal reflex was tested by placing the tip of a fine paint brush onto the cornea of each eye and recording the occurrence of a blinking response. Qualitative observations were also made on the startle response to auditory stimuli (inhaled air through the experimenter's pursed lips), head turning to visual stimuli (red-balled eyedropper moved rapidly through the visual field), posture, gait, and the occurrence and coordination of grooming. Rats were also routinely lowered towards a table top while grasped around the midsection to evaluate the integrity of the visual and tactile placing responses. Arm extension and paw flexion were taken as indicative of normal orientation.

The above series of sensorimotor-reflex tests were administered at least twice preoperatively, and at least once per week postoperatively until recovery of preoperative performance was attained on all measures. The order of testing was as follows: extraoral responses to stimulation (those tests that required picking the rat up were done last), observations on the condition of the mouth, and oral responses to stimulation (paw and tail pinch were done last).

2. Food and water intake and body weight - Fresh food was presented daily in containers placed on the grid floor of the home cage. Solid foods were presented in 375ml heavy circular glass dishes (wt.=

358g, 10.5cm wide X 4cm high) with semi-liquid foods presented in 90ml plastic Petri dishes (wt.=10.5g, 9cm wide X 1.3cm high). Food was weighed to the nearest 0.5g with a Mettler balance. Weight of the food offered minus the weight retrieved 24 hours later determined intake. Appropriate evaporation constants were calculated and subtracted from the daily food intake records.

Fresh tap water was presented daily in Wahmann 100ml calibrated glass rat water bottles, with the metal sipper tube approximately 1½ inches above the cage floor, in a conspicuous, consistent location. Water intake was read directly from the meniscus line of the calibrated water bottle to the nearest 0.5ml. No attempt was made to control for spillage or evaporation.

After a minimum of seven days adaptation to the laboratory, intake and body weight were recorded for 10 consecutive days. Data were recorded daily (including weekends) between 9AM-2PM with each rat's data collected at approximately the same time every day. Body weight was measured to the nearest 0.5g on a Fisher Dial-O-Gram balance.

Preoperatively, one group of rats was offered an array of foods varying in texture, taste, and ease of oral manipulation. These diets allowed for study of the interaction between deafferentation effects and the sensory properties of the diet. The "_cafeteria diet_" included:

(1) _Mashes_: to provide foods which do not require grasping, gnawing, or biting two mashes were used which are of similar texture but different taste; Pablum (20 parts water + 10 parts Carnation Evaporated Milk + 6 parts Gerber or Beechnut Mixed Cereal For Babies, by weight) and Rat Chow Mash (20 parts water + 9 parts Purina Micro-Mix For Rats).

(2) Bite-size pellets: these consist of hard (Purina Cat Chow, liver) and soft (Purina Tender Vittles, liver) pellets which are approximately the same size, equally easy to manipulate, similar in taste, yet differ in their requirements for mastication.

(3) Purina rat chow pellets: while equivalent in taste and nutrient value to the rat chow mash, the standard rat laboratory diet makes the greatest demand on the rat's sensorimotor capacities since their ingestion requires a complex sequence of oral grasping, holding in the forepaws, shaving off small pieces with the incisors, mandibulation, and chewing. Rat chow pellets were always available ad-lib, but the amount of the special diets offered was maintained at a level which insured that a rat must ingest some standard rat chow pellets in order to gain or maintain body weight; 10g of dry cat chow, moist cat chow, and pablum were presented fresh daily, while 30g of rat chow mash was presented in addition to the above on alternate days.

In order to determine whether the restricted availability of "palatable" foods was responsible for the obtained intake and body weight functions, three additional groups of rats were offered, ad-lib, only one diet type: rat chow pellets, rat chow mash, or pablum. Intake and body weight were recorded in each of these three groups when either of these three diets was offered as the sole diet available. This "single-choice" condition provided data on deafferentation effects upon the "absolute palatability" of these three diets; as opposed to the cafeteria condition which was addressed to deafferentation effects upon the "relative palatability" of the diets. For the single-choice pablum group the diet mixture was slightly altered to give the animals some roughage and prevent diarrhea (20 parts water + 10 parts milk + 6 parts cereal + 1.25 parts Micro-Mix For Rats).

Postoperatively, food and water were made immediately available to all animals. Intake and body weight were recorded daily (including weekends) for at least 50 days, or until impending starvation required that rats be sacrificed. When body weight fell to below 65% of preoperative level, pablum and rat chow mash were offered in greater amounts; once body weight returned to 65% of normal the standard cafeteria regimen was reinstituted. Subjects in the cafeteria diet condition were offered these foods for at least 30 days and subsequently until rat chow pellet intake regained preoperative levels. At that point they were offered only rat chow pellets, ad-lib. Subjects in the single-choice condition were offered only that diet.

a. <u>interaction of food and water intake in "recovered" rats</u> - After having demonstrated the ability to maintain approximately normal daily intake on rat chow pellets (greater than 20g) and water (greater than 30ml) for at least one week, "recovered" trigeminal orosensory deafferented rats were subjected to up to three repetitions of the following: 24 hour food deprivation followed one week later by 24 hour water deprivation. The effects of food deprivation upon water intake (prandial drinking) and water deprivation upon food intake were recorded. These data were compared to data obtained from sham operates under identical conditions of deprivation, across the same range of body weight and predeprivation intake.

b. <u>control procedures used to analyze effects upon body weight regulation</u> - (1) To provide baseline data on the rate of body weight loss in the absence of food and water intake for comparison with aphagic and adipsic experimental rats, a control group was subjected to sham surgery and then food and water deprived for five days. (2) To clarify the relation between long-term body weight regulation and the amount and types of food ingested postoperatively in deafferented rats, a "yoked for food intake" control group was used. A group of normal rats were offered only those types and amounts of food eaten daily by the deafferented rat to which it was yoked. Water was made available ad-lib to the control rats. Yoking of the diets was continued until the return of measureable rat chow pellet intake, at which point the control animal was "unyoked", i.e. allowed ad-lib access to rat chow pellets. (3) To study the ability of "recovered" deafferented rats to defend their body weight, trigeminal rats were subjected to 24 hour food or water deprivation up to three times in succession, separated by a minimum of one week. The number of days required to regain pre-deprivation body weight was recorded and compared to data obtained from a group of sham operates subjected to identical deprivation conditions.

3. Observations of feeding and drinking behaviors - All animals were observed daily, in the home cage, for at least one minute after fresh food and water were presented. In addition, many hours were spent observing deafferented rats during the course of laboratory maintenance. Notes were made on the organization of consummatory responses to food and water, the order in which the various diets were consumed, and general activity related to ingestion.

4. Feeding efficiency - In the present study the efficiency of the consummatory response to food was measured only with respect to the ingestion of solid foods (rat chow pellets, dry cat chow, moist cat chow). The measures used reflect the efficiency of the consummatory response at two different points in the ingestive sequence: (1) after

the removal of the pellet from the large food dish, and (2) during the act of mandibulation - the process by which bits of food shaved from the pellet surface are moved from the front to the back of the mouth prior to swallowing. Reductions in feeding efficiency during the first stage would be reflected in a reduction in the ratio of food ingested to food removed from the dish (food intake/food removed). Disruptions in mandibulation would be reflected in an increase in the ratio of uningested crumbs to total food intake. Housing conditions were such that dropped food (pellets and crumbs) remained available to the animal so that repeated attempts at ingestion were possible.

5. Responsiveness to food - Responsiveness to solid foods was measured by the total amount of food removed from the large feeding dishes. Since equal amounts of solid food were made available pre- and postoperatively (30g rat chow pellets, 10g dry cat chow, 10g moist cat chow), ratios were not required.

6. Quinine aversion - In order to clarify the possible relation between deafferentation effects and taste sensitivity, responsiveness to a quinine solution was tested. The method of limits, as well as a tracking procedure, were used to determine pre- and postoperative thresholds for quinine hydrochloride aversion (QHCl, #Q-1125, Sigma Chemical Corp.). A two-bottle preference procedure was followed with the following logarithmically equidistant concentrations: .0005, .0001, .00005, .00002, .00001, .000005, and .000002M (see Ables and Benjamin, 1960, for rationale). The bitter solution was presented in one bottle and distilled water in the other, with side preferences controlled for by an ABBA design. Fresh solutions were provided daily. Animals were randomly assigned so that, preoperatively, some received an ascending

series of QHCl concentrations while others received a descending series, with the start point changed for the various animals. One concentration was available over two days, one day for each side; and the ascending or descending series was repeated twice, providing four days of relative intake at each concentration. Thresholds were then defined as lying at the midpoint between that concentration where the four day relative QHCl intake was less than 25% and that concentration where the discrimination was lost, greater than 25%.

Postoperatively, only one ascending or descending series was run in order to rapidly bracket the threshold. Once detection or nondetection of QHCl became statistically evident ($<$ or $>$ 25% relative intake), the direction of the series was reversed until non-detection or detection occurred, respectively; thus providing at least two threshold determinations over time. To summarize, the procedure considered the effects of surgery and postoperative day upon relative QHCl intake, which determined the subsequent QHCl concentration made available.

Four trigeminal rats were studied; however, postoperative aversion thresholds were not evaluated until that point in recovery where water intake was greater than 30ml for a one week period. One rat was not tested preoperatively.

F. Treatment Groups

The present results are based upon a variety of measures collected from 74 rats, divided into the following treatment groups:

1. Experimental - Four different types of trigeminal orosensory deafferentation were carried out:

a. bilateral complete orosensory deafferentation (V deaff.: complete), N=23.

b. bilateral complete orosensory deafferentation with the lingual nerves intact (V deaff.: _lingual intact_), N=19. This group was included to clarify the contribution of tongue somatosensory deafferentation to the deficits seen after complete trigeminal orosensory deafferentation.

c. bilateral anterior superior alveolar and inferior alveolar nerve sections (V deaff.: _alveolar only_), N=6. This group provided a preparation in which the deafferentation was largely limited to the rostral buccal cavity and lower lip line.

d. unilateral complete orosensory deafferentation (Uni V deaff.), N=3.

2. _Surgical controls_ - The following surgical control groups were prepared:

   a. sham surgery, N=8.
   b. bilateral infraorbital nerve sections, N=5.
   c. bilateral ethmoid nerve sections, N=2.
   d. teeth clipping, N=2.

3. _Behavioral controls_ -

   a. "yoked for food intake", N=8.
   b. five day total food and water deprivation, N=7.

All experimental and control groups provided data on daily food intake and body weight (cafeteria diet), while water intake, efficiency, and responsiveness were noted in all groups but only for those animals offered solid foods. Selected groups were evaluated under the remaining behavioral conditions as follows (for sample sizes see Results):

1. V deaff.: complete - single diet choice (rat chow pellets, rat chow mash, and pablum), body weight with yoked controls, 24 hour

food and water deprivation tests, sensorimotor-reflex testing, and quinine aversion.

2. V deaff.: lingual intact - same as in (1).
3. V deaff.: alveolar only - sensorimotor-reflex testing.
4. Infraorbital - sensorimotor-reflex testing.
5. Sham surgery - 24 hour food and water deprivation tests.

Five of the 15 behavioral control subjects served as experimental subjects after regaining their original body weights. Two completely deafferented, two sham operates, and two infraorbitals provided intake and body weight data while living in Wahmann activity wheels.

RESULTS

A. Neuroanatomical Data

The HRP data verified the projections of the sectioned trigeminal orosensory nerves upon the Gasserian ganglion. Figure 9 presents horizontal sections through the ventral area of the ganglion, illustrating the labeling produced after HRP treatment of the inferior alveolar and lingual nerves in one rat and the anterior superior alveolar and sphenopalatine nerves in another.

Insert Figure 9 Here

HRP uptake was extremely dense in the lateral portions of the ganglion following mandibular orosensory nerve treatment, encompassing the entire posterolateral extent, save for those ventral areas making up the trigeminal motor root. Retrograde transport of HRP following maxillary orosensory nerve treatment was more diffuse than after treatment of the mandibular branches, spanning the entire mediolateral extent of the rostral pole of the ganglion.

These data are in close agreement with the somatotopic organization of the ganglion as revealed by degeneration procedures following identical nerve sections (Gregg and Dixon, 1973). A composite schematic of their cell columns is presented in Figure 9 for comparison. The present mandibular cell body distribution extended into far lateral areas of the ganglion apparently not examined by Gregg and Dixon. Also, labeled cells in the medial region could represent sphenopalatine areas not studied by these authors.

Appendix A presents a series of coronal sections through the ganglion illustrating the labeling produced by HRP treatment of the mandibular and maxillary nerves.

Post-mortem analyses of perfused tissue carried out within the first postoperative week indicated that intended nerve sections were typically complete with little or no damage to adjacent neural tissue. Post-mortems carried out between weeks 4-16 revealed a fanning of regenerating tissue into areas occupied by muscle, blood vessels, bone, adjacent nerves, and the distal cut ends of the originally sectioned nerves. No distinction could be made between regenerating inferior alveolar vs. lingual nerves if both were cut initially at the same time. The anterior superior alveolar never showed signs of regeneration, while some regrowth was seen in the sphenopalatine and posterior superior alveolar regions. The functional significance of these morphological changes is presently unclear (but see p. 72).

B. Effects Upon the Condition of Oral Structures

Tables 1 and 2 describe the effects of deafferentation upon incisor length and the condition of the tongue, lower lip, and palate. Means are provided where more than one measurement or rating was taken.

Insert Tables 1 & 2 Here

The most obvious result of complete trigeminal orosensory deafferentation was a rapid deterioration of the condition of the mouth. Incisor overgrowth became obvious within the first postoperative day, accompanied by a shift in the resting position of the mandible to a more receded position. The incisors became brittle and discolored over the first few postoperative weeks, the uppers often separated by as much as 2mm, and one or more were observed to crack at the gum-incisor junction and fall out (though incisor loss typically didn't occur until the second postoperative month). With the exception of one case, the incisors always grew back, though often in an oblique position. While normal rat's incisors are very sharp and even, deafferented rat's incisors became blunt, thick at the base, and often uneven. Incisor length increased up to 4mm weekly, producing mild to severe abrasions in the rostral palate, lower lip, and tongue. To minimize these abnormalities, the incisors were filed weekly to remove from 2-6mm. The amount filed depended upon the extent and orientation of the deafferented rat's incisor bruxism, the resting position of the mandible, and the extent of the oral abrasions. Often normal incisor length was accompanied by extensive palate and lower lip abrasions, apparently due to misdirected gnawing, necessitating incisor filing to a shorter than normal length. The incisor condition of the deafferented rat never recovered completely in the six month maximum observation period, though after week four the amount of filing required was lessened. Maximum recovery was characterized by month-long periods where the incisors were kept at normal lengths, but the condition then deteriorated and filing was required.

Complete orosensory deafferentation invariably resulted in lesions of the anterior tip of the tongue. Tongue damage was quite variable in extent. Lesions ranged from mild abrasions with rapid recovery, to biting off the tip and extensive scarring which required up to two months to heal. Infections were never observed. Swelling of the tip of the tongue was common, though rarely to an extent that would hinder gnawing behaviors.

All completely deafferented rats exhibited some form of palate and lower lip abrasions, leading to minor scarring. The extent of the lesions was related to the length of the incisors. The four rats whose oral condition was systematically observed exhibited complete recovery from palate, lower lip, and tongue abrasions by the seventh postoperative week. However, infrequent episodes of incisor overgrowth in "recovered" rats resulted in mild palate and lower lip abrasions.

With decreasing magnitudes of bilateral deafferentation, more precise control of incisor length was exercised, though all three preparations sustained complete deafferentation of the incisors. Consequently, palate and lower lip abrasions were less severe and recovered more rapidly. Tongue abrasions were rarely seen in the "lingual intact" and "alveolar only" groups.

Though no quantitative data is available, unilateral orosensory deafferentation also resulted in incisor abnormalities. Clipping was rarely required (tri-weekly), though the incisors were consistently uneven, with the incisors on the deafferented side exhibiting the overgrowth. Tongue abrasions were never seen and palate and lower lip abrasions were rare. The infraorbital group exhibited only superficial and transient abrasions of the rhinarium and upper lip. The condition of the mouth appeared normal in the other surgical controls and in normal rats maintained for prolonged periods on semi-liquid food.

There does not appear to be any systematic relationship between damage to oral structures and food and water intake. Figure 10 presents these same subjective ratings on the extent of damage to the tongue, lower lip, and palate in four completely deafferented rats, as well as their solid food intake (rat chow pellets, dry cat chow), semi-liquid food intake (rat chow mash, pablum), and water intake.

Insert Figure 10 Here

Though the general shape of the two sets of functions look similar, closer examination indicates that neither of the morphological symptoms is a good predictor of intake, save for the similarity in the amount of tongue damage and water intake. Note that semi-liquid food intake recovers in a negatively accelerated fashion to preoperative levels by week five, while the condition of the mouth took seven weeks to recover completely. Second, solid food and water intake returned during week four, while the degree of morphological damage did not change significantly. Third, even with complete oral recovery, solid food and water intake remained below preoperative levels. Fourth, "lingual intact" rats exhibited no tongue damage, yet did not differ from "complete" rats with respect to the severity of the intake deficits.

Furthermore, two cases of naturally occurring incisor overgrowth were discovered, resulting from bite malocclusions. Though the incisors had grown deeply into the palate, rat chow pellet and water intake were not noticeably lower than normal rats. Table 3 provides a sample of their daily food and water intake, body weight, and feeding efficiency over a five day period. It should also be pointed out that teeth clipping did not seem to traumatize any of the experimental or control animals. Mashes were often ingested immediately after the teeth had been clipped.

Insert Table 3 Here

C. Effects Upon Sensorimotor-Reflex Function

1. Oral responses to stimulation - Deafferented rats, with

and without oral abrasions, exhibited an unquestionable ability to bite, lick, chew, and swallow; however, the probability of occurrence and the sequencing of these reflexes into coordinated response chains were altered by trigeminal orosensory deafferentation. The extent of these disruptions depended largely on the modality, locus, and intensity of the stimulus array.

a. intraoral stimuli - Normal rats periodically exhibit a highly stereotyped gnawing and grinding of the lower incisors against the back surface and tips of the upper incisors (bruxism). These behaviors are accompanied and identifiable by a chattering sound, periodic bulging of the eyes, and medial to lateral and rostral to caudal mandible movement. As a result of bruxism, incisor length is controlled within very fine limits. Deafferentation disrupted the frequency, topography, and orientation of bruxism in the following way: (1) The start point was shifted, in space, to a more caudal position as a result of the change in the resting position of the mandible. (2) Subjective observations suggest that the frequency of incisor bruxism decreased. (3) Overbites and malocclusions typified those instances where bruxism did occur, resulting in palate and lower lip abrasions. Thus, the orientation of the upper and lower incisors in gnawing behavior was disrupted by elimination of cutaneous sensations. The fact that abrasions appeared on the tongue, palate, and lower lip is clear evidence that tongue and jaw movements had occurred.

i. tactile - As shown in Table 4, tactile stimuli delivered to the oral region with a Q-Tip were no longer as effective elicitors of mouth opening, lapping, or biting in the completely deafferented and "lingual intact" groups, though clearly these responses were performed. No effect was observed in the "alveolar only" group nor in the infraorbital controls.

Insert Table 4 Here

---

ii. gustatory - No appreciable change in the frequency of mouth opening, lapping, and swallowing was seen in any of the subjects when chocolate-flavored Nutriment was placed on the tongue (Table 4). No deficits were observed in the capacity for maximum tongue extension or gape size. However, deafferented rats often exhibited misdirected and seemingly slower tongue movements.

b. extraoral stimuli - The degree of disruption in the biting and licking sequences increased as the stimulus moved away from intraoral regions, save for the tail pinch. Neither the components nor the sequencing of biting in response to noxious tail pinch stimulation were disrupted in either of the orosensory deafferentation groups (Table 4). However, the biting sequence to a paw pinch stimulus was disrupted in both the completely deafferented and "lingual intact" groups. The probability of head turning towards the stimulus did not change, while the probability of mouth contact, mouth opening, and biting decreased. Biting in response to a Q-Tip rapidly placed on the lip-line also decreased in all orosensory deafferented rats.

Such biting as did occur under any of these three circumstances often was sufficiently forceful to produce deep incisor indentations in the Q-Tip or the experimenter's finger. However, the latency to bite usually increased, bite force became more variable, the amount of force required in the tail or paw pinch was usually greater than necessary preoperatively, and rapid waning of biting on repeated presentation of noxious stimulation was observed.

The data in Table 4 suggests that recovery of the components of the biting sequence occurred in mouth contact first and biting last, through the sequence in which they naturally occur. The sequence became reorganized over time, exemplified by the many instances of head turning without mouth contact, mouth contact without mouth opening, and mouth opening without a bite.

2. Extraoral responses to stimulation and general motor abilities - Deafferented rats did not show gross postural impairments, muscular rigidity, tremor, flaccidity, or involuntary movements. Escape responses were brisk and rearing and climbing in a semi-novel cage were normal. Sniffing behavior and vibrissae whisking were often exhibited. Visually- and tactually-guided placing responses appeared normal, as did the head turn response to visual or auditory stimuli. The corneal reflex remained intact, as did appropriate use of the limbs (except for infrequent cases of poor adjustment to a suddenly inverted wiremesh cage, in the completely deafferented rat).

As shown in Table 5, completely deafferented and "lingual intact" animals showed deficits in orienting to an ammonia-soaked swab (possibly due to sphenopalatine and ethmoid nerve damage, which did not occur in the "alveolar only" procedure). These two groups also manifested a reduced probability of orienting toward a source of vibrissal displacement (possibly due to inadvertent damage to the infraorbital nerve, which was only slightly retracted in the "alveolar only" procedure).

Insert Table 5 Here

Infraorbital controls did not show deficits in oromotor responses but had difficulty orienting to vibrissal displacement and olfactory stimuli. Their most noticeable deficit was a postural one. They developed an extremely hunched posture, with their snouts pressed against the ground or cage wall whenever locomoting, and would frequently walk into the walls of the cage. This resulted in abrasions on the upper lip and rhinarium. The tactile placing response could not be elicited unless the lower lip or chin hairs made contact with the surface of the table top.

It is clear from all of the above observations that the elementary components of ingestive behavior (biting, chewing, licking, swallowing) are still intact in these rats. Trigeminal orosensory deafferentation, however, has disrupted somatosensory inputs which normally control the sequential organization of feeding and drinking.

D. Effects Upon the Organization of Consummatory Responses to Food and Water

Complete trigeminal orosensory deafferentation produced profound disruptions in the consummatory response sequences necessary for food and water intake. These disruptions paralleled the postoperative reductions in food and water intake. Therefore, for clarity's sake, observations of home cage ingestive behaviors in the completely deafferented rat will be separated into the four stages that best describe the reduction and gradual recovery of intake.

1. Stage I (adipsia + aphagia) - The approach to food was hesitant, though proper orientation of the mouth with respect to the food was achieved. However, the head was not lowered sufficiently for contact to be made with the food. Mouth opening and/or tongue extension did not occur as the snout hovered over the food. Vigorous sniffing and

occasional paw swiping through the food ensued, and the rat quickly left the food source. If the food was semi-liquid mash then the animal departed with food on the paws.

The approach to water in a sipper tube or dish was also hesitant. As with food, the initial orientation of the snout was normal, yet neither mouth opening or tongue extension occurred as the snout hovered over the water dish or circled the sipper tube and the approach sequence aborted just prior to contact. After a few seconds most deafferented rats grabbed the sipper tube with both paws, turned the snout 90°, and pushed the upper lip against the metal tube. Again, mouth opening or tongue extension failed to occur and the rat quickly left the water source. One animal was even observed, on his first postoperative experience with water, to walk up to the sipper tube, bite it, and quickly walk away.

2. Stage II (adipsia + solid food aphagia + semi-liquid food hypophagia) - The return of semi-liquid food intake was accompanied by development of alternative modes of feeding which included either shoveling the snout through the food or using the paws to scoop up mash, bringing it against the lower lip and incisors, where it was pushed through, eliciting very weak lapping movements and minimal mouth opening. It's important to note that all bilaterally deafferented rats used their paws to aid in ingestion. Some developed this "scooping" strategy. Most of the others retained the paw swiping sequence typical of the aphagic period, though here it seemed to develop operant characteristics different that that of the above-described "scoopers". Feeding by shoveling the snout through the smooth-surfaced mash required immersion of nearly the entire oral-perioral region. "Shovelers" spared themselves

this seemingly "unpleasant" bathing by first paw swiping, which provided either a rough edge to the mash or coated the sides of the dish, followed by oral shoveling through the heightened edges of the food or the sides of the dish. All of the above techniques served to facilitate intake without normal mouth opening and tongue extension. During this stage mash was always found all over the cage and animal, resulting in inflated food intake measures. Mash was also reliably found between the lips and gums as well. Occasionally, deafferented rats removed solid foods from the dish with their forepaws, but it was immediately dropped and left uneaten. Approaches to solid food and the water spout during this stage were too rare to make systematic observations.

3. Stage III (hypodipsia + solid food hypophagia + semi-liquid food hypophagia) - The recovery of solid food intake, and water intake, was marked by the return of extensive mouth opening and biting in response to food contact. It was also marked by the return of solid food removal from the dish via the incisors, where previously this had been accomplished with the paws. Removal often required repeated bites at the pellet, as it often fell out of the mouth. Occasionally the paws were used to aid in the carrying of food in the incisors. Many instances were observed where the rat hovered over a pellet making chewing movements and finally partial mouth openings before a wide enough gape was achieved to bite and carry the pellet. Consummatory responses to semi-liquid food remained as described in Stage II.

Drinking was eventually accomplished without the aid of normal tongue extension. Rats were often seen with the head and body in contorted positions, either rubbing their lower or upper lip against the sipper tube, which served to remove water from the bottle, or exhibiting weak and slow tongue extension. Most of the animals used their paws to guide the mouth to the sipper tube. There were many instances of licking and missing the sipper tube, while a few rats were observed biting and yanking the sipper tube, then turning their heads and letting the water trickle down their throat. Surprisingly, most rats managed quite efficient drinking with these techniques; rarely were excessive amounts of spilled water seen on the cage floor.

4. Stage IV (normal food + water intake) - Many bilaterally deafferented rats never recovered to this stage, even in the six month maximum observation period. Those that did so exhibited normal ingestive behaviors to solid and liquid foods and water, as determined by gross observations. However, no rat displayed normal consummatory behavior for extended periods of time (greater than six weeks). Biting abnormalities, manifested in incisor overgrowth, periodically produced relapses into Stage III consummatory behavior. Usually teeth clipping was followed by rapid recovery of normal ingestive behaviors.

All of the above stages were observed not only in completely deafferented rats but also in subjects with intact tongue somatosensation ("lingual intact"); nor did the two groups differ in the rate of recovery. (See section on food and water intake for mean durations of the above stages.) The "alveolar only" group did not display Stage I consummatory deficits; they went immediately into Stage II, followed soon thereafter by Stage III. At these various stages of recovery the "alveolar only" group did not appear to differ from the more severely deafferented groups with respect to consummatory behavior. The only difference was in rate of recovery through the various stages.

Importantly, the order in which these stages occurred was not necessarily ordered as above; e.g. adipsia often followed a period of hypodipsia; though the above-described sequence was the rule.

Control infraorbital nerve sections produced totally different effects upon the organization of consummatory responses. While the orally deafferented rat reliably immersed its lower lip in mash while feeding, the infraorbital rat always immersed the denervated upper lip and rhinarium. This made sustained feeding difficult because of respiratory impairment. Drinking postures were also assumed which facilitated lower lip or cheek contact with the sipper tube, while tongue movements seemed normal. Biting behaviors were unimpaired, as evidenced by the rapid recovery of solid food intake.

E. Effects Upon Feeding Efficiency

Figure 11 presents data for two measures of feeding efficiency reflecting different stages of the ingestive sequence: (1) the ratio of solid food ingested to solid food removed from the dish, and (2) the ratio of uneaten crumbs to solid food intake. Since subjects in all four surgical control groups showed only mild and relatively transient effects upon both of these measures, their data are not included. Experimental groups showed deficits proportional to the extent of the deafferentation.

Insert Figure 11 Here

Deafferentation reduced both the probability that food removed would be eaten and the probability that bits of food shaved off the pellet surface would be mandibulated and swallowed. Because, in most cases, the dropped food was accessible for continued attempts at ingestion, the efficiency ratios actually underestimate the actual deficits. Note that the bilaterally deafferented rats gradually exhibited complete recovery on measure A, but never on measure B.

F. Effects Upon Responsiveness to Solid Foods

Figure 12 indicates that responsiveness to solid foods, as measured by the amount of food removed from the dish, was drastically reduced following orosensory deafferentation. As with efficiency, experimental groups showed deficits proportional to the extent of the deafferentation. No such deficits were seen in any of the control groups. Recovery of responsiveness was gradual in all experimental groups and its time course depended on the severity of the deafferentation.

Insert Figure 12 Here

Since deafferented rats have demonstrated their ability to remove at least some solid food from the large food cups with their paws, the amount removed is a measure of responsiveness, relatively unconfounded by disruptions in the consummatory response. Furthermore, deafferented rats began ingesting solid foods within the first postoperative month, thus demonstrating the ability to bite and carry food. The "alveolar only" group is particularly useful in this regard because solid food intake returned in the first postoperative week, making intake a legitimate measure of responsiveness in these cases.

G. Effects Upon Food Intake

All orosensory deafferentation procedures were followed by a reduction in food intake whose magnitude and persistence was a function of the locus and extent of the denervation and the sensory properties of the available diets. Note that most of the intake data to be reported here underestimates the severity of the deficits produced by complete orosensory deafferentation since many animals had to be sacrificed prior to imminent starvation, within the first postoperative month.

1. Duration of aphagia - Figure 13 presents the mean number of days of aphagia (intake of one gram or less) for each of the five diet types when presently concurrently (cafeteria diet). The duration of aphagia was a joint function of the type of deafferentation and the diet type. Differences between groups were most evident with respect to solid food aphagia, in that neither of the deafferentation groups exhibited profound aphagia on pablum or rat chow mash. Aphagias were maximal following deafferentation of both the upper and lower mouth including the tongue, minimal when restricted to infraorbital denervation and sham surgery, and nonexistent following ethmoid nerve sections and teeth clipping.

Insert Figure 13 Here

2. Recovery of intake: time course and diet determinants -

a. cafeteria diet - As Figure 13 indicates, recovery of intake takes place gradually and involves an orderly progression through the diet types, from (1) soft tasty pablum and soft bland rat chow mash, to (2) moist bite-size liver-flavored cat chow, and finally to (3) dry bite-size liver-flavored cat chow and the large bland rat chow pellets. This progression was statistically reliable. When all three bilateral trigeminal orosensory groups were combined, rat chow mash and pablum were indistinguishable with respect to days of aphagia ($\underline{t}(21)=0.68$, $\underline{p} > .10$), rat chow mash intake recovered before moist cat chow ($\underline{t}(16)= 3.51$, $\underline{p} < .01$), moist cat chow recovered before dry cat chow ($\underline{t}(19)= 3.77$, $\underline{p} < .01$), and dry cat chow and rat chow pellets were indistinguishable (*t*(18)=1.49, $p > .10$). Neither of the surgical controls exhibited this characteristic progression through the diet types.

Table 6 also describes the order of recovery through the diet types.

Insert Table 6 Here

By analyzing individual animals and computing the number of rats that began ingesting which diets 1st, 2nd, 3rd, etc., it also became apparent that the mashes are ingested 1st and 2nd, moist cat chow 3rd, and the dry pellets 4th and 5th. Note that while dry cat chow and rat chow pellets did not statistically differ, 53% of the animals resumed eating dry cat chow fourth in the recovery sequence vs. 24% that ate rat chow pellets, while 59% ate rat chow pellets last vs. 18% that ate dry cat chow last. This trend may indicate that the size and taste of food are important in determining which diet is preferred when by the deafferented rat.

The speed of recovery of intake, within a given diet type, depended on the severity of the deafferentation (also see Figure 13). The following represent some of the more salient differences (*t*, $p < .05$): *rat chow pellets* (complete recovered last vs. alveolar, lingual intact vs. sham, alveolar vs. sham, unilateral vs. sham), *dry cat chow* (complete recovered last vs. alveolar, lingual intact vs. alveolar), *moist cat chow* (complete recovered last vs. lingual intact, lingual intact vs. sham, alveolar vs. sham). Also, none of the experimental groups differed from sham operates with respect to duration of aphagia on pablum or rat chow mash.

Deafferentation effects upon the "relative palatability" of these diets is illustrated in Figures 14 and 15, for representative "lingual intact" and "alveolar only" rats.

Insert Figures 14 and 15 Here

These composite figures demonstrate three additional points: (1) the relationship between the recovery of solid food intake and the recovery of water intake, (2) the lack of a significant effect of teeth clipping upon food and water intake in deafferented rats, and (3) the lack of compensatory overeating once all of the diets were readily consumed.

b. <u>single-choice diet</u> - The relation between diet type, food intake, and body weight in deafferented rats is seen even more clearly in a test situation in which only a single food is offered. Figure 16 presents these data. Since no differences were observed between the "complete" and "lingual intact" groups, their data were combined.

Insert Figure 16 Here

Faced with rat chow pellets as the only source of food, deafferented rats starved to death. Although other rats sustained themselves on pablum or rat chow mash, food intake dropped 25-75% and remained low for prolonged periods. Deafferentation effects upon the "absolute palatability" of pablum and rat chow mash differed only in that pablum intake returned to preoperative levels by day 40, while rat chow mash intake remained low indefinitely.

c. <u>intake analyses when diet conditions are combined</u> - Figure 17 combines the intake and body weight data obtained under all diet conditions for each experimental and control group. Only the solid food intake is plotted because many of the experimental rats in the cafeteria situation were supplemented with increased mash to insure survival, confounding the within and between group comparisons. Sample size differences within a given group for separate measures reflects the inclusion of body weight data from rats in the single-choice mash conditions and the fact that some rats did not provide water intake data.

Insert Figure 17 Here

Decreased solid food intake was observed in all orosensory deafferentation groups. These reductions were strikingly proportional to the magnitude of deafferentation, with unilaterals not differing significantly from surgical controls, and complete bilaterals showing prolonged aphagia, hypophagia, and gradual recovery of normal intake. Examination of the intake data from individual rats indicates that gradual recovery is a grouping artifact; recovery of solid food intake was abrupt within a given diet yet gradual between the different diets.

H. Effects Upon Water Intake

1. Duration of adipsia - Deafferented rats exhibited relatively short periods of adipsia, i.e. postoperative days to first water intake (greater than one milliliter). The shortest duration was seen in the unilateral group and the longest in the "complete" group; however, only the "complete" ($t(16)=2.08$, $p < .05$) and the "lingual intact" groups ($t(13)=1.86$, $p < .05$) differed from sham controls. In addition, none of the bilateral orosensory deafferented groups differed from each other.

Insert Table 7 Here

Deafferented rats also reliably exhibited subsequent periods of adipsia following the first instance of intake.

These data are also presented in Table 7. Statistically significant differences were found when the "days to first intake" and "total days of adipsia" measures were compared in the "complete" ($\underline{t}(8)=2.36$, $\underline{p} < .05$), "lingual intact" ($\underline{t}(6)=3.57$, $\underline{p} < .02$), and "alveolar only" groups ($\underline{t}(5)=2.24$, $\underline{p} < .05$). In other words, water intake waxed and waned until that point where preoperative levels of water intake were exhibited.

2. Recovery of intake: time course - As Figure 17 indicates, water intake eventually returned to preoperative levels in all groups: by day 50 in the "complete" group, by day 40 in the "lingual intact" group, by day 30 in the "alveolar only" group, and by day 10 in the unilaterals. The unilaterals did not differ from the surgical controls whose intake also required up to 10 days to regain preoperative levels. Grouping the data in Figure 17 masks the persistence of the adipsia and the rather abrupt recovery of water intake in the majority of the animals (see Figures 14 and 15 for representative data). However, it does point out the parallel nature of the water intake and solid food intake functions, and the prolonged periods of hypodipsia. These curves also suggest that complete recovery of water intake preceded complete recovery of solid food intake in all three bilateral orosensory groups.

I. Relationship Between Food Intake, Responsiveness, & Efficiency

Figure 18 describes these relationships in the "complete", "lingual intact", and "alveolar only" groups, while Table 8 shows how they are correlated. For all three experimental groups, responsiveness to solid food always predicted solid food intake, one or both efficiency measures always predicted intake, and one or both efficiency measures always predicted responsiveness.

Insert Figure 18 Here

Insert Table 8 Here

Not only were these three measures good predictors of each other, but the extent and persistence of the deficits were similar for each measure within a given experimental group, save for the mandibulation measure (efficiency B).

J. Effects Upon Body Weight

Figure 19 describes the mean maximum weight loss and the mean number of days where weight was maintained below ad-lib levels for all treatment groups offered the cafeteria diet. (Weight at surgery was defined as the ad-lib point.) Weight loss and subsequent retardation in weight gain was most severe in the "complete" group which lost, on the average, 35.6% of its weight (SE=3.6) and took 67.1 days to regain it (SE=16.7). No such weight loss was found in either of the control groups, though infraorbitals required nearly a month to regain lost weight (which was probably an artifact of their shallow preoperative rate of weight gain; see Figure 17). Again, the magnitude of the deficit was clearly related to the extent of the orosensory deafferentation.

Insert Figure 19 Here

The following represent salient statistical differences (*t*, $p < .05$) with respect to *maximum weight loss*: complete vs. alveolar, complete vs. unilateral, complete vs. sham, lingual intact vs. alveolar, lingual intact vs. unilateral, lingual intact vs. sham, alveolar vs. sham, and unilateral vs. sham. *Days to regain lost weight* also differentiated the following groups (*t*, $p < .05$): complete vs. alveolar, complete vs.

unilateral, complete vs. sham, lingual intact vs. alveolar, lingual intact vs. unilateral, lingual intact vs. sham, alveolar vs. unilateral, alveolar vs. sham, and unilateral vs. sham.

When pablum or rat chow mash were offered ad-lib (single-choice), weight losses were slightly less than that of animals maintained on the cafeteria diet (see Figure 16). Thus, severe weight losses in the cafeteria groups were not due to restricted availability of "palatable" foods. The single-choice pablum group did not differ from the single-choice rat chow mash group with respect to initial weight loss. However, they did exhibit differential recovery functions, with the pablum group displaying preoperative rates of weight gain after day 25. The rat chow mash group consistently maintained their weight at approximately 80% of ad-lib.

1. <u>Short-term effects</u> - Rats made aphagic and adipsic by trigeminal deafferentation lost weight at the same rate as normal rats, sham-operated and deprived of food and water for equivalent periods (Table 9).

Insert Table 9 Here

Another measure of the deafferented rat's ability to control weight over relatively short periods is seen in Table 10. Following 24 hr. food or water deprivation, "recovered" deafferented rats (preop intake for at least one week) regained lost weight as rapidly as normal rats after identical deprivation conditions. Since "lingual intact" and "complete" groups did not differ, their data were combined.

Insert Table 10 Here

2. <u>Long-term effects</u> - Once solid food intake resumed, weight

recovery was considerably retarded in the experimental groups. Even when rat chow pellets were being ingested in substantial amounts, food intake remained insufficient to permit the recovery of body weight to control levels. Indeed, when compared to "yoked for food intake" control rats given identical types and amounts of food over the same postoperative periods, deafferented rats appeared to regulate body weight at a lower level (Figure 20).

Insert Figure 20 Here

Body weight curves for four pairs of rats are presented to demonstrate two crucial points: (1) once rat chow pellet intake returned in the deafferented rat and the control rat was "unyoked", equal *initial* rates of weight gain were displayed in all pairs; and (2) deafferented rats ceased their rapid weight gain long before control animals did in three of the four pairs.

K. *Effects Upon the Interactions of Food and Water Intake and Body Weight*

In normal rats, food and water intake and body weight are interdependent and the ratios of nutrient intake to body weight, or food to water intake, are maintained constant over a wide range of deprivation conditions (Collier, 1969). Table 11 presents food to body weight, water to body weight, and water to food ratios for nine representative deafferented rats over a 10 day hypophagic period in which body weight had leveled off at sub-normal levels. Postoperative ratios are significantly below equivalent 10 day preoperative ratios (t, $p < .05$).

Insert Table 11 Here

Table 12 presents the same pre- vs. postoperative comparisons in four "yoked for food intake" control rats at similar hypophagic periods. Unlike deafferented rats, the W:F ratios remained constant even though the amount and type of food intake had changed, suggesting a genuine effect of deafferentation upon the amount of water consumed per food intake. However, control rats similarly showed decreases in F:BW and W:BW ratios. Though small sample sizes prohibited statistical analyses, all four controls decreased their F:BW ratios and three of the four controls decreased their W:BW ratios. Thus, control and deafferented rats did not maintain constant nutrient intake:BW ratios.

Insert Table 12 Here

These data suggest that the present experimental conditions (e.g. diet type, preoperative growth rate, etc.), rather than deafferentation, were responsible for producing reduced F:BW and W:BW ratios.

"Recovered" deafferented rats did not exhibit prandial drinking, as evidenced by normal levels of water intake during 24 hour food deprivation (Table 13). However, there was a significant decrease in solid food intake during 24 hour water deprivation when compared to sham-operated controls ($t(20)=2.29$, $p < .05$). Pre-deprivation differences were not significant. Both "complete" and "lingual intact" groups exhibited an effect upon food intake while water deprived, so their data were combined.

Insert Table 13 Here

L. Effects Upon Quinine Aversion

As Figure 21 indicates, detection of a QHCl solution was markedly impaired in both the completely deafferented and "lingual intact" groups.

Insert Figure 21 Here

While preoperative detection thresholds ranged between 2 X 10^{-6} and 2 X 10^{-5} M, postoperative thresholds rose to between 1 X 10^{-4} and 5 X 10^{-4} M for rat #'s 78-13, 78-15, and 78-17. These changes represent between one to two orders of magnitude increase in QHCl aversion thresholds, unattributable to lingual denervation. Rat # 78-44 did not exhibit a threshold change on the descending series, while tolerating much stronger concentrations on the subsequent ascending series. The above threshold changes probably underestimate the actual deficit produced in the immediate postoperative period since these measurements could not be obtained until water intake had recovered (days 42-72). Though one rat was not tested preoperatively, a postoperative impairment was indicated by comparison with the threshold range of these and other rats tested preoperatively (see Experiment 2 for additional data on normal aversion thresholds).

M. Effects of Trigeminal Deafferentation Carried Out In Several Stages

Three tactics were used in a preliminary study of the neural basis for recovery of function: (1) addition of the second stage to a previous unilateral orosensory deafferentation after variable periods of time and monitoring the speed of behavioral recovery; (2) resection of regenerating conections in rats showing maximum behavioral recovery from bilateral trigeminal orosensory deafferentation; and (3) sectioning originally unaltered nerves (infraorbital, gustatory) in another population of "recovered" trigeminal rats.

Three rats received the second stage trigeminal orosensory deafferentation at the following intervals post-stage I unilateral surgery: 14, 26, and 88 days. The first rat (14 days) exhibited all the characteristics of complete deafferentation; however, it recovered completely on day 17 which is uncharacteristically rapid for the bilateral preparation. The second also exhibited the entire syndrome to such an extent that he had to be sacrificed prematurely on day 20 post-stage II, thus not allowing for analysis of the time course of recovery of function. The third (88 days) exhibited no more than the characteristic unilateral deficits. Thus, the length of the interoperative interval seemed to determine the severity and persistence of the second operation.

Bilateral resection of all three maxillary orosensory nerves was accomplished in two "recovered" trigeminals, while bilateral resection of both mandibular orosensory nerves was done in three other "recovered" rats. Both procedures totally reinstated the entire syndrome of sensorimotor-reflex deficits (oral abrasions, incisor overgrowth, decreased probability and coordination in biting, etc.), yet food and water intake and efficiency were not as severely disrupted; rat chow pellet and water intake persisted, though at a reduced level. Thus, intake occurred even though maximum sensorimotor-reflex deficits were exhibited.

The addition of bilateral three-branch gustatory deafferentation in two "recovered" trigeminals produced no more than the 10-20% body weight loss typical of the gustatory syndrome (see Exp. 2 for details). However, adding infraorbital nerve sections to three "recovered" trigeminals reinstated the characteristic trigeminal orosensory syndrome: solid food aphagia and adipsia, decreased responsiveness to food, depressed oromotor reflexes, and feeding and drinking inefficiency. As you recall, infraorbital nerve sections, by themselves, produced only mild and transient effects upon ingestive behaviors.

DISCUSSION

Bilateral trigeminal orosensory deafferentation produces an array of behavioral and morphological changes whose magnitude varies with the number of orosensory nerves sectioned. This procedure: (1) affects the general condition of the mouth. Bite malocclusions, in combination with a reduction in the rat's typical gnawing behavior, result in incisor overgrowth and abrasions of the palate and lower lip. Moreover, lingual nerve sections are followed by damage to the tongue, ranging from minor abrasions to biting off the tip. (2) By removing an afferent limb of the mouth opening and tongue extension reflexes, deafferentation disrupts the sequential organization of consummatory behaviors (biting and licking), and subsequently reduces the efficiency of eating and drinking. The extent of these disruptions depends largely on the modality and locus of the stimulus presented. Deafferented rats, therefore, develop alternative modes of eating and drinking. (3) Correlated with decreased efficiency is a reduced responsiveness to food and water. (4) Deafferentation results in a profound reduction in food intake whose magnitude and persistence is a function of the texture, and possibly the size and taste, of the available diets; and (5) a similar reduction in water intake. Though the initial periods of adipsia are relatively brief, intake remains low for prolonged periods. (6) When semi-liquid foods are available, deafferented rats resume sufficient intake to regulate body weight at reduced levels. Control procedures suggest that chronically reduced body weight is a direct effect of decreased intake. (7) Normal food and water intake eventually returns, though the lack of compensatory overingestion deters rapid body weight gains. Finally, (8) the "recovered" deafferented rat exhibits impaired sensitivity to

QHCl solutions, reduced food intake while water deprived, and periodic relapses into earlier stages of recovery.

The following discussion will address some of the more obvious hypotheses which might account for the reduced intake produced by trigeminal deafferentation.

A. Changes in Oral Morphology

It must be stressed at the outset that the abrasions, incisor overgrowth, and subsequent teeth clipping do not contribute significantly to the intake deficits observed after trigeminal orosensory deafferentation. Several lines of evidence support this conclusion: (1) Naturally occurring malocclusions and subsequent incisor overgrowth and palate abrasions of comparable severity are sometimes found in otherwise normal rats; however, they are not accompanied by reduced food (rat chow pellets) or water intake. (2) Tongue abrasions do not occur when the lingual nerve is left intact, yet no significant differences in ingestive behavior were observed between this group and the completely deafferented group. (3) There is no apparent relationship between the condition of the mouth in deafferented rats and the severity of the ingestive behavior deficits; though it is true that morphological changes always accompany intake deficits. (4) No effects upon ingestive behavior were observed when a separate group of normal rats were subjected to frequent teeth clipping. (5) Feeding and drinking often recovered completely, while incisor abnormalities recovered only temporarily. (6) "Recovered" deafferented rats subjected to resectioning of either mandibular or maxillary branches exhibited all of the original abrasions and incisor problems typical of the completely deafferented rat, yet rat chow pellet and water intake were maintained, albeit at a reduced level.

All of the above leads me to believe that morphological changes cannot account for the disruptions in ingestive behavior seen after trigeminal orosensory deafferentation.

B. Aversive Sensations

Deafferentation could conceiveably be producing abnormal or painful sensations in the oral region which makes ingestion aversive in the immediate postoperative period, but which diminishes during recovery. This hypothesis is unlikely in view of the following: (1) Intraorally administered semi-liquid food elicits vigorous mouth opening, lapping, chewing, and swallowing movements. (2) Some diets are readily ingested during the immediate postoperative period while others are not. If ingestion was aversive, then one wouldn't expect intake to occur as readily in either of the above situations. (3) Teeth clipping in normal animals appears painful, is highly abnormal, and might make ingestion aversive, yet intake is unaffected. (4) The data on conditioned taste aversions (Rozin and Kalat, 1971) indicates that rats will begin ingesting foods which signal illness long before inanition is imminent. (5) Unilateral trigeminal deafferentation produces minimal deficits compared to those seen after adding the second side, though unilateral sections would clearly produce abnormal sensations. (6) Surgical and nerve section controls (sham, teeth clipping, infraorbital, ethmoid) did not exhibit the types and amounts of deficits seen after orosensory deafferentation, though they were also subjected to abnormal conditions, especially the infraorbital group which sustained a massive elimination of orientational information.

An additional set of observations could be taken to indicate that the feeding situation is aversive. During the approach to the food dish, and while engaging in feeding on semi-liquid foods, deafferented rats often exhibit paw flailing, paw pushing (wiping the forepaws of the cage floor), head shaking, and/or teeth chattering. Miller (1980, personal communication) has independently confirmed these observations, noting their similarities to the behaviors which appear in normal rats in response to intraorally-delivered quinine (Grill and Norgren, 1978). These behaviors could represent the response to an aversive stimulus, or a set of behavioral adjustments to alterations in the rat's own stimulus inputs and sensorimotor capacities. I prefer the latter interpretation in light of the following: (1) High-speed cinematography has shown that normal rats grind their incisors or chew while approaching food (Jacquin and Zeigler, in preparation); observations of teeth chattering could therefore reflect the slowing down of a normal response pattern because of inappropriate sensory feedback, thereby becoming noticeable to the naked eye and ear. (2) Deafferented rats lack the normal reflex controls for mouth opening and tongue extension, resulting in their passing the snout over the food without actually making contact. In a sense, the food has disappeared. Deafferented rats adjust to their "tactual blindness" by groping for the food with their forepaws in a paw pushing fashion. Food becomes pasted all over the animal's forepaws and could conceiveably constitute an aversive state to the animal. Paw pushing on the cage floor or rubbing the paws against the mouth then serves to remove the irritant stimulus. Thus, paw pushing could represent a grooming sequence. (3) Those rats that have groomed their mash-covered paws suddenly develop a new food-reinforced operant chain. Paw pushing through the food, followed by grooming, is an effective way to get food into the mouth when normal reflex controls are ineffective. Those rats that fail to develop this "scooping" strategy soon learn that paw pushing through the food provides a heightened edge which spares them having to immerse the entire perioral region into the mash while feeding. Either way, mash ends up on the rat's snout and paws. Paw flailing and head shaking then represent a way to lessen this irritable condition. (4) Rats sustaining trigeminal motor root sections (Jacquin, in preparation) exhibit all of the above-described abnormal behaviors (except teeth chattering), yet remain highly responsive to food, as measured by time spent trying to feed. Thus, these awkward behaviors are not sufficient to force the animal out of the feeding situation.

I conclude that these behaviors reflect indirect consequences of orosensory deafferentation which serve to maximize feeding efficiency and body hygiene, rather than reflect an aversion to feeding.

C. Orosensorimotor Deficits and the Disruption of Consummatory Responses

The deafferented rat is clearly capable of biting, chewing, licking, and swallowing in response to intraoral gustatory and tactile stimuli, such as liquid food, water, a Q-Tip, or an intragastric feeding tube. These observations confirm previous reports by Miller (1977, 1978b). Biting can also be elicited by tail pinch or paw pinch stimulation, and bites made under these conditions can have considerable force (our many punctured fingers can attest to this). However, in contrast to the relative ease with which licking and biting can be elicited by *intra*oral stimuli, it is extremely difficult to elicit these responses using the *peri*oral stimuli which normally elicit them. Tactile stimulation of deafferented rat's perioral areas (e.g. lip line, vibrissae) with food, water, or a Q-Tip elicits few attempts to bite or lick and such bites as are emitted are often disoriented and lacking in vigor.

Observations of the consummatory responses made by deafferented rats to rat chow pellets, pablum, and water indicate that during the aphagic-adipsic period the organization of feeding and drinking response sequences has been seriously disrupted. Although the initial response to the pellet is normal and the snout may be appropriately oriented to it, the rat's mouth fails to open and the sequence is aborted without biting taking place. A deafferented rat will approach the water tube and properly orient its snout, but the mouth fails to open and the tongue does not extrude, and the drinking sequence is aborted. The same deficits are evident in deafferented rats given semi-liquid mashes, so that although they pass their snout across the surface of the mash, they fail to make tongue contact.

During recovery many animals make postural adjustments to the sipper tube which, although contorted, facilitate the ingestion of water by bringing the tube into contact with those areas sustaining somatosensory innervation. Similarly, many deafferented rats develop alternative idiosyncratic response patterns to food, including using the paws to scoop up small amounts of mash or shoveling the mouth through the mash. Kittens which have sustained section of the trigeminal sensory root show similar behaviors (Kerr, 1975).

The final stage of recovery is characterized by normal intake, though deficits in masticatory behavior persist, as evidenced by increased ratios of chewed crumbs to total food intake and periodic incisor overgrowth. The former represents a deficit in mandibulation, thus implicating orosensation in the coordinated spatiotemporal organization of the lips, jaw, and tongue in the placement and continual repositioning of a food bolus during mastication.

It is clear from all of the observations that while the elementary components of ingestive behavior are still intact, trigeminal orosensory deafferentation disrupts somatosensory inputs which normally control the sequential organization of eating and drinking reflexes. As such, this represents a fundamental explanation for reduced intake; a necessary component of the feeding and drinking sequences has been eliminated, oral tactile stimulation.

It's important to emphasize at this point that we are, in fact, dealing with a "sensory" rather than a "motor" deficit. This is clear from two additional lines of evidence. First, the trigeminal sections spare all efferents to the muscles of mastication or the tongue (a conclusion supported by HRP studies of the central projections of the sectioned nerves). Second, bilateral sections of the trigeminal motor root and/or the hypoglossal nerve produces very different preparations (Jacquin and Zeigler, 1978, 1979). After trigeminal motor root section the mandible becomes fixed in the resting almost-closed position, reflecting elasticity in the jaw closing musculature and connective tissue in the cheek region (Weijs and Dantuma, 1975). Reduced food and water intake is a result of a "motor" deficit, since the animal is incapable of mouth opening or tongue extension (although tongue movements within the mouth occur). After hypoglossal nerve sections, the tongue becomes fixed in its resting position directly behind the lower incisors, while jaw movement is unimpaired. Reduced intake also reflects a "motor" deficit, since food or water cannot be moved from the front to the back of the mouth.

All of the observations on the effects of "sensory" nerve sections upon motor output patterns are in accord with the wealth of data on the role of oral afferents in oromotor reflexes. Sherrington (1917) first described the jaw opening reflex as part of a total reflex pattern evoked by a cutaneous oral stimulus. Recent workers have demonstrated reflex activity in jaw opener muscles (digastric) upon stimulation of intraoral sites in the cat (periodontium and tooth pulp, Sessle and Greenwood, 1976b; Sessle, 1977b; tooth and palate, Thexton, 1973), as well as summation of the reflex response with simultaneous stimulation of multiple oral receptors. The latter may explain the graded effects upon biting reflexes with varying magnitudes of trigeminal deafferentation. The jaw opening reflex can also be elicited by electrical stimulation of nerves carrying gustatory information (glossopharyngeal and superior laryngeal) and from the temperomandibular joint and the hypoglossal nerve (Greenwood and Sessle, 1976b; Schwaluk, 1971; Lindquist and Martensson, 1969). The former may explain the ability to elicit mouth opening in deafferented rats using gustatory stimulation. Stimulation of these intact nerves may also mediate the deafferented rat's mouth opening response to intraoral tactile stimulation.

That extraoral stimuli failed to elicit reliable mouth opening is in accord with work by MacDonnell and Flynn (1966). They showed that tactually-elicited mouth opening in cats was disrupted by inferior alveolar and infraorbital nerve sections. Their observations confirmed that the disruption was mediated by removal of the afferent limb of lower lip and muzzle cutaneous receptive fields necessary for biting attack. In addition, Kidokoro, et al. (1968) reported that the jaw opening reflex recorded in the digastric nerve could be elicited by inferior alveolar stimulation at strengths that are only slightly above the nerve's threshold. Thus, inferior alveolar nerve sections would be expected to produce disruptions in extraorally elicited reflexes. This was indeed the case in the present work.

Impairments in tongue extension and tongue coordination are also explicable in a reflex framework. Since the tongue operates no joints and probably contains no muscle spindles (Cooper, 1953), cutaneous mechanoreceptors may be the major source for identifying tongue position (Yokota, et al., 1974). In fact, Kawamura (1964) has found the hypoglossal nucleus to display either activation or depression upon stimulation of oral fields. Changes in the contraction of tongue muscles, EEG alterations, and responses in the hypoglossal nerve occur with touch, deformation, or any stimulus that produces afferent input in the nerves from the tongue. It's been shown that a major source of activation of tongue extensor motoneurons comes from stimuli coincident with mouth opening. Lowe and Sessle (1973) and Lowe (1976) have demonstrated a strong control over tongue extension by temperomandibular joint receptors. These movements can be recorded by opening the jaw as little as four millimeters. Masseter nerve stimulation has been shown to elicit tongue extension (Sumino and Nakamura, 1974), and not via the trigeminal mesencephalic-hypoglossal nucleus pathway, since mesencephalic lesions do not alter the synaptic potentials recorded from hypoglossal motoneurons. Finally, Blom (1960) found that reflex tongue activity is abolished by bilateral anesthesia of the mandibular nerves. The above findings, therefore, provide an explanation for the observed effects of trigeminal orosensory deafferentation upon tongue extension, even when the lingual nerves are spared. Apparently, jaw movement-produced feedback exerts powerful control over tongue movement.

In addition, peripheral stimuli, such as a food bolus, have been shown to be able to sum with the central masticatory pattern generator, even in the paralyzed animal (Lund and Dellow, 1973); e.g. stimulation of the teeth can interrupt chewing. In addition, a low intensity stimulus to the lingual nerve can facilitate cortically-induced rhythmic tongue movements (Morimoto and Kawamura, 1973). These findings implicate tactile stimuli in the control of mandibulation. It's of interest, therefore, that the hypothesized site of the masticatory pattern generator (pontine reticular formation) receives a massive orofacial afferent input and projections from many forebrain areas previously shown to play a role in gnawing behavior; e.g. limbic areas, motor cortex, basal ganglia (Dellow and Lund, 1971; Berntson and Hughes, 1974).

I have since further investigated the nature of the consummatory deficit in deafferented rats using close range, high speed, videotape recording (Jacquin and Zeigler, in preparation). These data confirm the original observations that lower lip and chin hair denervation results in an aborted consummatory response; the mouth does not open and the tongue is not extended. Rarely, however, did the deafferented rat get so far as to make oral contact with the food pellet or sipper tube. Usually the approach ceased long before contact and persistent chewing movements ensued. In observing these films one gets the impression that the rat is "stuck" in a phase prior to food or water contact. Does this mean that deafferentation has also affected the rat's responsiveness to food and/or water?

D. Feeding Inefficiency vs. Decreased Responsiveness to Food

By examining changes in the species-typical response chain, it is possible to experimentally dissociate deafferentation effects upon intake attributable to a decrease in the efficiency of the consummatory responses or to a reduction in the frequency or persistence of the rat's response to food. (Whether the neural mechanisms responsible for guiding the consummatory response to completion vs. responsiveness to food are separable is another matter; see General Discussion.) In such an attempt at dissociating causes for reduced intake, one must carefully consider just what is being measured.

The species-typical response of a rat to solid food in a container is to first remove it with the incisors and then carry it to a corner where he begins shaving off small pieces. The ingestive sequence could conceiveably abort prior to food contact, after contact but before removal from the dish, after removal but before actually shaving pieces off the pellet, or after shaving but before mandibulation. Any of these disruptions could reflect either a decline in responsiveness or reduced efficiency or both. In the present experiment the following was measured: (1) the probability of removing food from the dish, (2) the probability of intake once food was removed, and (3) the probability of intake once shavings were gnawed off the pellet surface. Deafferentation produced deficits in all three measures.

I interpret decreased food removal as a responsiveness deficit, simply because removal of food from a glass dish can involve the use of the rat's paws, a response chain unconfounded by disruption of the efficiency of the oral apparatus. Support for this interpretation comes from recent observations on the effects of trigeminal motor root section in the rat (Jacquin, in preparation). Such a preparation literally cannot open its mouth, yet food is removed with the paws in large amounts.

On the contrary, I interpret decreased intake/food removed as an efficiency deficit since the lack of intake can only mean that the jaw apparatus did not function properly. This interpretation is again supported by trigeminal "motor" rats that remove food, leave it uneaten, and can only be characterized as inefficient eaters. It is possible for a hoarding animal to be inaccurately depicted as inefficient, though hoarding is always accompanied by intake and the animal would therefore appear relatively efficient.

Similarly, I interpret an increase in uneaten chewed crumbs/intake as indicative of an efficiency problem, namely a mandibulation deficit, since the lack of intake can only mean that the tongue did not function properly. Support for this interpretation comes from rats subjected to hypoglossal motor nerve sections (Jacquin, in preparation). Such a preparation cannot move its tongue and large amounts of crumbs are left uneaten, indicative of a mandibulation deficit.

The consequences of such severe deficits in feeding efficiency may be sufficient to account for the reduced intake of the deafferented rat. As such, the following hypotheses may be advanced in constituting a general "consummatory deficit hypothesis".

1. Extinction hypothesis - By reducing the efficiency of the consummatory response, deafferentation could be abolishing the primary reinforcement normally provided by food intake, leading to extinction of feeding behavior. This hypothesis is incompatible with the following data: (1) Responsiveness to food is lowest immediately following deaf-

ferentation. If an extinction schedule was operating then one would have expected the food to be strewn all over the cage with little or no ingestion, followed by waning of responsiveness, which clearly did not occur with either solid or semi-liquid food. In recovery, increased efficiency and subsequent intake would have caused an abrupt reversal in the amount of food removed, which also did not occur. However, if decreased responsiveness was a causal factor for reduced intake, then absence of intake would be paralleled by a significant reduction in the amount of food removed during the aphagic period, followed by a gradual increase in the amount removed. This is exactly what happened, making decreased responsiveness the viable explanation, not extinction. (2) Intake and body weight remain below control levels despite gradual improvement in feeding efficiency. (3) Intake of semi-liquid foods does not drop out completely as would be expected if extinction was operating; instead, deafferented rats offered ad-lib "ingestable" foods (mashes) exhibit prolonged hypophagia. I assume that subnormal mash intake is indicative of decreased responsiveness, since ingestion of some should indicate an ability to ingest more. (4) Partially deafferented rats ("alveolar only") begin ingesting substantial amounts of solid food within the first postoperative week, yet responsiveness remains low. (5) "Alveolar only" subjects exhibit only a minor efficiency deficit (intake/removed), yet show major deficits in food intake.

All of the above suggests that extinction is not operating following deafferentation, and that the most severe consequence of feeding inefficiency, lack of intake, is not sufficient to explain the observed changes in ingestive behavior. However, deficits in efficiency, responsiveness, and intake are usually correlated, suggesting that they are mediated by similar mechanisms, namely trigeminal orosensory stimuli.

Additional experiments have been carried out to clarify the extent to which the reduced intake seen after trigeminal orosensory deafferentation reflects a disruption of orosensorimotor mechanisms, "motivational" processes, or some complex combination of both. With respect to the "extinction hypothesis", I have subsequently compared the effects of deafferentation to four groups of control rats, each subjected to a different extinction situation: (1) Trigeminal deafferented rats spent far less time feeding, or trying to feed, than sham operates whose access to each of the available diets was prevented via a wire mesh cover over the top of the dish. Videotaped observations indicate that deafferented rats initiate fewer meals and decrease meal size when compared to "extinction controls" (Jacquin, Olazabal, and Zeigler, in preparation). Moreover, deafferented rats exhibited decreased feeding time equally across the entire day, unlike what one would have expected if extinction was operating. (2) Deafferented rats spent far less time feeding, or trying to feed, and removed far less food from a dish, than "extinction control" rats subjected to bilateral trigeminal motor root sections, or (3) bilateral hypoglossal nerve sections. Thus, rats that can't eat remain highly responsive to food. Maximum feeding inefficiency is therefore not sufficient to deter responsiveness to food (Jacquin, in preparation). (4) Deafferented rats pressed a lever and magazine approached significantly less often on a daily VI60" schedule of mash reinforcement than sham operates on an extinction schedule. Decreased efficiency is therefore not sufficient to account for impaired food-reinforced operant behavior (Jacquin, 1978). In addition, despite the fact that they were being tested at 65-85% of their ad-lib weight, deafferented rats frequently spent a large part of each test session asleep in the operant chamber, something never seen in "extinction controls".

Using a tunnel feeding apparatus equipped with a photocell entrance detector, Miller (1978b) reports that deafferentation reduces the approach frequency to food pellets. She also concludes that the rat's "propensity" to eat has been affected, in combination with impaired consummatory behavior.

2. Hypothesis: deafferentation increases the effort required for ingestion and thereby reduces the reinforcing properties of food - This hypothesis takes into account the fact that deafferented rats do ingest, yet the effort required to ingest significantly decreases the probability of feeding, i.e. reduces the reinforcing properties of food. For example, Collier, et al. (1972) report that cats will work only so hard before intake and body weight start to decline, though this point wasn't reached until thousands of daily lever presses were required for access to a single meal. In a sense, this hypothesis is inconceiveable in view of the fact that control rats placed on extinction spend more time trying to feed than deafferented rats that are ingesting some food. One could argue, however, that the consequences of increased effort for little reward are sufficient to inhibit feeding even further than that which would follow extinction. This hypothesis is, at present, irrefutable, though one recent operant experiment provides data bearing on this question (Jacquin, 1978). A group of deafferented rats that did manage to ingest a measureable quantity of food during lever pressing sessions were compared to a sham operate control group matched for intake and effort. Postoperatively, control rats were required to extend their tongues through the food magazine apperture to obtain mash reinforcement

on an identical schedule to that of deafferented rats. The extent of tongue extension required was predetermined in order to reduce intake to the level of a matched deafferented rat, subsequently increasing the effort required to obtain less food. Control rats receiving less food for greater effort lever pressed and magazine approached at a significantly higher rate than deafferented rats matched for intake. Interestingly, deafferented rats did not differ from the "extinction control" group with respect to either behavioral measure; i.e. deafferented rats that did ingest reinforcement behaved like normal animals on extinction.

The "effort hypothesis" is therefore unsupported, since both ingesting deafferented subjects and "increased effort + decreased intake" control subjects worked harder than non-ingesting deafferented and "extinction control" rats. These data do suggest the possibility that ingested food is no longer reinforcing to the deafferented rat, in that ingesting deafferented rats behaved as if they were on an extinction schedule. I cannot agree with this hypothesis, given the fact that ingesting deafferented rats exhibited higher rates of operant behavior than the non-ingesting rats.

These observations do suggest that trigeminal deafferentation reduces the <u>effectiveness</u> of food reinforcers in maintaining operant behavior. One could argue that decreased intake of "ingestable" foods (mashes), in the home cage, is due to the reduced effectiveness of food as a reinforcer. Thus, cutaneous orosensation accompanying food in the mouth appears to be a critical component of the stimulus array constituting food reinforcement in the rat.

3. <u>Hypothesis</u>: <u>deafferentation necessitates the development of an alternative ingestive sequence which could reduce food intake</u> -

Since the normal reflex controls of ingestion are rendered ineffective by deafferentation, rats are forced to develop alternative feeding strategies. Having to relearn how to feed may be sufficient cause for reduced intake. To test this hypothesis I pretrained a group of rats to obtain food via the response modality chosen by most deafferented rats - reaching one paw into a food magazine and "scooping" out mash (Jacquin and Zeigler, 1979). Since pretraining eliminates their having to stumble upon "scooping" as a successful response, this hypothesis would predict that the effects of deafferentation would be lessened or eliminated.

The results of this study do not support this hypothesis. Following complete trigeminal orosensory deafferentation "scoopers" exhibited periods of aphagia and hypophagia comparable to that described earlier. In addition, "scoopers" provided data on meal patterns, elucidating some additional mechanisms responsible for reduced intake. During the immediate postoperative period reduced intake was mediated by a striking decline in the frequency and duration of feeding bouts. The return of substantial intake was attributable to extraordinary increases in meal duration, while meal frequency remained low. Pretrained "scoopers", however, persisted in their consummatory inefficiency yet these impairments cannot account for the persistent reduction in meal frequency nor the increase in meal duration since rats with hypoglossal nerve sections were much more inefficient yet sustained normal meal patterns.

For our present purposes, the significance of these findings lies in the clarification of some of the behavioral mechanisms mediating reduced food intake in deafferented rats, as well as the relation between sensorimotor and motivational deficits following deafferentation.

Trigeminal sections produced both types of deficit, but the reduced intake did not simply reflect a disruption in the sensorimotor control of feeding. Moreover, decreased meal frequency and increased meal duration were evident even in"alveolar only" subjects who showed no change in feeding efficiency. Thus, the reduced responsiveness of trigeminal rats was evident even when the response measure used involved the forelimb rather than the mouth and even when pretraining eliminated the necessity of having to develop a new response modality. In contrast, hypoglossal rats with profound disruptions in oromotor control, remained highly responsive to food. These data suggest that trigeminal inputs make a major contribution to the motivational control of feeding, i.e. to the initiation and termination of the meal.

E. Impaired Sensitivity to Taste Stimuli

Surprisingly, trigeminal orosensory deafferentation resulted in increased QHCl aversion thresholds. It is conceiveable that these sensitivity changes represent some fault in our psychophysical detection procedure (Frank, 1978, personal communication), since an animal so orally disoriented may not attend to such subtle gustatory cues. Additional signal detection experiments would be required to test this hypothesis, with reinforcement contingent upon quinine detection.

By whatever mechanism, the deafferented rat does not respond normally to this gustatory stimulus and this could represent a general decreased sensitivity to all gustatory stimuli. Since gustation has been shown to be a potent determinant of food intake (see General Introduction), such a disruption could account for the reduced intake in the deafferented rat. Experiment 2 is, in part, an attempt at answering this question.

With respect to the elevated QHCl aversion thresholds, Sessions, Miller, and Zoellner (in preparation) demonstrated that trigeminal mandibular orosensory nerve sections did not affect preference-aversion thresholds for saccharin or quinine. By contrast, the present study has shown that combined mandibular and maxillary nerve sections increases QHCl aversion thresholds. This finding is explicable by recent anatomical studies (I. Miller, 1977; 1979, personal communication) demonstrating a significant innervation of naso-incisor duct and possibly soft palate taste buds by greater superficial petrossal fibers (VII) passing through the floor of the orbit, namely the sphenopalatine ganglion. Though they represent only a small percentage of the oropharyngeal complement of taste buds (less than 10%), human work suggests that these taste buds are best-responsive to quinine (Collings, 1974; Henkin and Christianson, 1967a,b). Damage to the sphenopalatine ganglion was likely in the maxillary deafferentation procedure used in the present study, thus resulting in denervation of possibly quinine-best fibers.

Since a systematic evaluation of the effects upon sour, salt, and sweet sensitivity was not carried out, little can be said concerning the role of palatine taste bud denervation in the deficits in ingestive behavior reported here. Further work is required to determine the effects of petrossal nerve sections upon preference-aversion behavior and intake control. However, one could speculate that decreased sensitivity to the bitter properties of food would lessen the potentially aversive properties of some foods and subsequently result in exaggerated food intake. Clearly this did not occur following deafferentation.

F. Heightened Sensitivity to the Textural Properties of Food

The present experiments, and those of Miller (1977, 1978b), suggest that the effects of trigeminal deafferentation upon food intake are a joint function of the extent of the deafferentation and the sensory properties of the diet. The most severe deficits are seen when deafferented rats have access to only rat chow pellets. The mildest deficits are seen when they are offered only semi-liquid mashes.

When the relationships between diet, intake, and body weight are explored more systematically, it is clear that the duration of aphagia, the initial postoperative weight loss, and the subsequent level of body weight regulation are directly related to diet texture, and possibly size and/or taste. Therefore, a reasonable hypothesis is that the severity of the reduced food intake reflects a continuum of disability. The absence of solid food intake may reflect an inability to orally manipulate these foods, given the absence of appropriate mouth opening reflexes. The reduced frequency and persistence of ingestive behavior (trying to eat) can only reflect a reduced responsiveness to food. I would contend, though, that once a strategy has been worked out for achieving intake, the subsequently reduced level of food intake reflects decreased responsiveness rather than inability.

Historically, the elicitation of intake by various foods has been labeled its "palatability". Lesion effects upon the palatability of different diets have received a great deal of attention (e.g. Teitelbaum and Epstein, 1962; Teitelbaum, 1955). Preliminary results from our laboratory suggest that the intake of normal rats progresses through a texture, taste, and size gradient when evaluated over a 24 hour period (Jacquin, Olazabal, and Zeigler, in preparation). Thus, deafferented rats are just not accepting solid foods that normal rats would have left for the latter part of the day; i.e. the "relative palatability" of the diets had not changed with deafferentation. However, the effects upon "absolute palatability" are striking. While normal rats exhibited no absolute preference when presented either of these diets ad-lib, deafferented rats "do or die" depending on the textural properties of the sole diet available. But does it make sense to talk about palatability when lack of intake may simply reflect an inability to eat? The historical emphasis placed upon taste in determining palatability may have clouded our conceptions about what constitutes palatability. The present results suggest that the somatosensory properties of food may be equally or more important in determining intake, and that previous reports of lesion effects upon palatability may similarly reflect a continuum of oromotor disability.

G. Is Reduced Water Intake An Indirect Effect?

Trigeminal orosensory deafferentation also produces a severe disruption in drinking behavior. However, effects upon water intake are more difficult to interpret because deafferentation also produces drastic changes in quantitative and qualitative aspects of food intake, as well as severe orosensorimotor impairment and its consequences.

1. *Hypothesis: altered food intake might cause reduced water intake* - Since water and food intake are interdependent (Bolles, 1961; Kutscher, 1969; Collier, 1969), the failure of the deafferented rat to eat dry foods and its dependence upon the other special diets makes it difficult to distinguish those effects upon water intake which are a direct result of deafferentation and those which are an indirect consequence of changes in the amount and types of food consumed. Three lines of evidence mitigate against the latter interpretation: (1) Normal rats totally food deprived for prolonged periods drink substantial amounts of

water (Collier, 1969), as opposed to the adipsia-severe hypodipsia found in the first week following trigeminal deafferentation. (2) "Yoked for food intake" controls, given identical types and amounts of food as trigeminal rats for equivalent postoperative periods drink significantly more water than their trigeminal partners (Jacquin and Zeigler, 1978). The differences between the two groups persisted until the point at which trigeminal rats began ingesting solid foods, suggesting that water intake does recover completely. (3) During the stable hypophagic-hypodipsic period, the water to food ratios are lower than preoperatively, something not seen in "yoked for food intake" control rats at equivalent periods.

2. Hypothesis: orosensorimotor impairment produces extinction of drinking - As in feeding, the consequences of drinking inefficiency, namely lack of reinforcement, may be sufficient to abolish drinking behavior. However, the following experiment indicates that while a sensorimotor deficit is sufficient to abolish intake, it is not sufficient to reduce drinking behavior (Jacquin and Zeigler, 1978).

A standard drinkometer dircuit, providing a record of both the frequency and duration of contacts with the sipper tube, allowed us to dissociate deafferentation effects upon responsiveness to water from their disruptive effects upon the sensorimotor control of drinking. Total contact time served as a measure of responsiveness, while the ratio of contact time to water ingested provided a measure of drinking efficiency. We compared the drinking behavior of deafferented rats with that of two orosensorimotor "extinction control" groups, one sustaining trigeminal motor root sections, and the other, hypoglossal nerve sections. All three preparations drank less efficiently; however, although the "motor" animals could hardly ingest water they were highly responsive to the sipper tube and showed significant increases in the duration of individual drinking bouts. In contrast, deafferented rats made only a few brief contacts and remained relatively unresponsive to the sipper tube until their abrupt recovery some weeks later. These effects were seen even in rats in which the lingual nerves were spared. The reduced intake of the three preparations reflects the operation of two different processes: "motor" animals can't drink, "sensory" animals don't try to drink.

A behavioral "extinction control" group was also studied in an attempt to match the reinforcement conditions of the deafferented rat. Provided only with an empty water bottle, control rats initiated significantly more drinking bouts than deafferented rats, yet their duration was markedly reduced. This suggests that trigeminal rats do not sustain a bout because the water has, in a sense, disappeared. We are thus left with a genuine effect of trigeminal deafferentation upon the initiation of drinking (Jacquin, Olazabal, and Zeigler, in preparation).

The disruptive effects upon drinking are even more striking in light of the fact that similar movement patterns are required for ingesting semi-liquid food, which recovers relatively fast. In addition, many deafferented rats do exhibit some intake during the immediate postoperative week, but intake usually wanes into a second adipsic phase, suggesting that water intake no longer serves as an effective reinforcer of successful drinking behavior.

Finally, data collected in the operant chamber further supports the hypothesis that deafferentation affects the reinforcing properties of water. In contrast to the effects of various surgical and matched intake control procedures, deafferentation produced significant reductions in lever pressing (Jacquin, in preparation).

H. Is Reduced Body Weight An Indirect Effect?

Body weight in deafferented rats appears to be regulated, but at a reduced level. The following evidence suggests that the effects upon body weight regulation are a direct result of reduced food and water intake, rather than the result of an undetermined metabolic or digestive deficiency: (1) During the aphagic and adipsic period, body weight declines at the same rate as control animals subjected to similar deprivation conditions. Weights then asymptote at very low levels. (2) Trigeminal rats maintain similar body weight functions to that of their yoked intake partners (absolute differences may be attributed to substantive water intake in the yoked controls and liberal yoking for food intake). (3) Once solid food intake recovers, normal rates of weight gain are displayed, but the weight acceleration ceases long before that of the now "unyoked" controls. (4) Normal rats, food deprived for prolonged periods, exhibit a rapid return to ad-lib weight and do not show any ill side-effects (Collier, 1969; Levitsky, 1970). (5) Trigeminal rats regain lost body weight as rapidly as controls following 24 hour food or water deprivation. (6) The decreased F:BW, W:BW, and W:F ratios indicate that the retardation in weight gain, once solid food intake recovers, is due to consistent and prolonged hypophagia and hypodipsia. All of these facts suggest that the digestive and metabolic processes of deafferented rats are functioning normally and that these rats are efficiently utilizing the available food.

The F:BW and W:BW reductions might appear to conflict with the fact that normal rats maintained at lower weights retain the same predeprivation log intake : log BW ratios (Collier, 1969). In fact, Zeigler and Karten (1973b) showed that central trigeminal lesioned pigeons maintain a reduced weight, yet retain preoperative intake:BW ratios. These discrepancies are reconcilable by similar reductions in intake:BW ratios in the yoked controls and by the fact that Zeigler and Karten's preoperative ratios were obtained in fully-grown adult animals, where lower intake, yet equivalent ratios of intake:BW would be expected to drop weight to a lower level. The present preoperative ratios were obtained from young, growing rats, thus demanding lower intake:BW ratios in order to consistently maintain lower postoperative weights.

A more general, theoretical discussion of the results of this study can be found in the General Discussion.

Verification and Generalizability of Prior Deafferentation Studies

By whatever mechanism, the present results directly implicate trigeminal orosensory afferents in the neural control of orosensorimotor processes, food and water intake, body weight regulation, feeding efficiency, and responsiveness to food. These data suggest that trigeminally monitored information contributes substantially to the sensorimotor and motivational control of ingestive behavior in the rat, thus confirming Marwine and Zeigler's (1975) original observations. Though their electrolytic lesions were not restricted to orosensory regions in the ganglion, they did produce a continuum of effects upon ingestive behavior varying from prolonged aphagia to varying degrees of hypophagia and hypodipsia. Decreased intake was attributed to both orosensorimotor and responsiveness deficits, which can now be traced to orosensory deafferentation.

The present report confirms and extends Miller's (1977, 1978b) original observations on the effects of trigeminal orosensory deafferentation. One discrepancy does exist with respect to the duration of aphagia and adipsia in completely deafferented rats. Miller reports adipsia and aphagia that persists for a minimum of five weeks, as opposed to the 5.4 day adipsia and 1.9 day aphagia reported here, using similar diets. However, the constituents of the pablum and rat chow mash used by Miller have yet to be described, and the types of dishes used to present these mashes restricts the flexibility of consummatory behavior (6.3cm diameter, 5.0cm deep). As I've pointed out, semi-liquid mashes presented in shallow wide-faced dishes allows for adjustments in deafferented rat's consummatory behavior; adjustments that are necessary for intake. Successful ingestion of mash might have facilitated attempts at water intake, though this attempt at reconciling the differences in adipsia is only speculative.

Miller (in preparation) has provided data on the effects of strictly mandibular or maxillary deafferentation. Interestingly, the deficits in food and water intake fell between the presently described "alveolar only" and unilateral groups; by the second postoperative week intake of all foods had returned to preoperative levels, with rat chow pellets being the last consumed. Body weight decreased to 88% of ad-lib, but required 3-5 weeks to recover.

Thus, it appears that deafferentation must be bilateral and encompass at least some of the upper and lower mouth for the production of severe intake deficits.

The present report also lends support to Daunton's (1977) observations of impaired discriminative control of bite force and decreased bite frequency for intraoral water reinforcement in rats sustaining local anesthetization of the rostral buccal cavity. Though collected in a strictly operant paradigm, her data likewise suggest a marked reduction in drinking and impaired sensorimotor control of biting, with no effect upon the ability to emit a forceful bite.

Finally, the effects of trigeminal deafferentation upon feeding behavior in the rat are quantitatively and qualitatively similar to the deficits encountered after similar denervations in the pigeon (Zeigler, 1975a; Miller, et al., 1978; Moon and Zeigler, 1979). The similarities are striking in light of the gross differences in the morphology of the ingestive apparatus, the trigeminal nerve distribution, and the types of consummatory behaviors used by rats and pigeons. The deficit in drinking behavior seen in the deafferented rat, but not in the pigeon, may reflect a genuine species difference in the organization of the neural mechanisms underlying water intake. The functional integrity of the pigeon's drinking response might require only lingual innervation, as opposed to the rat (Mendelson and Zec, 1972). Since tongue somatosensation is not disrupted by trigeminal deafferentation in the pigeon, this could explain the species difference. Furthermore, the fact that deafferented pigeons exhibit prolonged aphagia, while deafferented rats begin ingesting food within the first postoperative week could reflect differences in the flexibility of ingestive behavior (the rat being able to use its paws and ingest without mouth opening and tongue extension), differences in the textural properties of the available diets (no data is available on the deafferented pigeon's response to semi-liquid foods), or the denervation of nonoral areas in the pigeon deafferentation procedure (proportionately, the grossly aphagic bird sustains a far greater magnitude of sensory disruption). In any case, the magnitude and type of deficits produced in the rat lend some degree of generalizability to the pigeon work.

Recovery of Function: Behavioral Stages and Possible Morphological Basis

Though recovery is only of secondary interest in the present study, I can describe the way postoperative ingestive behavior changes over time and provide some hypotheses as to why these changes occur.

The "trigeminal syndrome" can be characterized as consisting of four separate, *though not necessarily sequential*, stages of recovery: (1) adipsia + aphagia, (2) adipsia + solid food aphagia + liquid food hypophagia, (3) hypodipsia + solid food hypophagia + liquid food hypophagia, and (4) normal preoperative levels of food and water intake. Many factors determine the time course of each stage, the likelihood of advancing or regressing into another stage, and what stage the animal starts in. Most importantly, maintenance conditions dictate the eventual recovery of ingestive behavior. Only if the incisors are properly cared for, and semi-liquid food is presented in wide-faced shallow bowls, will the animal survive the first postoperative week. Even then, approximately 20% of the completely deafferented animals starve to death.

Secondly, the magnitude and somatotopic locus of the deafferentation determines the initial start point and the length of time spent in a specific stage. For example, completely deafferented subjects always exhibit stage I deficits and spend anywhere from one week to indefinite periods in stage II. "Alveolar only" subjects barely show stage II deficits and move rapidly into stage III. Importantly, though, the groups are indistinguishable within a given stage suggesting that the effects of deafferentation are additive, but only in the sense that a large number of nerve sections forces an animal into an earlier stage for a longer period of time.

Thirdly, the deafferented rat's own behavioral adjustment to its orosensorimotor impairment can dictate the stage of recovery and its duration. Since responsiveness to semi-liquid food returns relatively fast (by at least the end of the first postoperative week; Jacquin and Zeigler, 1979; Jacquin, Olazabal, and Zeigler, in preparation), recovery into stage II only occurs when an effective alternative feeding strategy is developed, such as "scooping" or "shoveling".

Fourthly, body weight loss can only serve to facilitate responsiveness to food which then increases the variability of the consummatory response, making ingestion likely. A reasonable hypothesis is that the species-typical consummatory response wanes in frequency and is replaced by more effective means of acquiring reinforcement. A large body of evidence exists on the facilitatory effects of body weight loss on the variability of appetitive behavior exhibited under an extinction regimen (Kimble, 1961). I believe that this phenomenon occurs in the species-typical consummatory behavior following deafferentation.

Finally, the recovery of solid food and water intake is accompanied by the recovery of responsiveness to food, oromotor reflexes, and feeding efficiency. There must exist a morphological substrate for reestablishing the stimulus-response linkages necessary for approach to food and water, mouth opening, biting or licking, and ingestion. Preliminary data suggests that regeneration of sectioned nerves, sprouting from intact nerves, and behavioral compensation are responsible for recovery of function; and that neural reorganization reestablishes the necessary S-R linkages.

Behavioral compensation is indicated by the fact that resectioning regenerating tissue produced all of the original morphological changes and orosensorimotor impairments yet did not produce as drastic an effect upon efficiency and intake. Thus, the animal had somehow learned to solve the feeding task without cutaneous orosensation, though intake still remained low. The process of recovery of intake, therefore, might involve a slow stepwise acquisition of new methods of accomplishing the behavioral objective to replace the basis on which the behavior was previously elaborated. However, long-term residual deficits in ingestive behavior suggest that behavioral compensation is not sufficient to produce total recovery.

Neural reorganization is indicated by the fact that rats sustaining second-stage unilateral deafferentation required less time for recovery of ingestive behavior. This suggests that either regeneration or sprouting from the intact side during the interoperative interval was responsible for lessening the effects of the second unilateral operation. A sprouting hypothesis is also indicated by the total reinstatement of the trigeminal syndrome by infraorbital nerve sections. Sprouting of infraorbital fibers into denervated areas seems likely given their proximity to oral areas and the return of oral insensitivity following these nerve sections. This effect is qualitatively different than the "hyposensory agitation" which follows additional sensory deprivation in limb-deafferented monkeys (Taub, et al., 1977). Further anatomical and physiological work is required to demonstrate the functional integrity of these hypothesized connections.

EXPERIMENT 2

SELECTIVE GUSTATORY DEAFFERENTATION IN THE RAT: EFFECTS UPON FOOD AND WATER INTAKE AND WEIGHT REGULATION

INTRODUCTION

The present report addresses two fundamental questions: (1) What is the role of peripheral gustatory inputs in the control of food and water intake and body weight regulation in the rat? and (2) Can impaired gustatory sensitivity account for the reductions in food and water intake seen after trigeminal orosensory deafferentation?

The first question represents the major focus of this paper and was handled by evaluating the effects of gustatory nerve sections. The second is more complicated and involves an assumption that the increases in QHCl aversion thresholds in trigeminal deafferented rats are indicative of a real change in the response to flavor. As such, deliberate disruption of well-known gustatory afferents should provide some insight into the way gross changes in flavor perception contribute to the trigeminal syndrome.

The present study also represents an attempt to extend Pfaffmann's (1952) original work on the effects of two-branch gustatory deafferentation upon quinine aversion thresholds to a three-branch preparation, and to compare the deficits produced by peripheral nerve sections to prior reports of lesion effects at other levels of the gustatory neuraxis (Ables and Benjamin, 1960; Benjamin, 1959; Benjamin and Akert, 1959).

Prior studies of central gustatory lesion effects upon ingestive behavior led me to expect interesting changes following peripheral gustatory deafferentation. Oakley (1965) studied the effects of thalamic taste nucleus lesions on water and food reinforced lever pressing. Lesions were placed in thalamic areas responding to taste stimulation, and only those animals shown to be taste-deficient in a two-bottle quinine aversion series were used. When water deprived, taste-deficient rats pressed for water at a lower rate than control rats. When food deprived, they pressed well only for strong sucrose, and gave low rates for saccharin and weak sucrose solutions. Absolutely no responding was reported for two rats. Direct evidence is therefore provided that gustatory stimuli are important reinforcers of operant behavior. In addition, Oakley noted the gustatory rats to be thinner than controls, less efficient in their feeding on rat chow pellets, and poorly groomed. He also frequently found animals that would not eat at all when given rat chow pellets or rat chow mash.

Recent work by Emmers (1977) implicates the thalamic taste area in food and water intake and body weight regulation. After bilateral destruction of thalamic areas shown to be responsive to chemical stimulation of the tongue (nucleus semilunaris accessorius thalami), rats decreased their hourly water intake. Whereas, preoperatively, NaCl injection was very effective in producing an augmented water intake, this effect vanished following the lesions. Water intake decreased to approximately 1/3 of preoperative level and persisted for 21 days. Food intake also decreased and body weight was not maintained. Originally matched for weight, control lesions resulted in mean weights much higher (392 ± 8g) than experimental rats (266 ± 12g) after 21 postoperative days. Two rats starved to death. Emmers also presents evidence that single neurons in this nucleus receive not only excitations that originate from taste receptors, but also other excitations that are processed via the splanchnic nerves; thus being able to monitor the concentration of substances existing in the internal environment.

Based upon Norgren's neuroanatomical and neurophysiological investigations into ventral forebrain projections of pontine gustatory neurons; central amygdaloid, rostromedial zona incerta, and lateral hypothalamic lesion effects upon ingestive behavior take on added significance (see Pfaffmann, et al., 1979, for a review of these studies). Of immediate relevance are the reports of exaggerated sucrose intake following lesions of the gustatory neocortex (Kiefer and Braun, 1977), the parabrachial nucleus (Nowlis, Braun, and Norgren, 1977), and the amygdaloid projections of these third-order afferent gustatory neurons (Rolls and Rolls, 1973); the aphagia and adipsia produced by central amygdala lesions (Box and Mogenson, 1975) when rats were offered rat chow pellets; and the hypodipsia produced after rostromedial zona incerta lesions (Evered and Mogenson, 1976; Rowland, Grossman, and Grossman, 1979).

The few studies examining the effects of peripheral gustatory deafferentation were largely limited to preference-aversion behavior. Richter (1956), using normal and adrenalectomized rats, reported that combined glossopharyngeal and chorda tympani nerve sections did not alter the ability to detect salt. However, additional section of the lingual nerves resulted in a severe deficit in discrimination. The fact that lingual nerve sections produced such a deficit could be attributed to a generalized incapacity to lick rather than a specific loss of sensitivity (Pfaffmann, 1952), though Mendelson and Zec (1972) reported no deficits in air-licking following lingual nerve sections.

In examining preference-aversion behavior for NaCl and aversion behavior to quinine, Pfaffmann reported minor changes in discriminability following only chorda tympani sections, yet a more definite reduction in discriminatory behavior with the addition of glossopharyngeal nerve sections. Attempts to additionally sever the pharyngeal branch of the vagus nerve resulted in high mortality. No mention was made of possible impairments in daily food and water intake or body weight regulation following chorda tympani and glossopharyngeal sections.
Richter (1956) found that section of the chorda tympani, glossopharyngeal, or lingual nerves, singly, had no effect on the regulation of salt intake; while combined section of the glossopharyngeal, lingual, and pharyngeal branch of the vagus nerve resulted in an inabiltity to recognize the solution. More importantly, body weight curves were presented showing an abrupt halt to weight gain following combined chorda tympani and glossopharyngeal sections (the major innervation of lingual taste buds), though no mention was made of why this occurred.

I. Miller's (1977) recent work extends Pfaffmann's and Richter's earlier findings on residual gustatory preferences and aversions following chorda tympani and glossopharyngeal nerve sections by describing the distribution of palatine taste buds which presumably subserved the residual taste sensitivity.

The Pfaffmann (1952) and Richter (1956) work has been cited as evidence against an oropharyngeal control mechanism in the long-term quantitative control of food and water intake (Epstein, 1967; Teitelbaum and Epstein, 1963).

To determine the roles of gustatory input in ingestive behavior, the deafferentation procedure was chosen because the deficits observed are so unambiguously related to a specific denervation (as opposed to the intragastric-operant procedure or CNS lesion techniques). Admittedly, it is a near impossibility to surgically produce 100% pure taste loss via peripheral or central denervation. The innervation is too diffuse and likely mixed with other sensory, motor, and autonomic systems. Thus, to oversimplify the source of gustatory afferent input would likely lead to misinterpretation of the behavioral effects of lesions. This problem has been pointed out by workers in the field of taste physiology (Oakley and Benjamin, 1966) and taste neuroanatomy (I. Miller, 1977). An additional interpretive difficulty lies in the joint action of somatosensory and gustatory stimulation in perceived flavor. Human work has demonstrated the crucial role of temperature (Sato, 1963), texture, and viscosity (Amerine, et al., 1965) in taste sensitivity. Neurophysiological data also points to an interaction of gustatory and somatosensory stimuli. Most gustatory fibers in the chorda tympani nerve respond to changes in tongue temperature (Ogawa, et al., 1968), as do gustatory units in the medulla, pons, and thalamus (Benjamin, 1963; Norgren and Pfaffmann, 1975). Given these built-in limitations, deafferentation procedures can give valuable insights into the role of gustatory stimuli in ingestive behavior, if the preparation's gustatory capabilities are thoroughly evaluated. Varying degrees of impaired gustatory functioning can then be correlated with deficits in ingestion.

The deafferentation procedure used in this report involved the chorda tympani, glossopharyngeal, and pharyngeal branch of vagus nerves, in an attempt to produce a pure, yet substantial, gustatory deafferentation. At the time these experiments were run, I. Miller's (1977, 1978) experiments on the palatine taste bud innervation were not yet completed so I restricted the denervation to clearly defined lingual and pharyngeal gustatory pathways. Figure 22 (from I. Miller, 1977) describes the oropharyngeal taste bud distribution in the rat.

Insert Figure 22 Here

Bilateral section of the chorda tympani, glossopharyngeal, and the pharyngeal branch of vagus removes approximately 4/5 of the rat's entire oropharyngeal complement of taste buds by removing the innervation of regions A, B, C, and a small percentage of the posterior region of the soft palate. This was determined by examination of the extent of taste bud degeneration following single nerve sections (I. Miller, 1977). Residual taste sensitivity to QSO_4 and NaCl was reported by Pfaffmann (1952) following combined chorda tympani and glossopharyngeal sections, thus implicating the pharyngeal, palatine, and epiglottal taste buds in qualitative gustatory discrimination. The palatine and epiglottal taste buds were largely spared in the present study via their greater superficial petrossal and superior laryngeal innervation.

Taste afferents are usually sensitive to solutions that evoke all four of the basic taste modalities, though they will usually respond best to only one of these (Pfaffmann, et al., 1979). With regard to the present deafferentation procedure, the chorda tympani nerve contains sucrose-best, NaCl-best, and HCl-best fibers with NaCl-best units constituting about 50% of that population. The glossopharyngeal nerve contains units best-responsive to all of the four taste qualities, with quinine-best units constituting about 40% of that population. The physiological properties of the pharyngeal branch of vagus have yet to be studied. Thus, it can only be said that the presently used nerve sections deny the rat a broad range of sensitivity to all of the four generally accepted taste qualities. The unaffected palatine taste buds have not been systematically studied in the rat, though human work suggests that they may be best-responsive to bitter solutions (Collings, 1974; Henkin and Christianson, 1967a,b).

The behavioral paradigms used are nearly identical to that of the preceding trigeminal experiment, mainly for ease of comparison. It was not surprising that gustatory deafferentation resulted in changes in ingestive behavior, in that gustation has often been equated with palatability (but see Mook, 1974). However, comparing the types and amounts of deficits produced by the trigeminal vs. gustatory procedures has proven to be particularly enlightening given the historical emphasis placed upon the two systems in eliciting ingestive behavior.

METHODS

A. Subjects and Surgical Procedures

A group of 27 male albino Wistar rats were used, weighing from 350-600g at the start of the experiment. They were housed and maintained in the manner described in Experiment 1. Three-branch gustatory deafferentation was performed on 20 rats. Four died within a week after surgery, and one developed severe respiratory problems and was eliminated from the experiment.

General surgical procedures have been described in detail in the preceding article. The chorda tympani nerve was sectioned proximal to its junction with the trigeminal lingual nerve, approximately four millimeters distal to its entry into auditory bulla, at the point where it traverses the auriculotemporal nerve (see Figure 6). Figure 6 also describes the surgical approach and the approximate area of section. Section of the glossopharyngeal and the pharyngeal branch of vagus nerves required exposure of the neural plexis medial to auditory bulla. Figure 23 (from Richter, 1956, p.613) describes the surgical approach and the approximate area of section.

Insert Figure 23 Here

Because of the possibility of damage to the ascending ramus of the hypoglossal nerve in retraction, hypoglossal nerve sections were performed bilaterally in seven control rats.

The deafferentation procedure required approximately 30 minutes and did not produce excessive bleeding. The rats appeared active and alert within 24 hours.

No histological analyses were performed. Since sham surgery has been reported to have no effect upon quinine aversion thresholds (Pfaffmann, 1952), a threshold increase was taken to indicate successful deafferentation.

B. Behavioral Procedures and Experimental Design

All behavioral data were collected under conditions identical to that of the preceding trigeminal experiment. Ingestive behaviors were monitored daily (including weekends) for at least 10 preoperative and 40-60 postoperative days in all of the following treatment groups:

1. Experimental - Bilateral gustatory deafferented subjects were assigned to one of four dietary conditions:

a. cafeteria diet (N=6) - These rats provided pre- and postop data on body weight, food and water intake, responsiveness to solid foods, and two measures of feeding efficiency. In four of these rats, QHCl aversion thresholds were determined using the procedure described in Experiment 1. Since testing began immediately on day 1 postop, the threshold tracking procedure allowed evaluation of recovery of taste sensitivity. Once intake and body weight had stabilized (usually day 30 postop), all subjects were 24 hour food deprived. Water intake and the number of days required to regain predeprivation body weight were recorded. This was repeated in some rats from one-two weeks later.

b. rat chow pellets: single-choice (N=3) - Pre- and postop body weight, food and water intake, responsiveness to food, and two measures of feeding efficiency were recorded. One rat provided these data while living in a Wahmann activity wheel. The other two rats were also tested for QHCl aversion thresholds and the response to 24 hour food deprivation. In addition, these two rats were twice subjected to 24 hour water deprivation, separated by at least one week. Food intake and the number of days required to regain predeprivation body weight were recorded.

c. rat chow mash: single-choice (N=3) - Pre- and postop body weight and food intake were taken, as well as the response to 24 hour food deprivation, though only the number of days to regain weight was recorded. Two of these rats were tested for QHCl aversion, though minimal water intake precluded its use.

d. pablum: single-choice (N=3) - Pre- and postop body weight and food intake were taken, as well as the response to 24 hour food deprivation, though only the number of days to regain weight was recorded.

2. Control - Of the seven hypoglossal controls, five were studied while offered the cafeteria diet, and two while offered rat chow pellets (single-choice). Food and water intake, body weight, efficiency, and responsiveness to food were recorded. Imminent starvation forced their sacrifice between days 15-30 postop. Sham surgical effects (N=8) were reported in Experiment 1 and their data are also used here. Comparisons with gustatory rats are somewhat limited by the sham procedure: exposure of the entire trigeminal orosensory operative field.

All subjects (experimental and control) were inspected daily for oral abnormalities, general activity, and food- and water-related consummatory deficits. Sensorimotor-reflex testing was carried out (as described in Experiment 1) to determine the animal's ability to orient to sensory stimuli.

RESULTS

Bilateral three-branch gustatory deafferentation did not produce the oral abrasions or incisor overgrowth found in the trigeminal deafferented rat, nor did it impair the ability to orient to sensory stimuli. Visual, auditory, proprioceptive, olfactory, and tactile stimuli elicited appropriate species-typical responses. Moreover, the animal maintained a normal appearance, posture, and disposition. Biting reflexes in response to paw pinch and tail pinch stimuli seemed unaffected, as did the exploration and eventual biting of a Q-Tip waved in front of the cage. Chocolate Nutriment placed intraorally or on the floor of the cage, during the immediate postoperative period, elicited vigorous lapping movements and seemingly normal swallowing movements. Importantly, both the components and the sequencing of ingestive responses appeared normal, for all diets.

By contrast, hypoglossal controls did not extend their tongue under any circumstance. This was expected since the nerve sections disrupted the motor control of tongue movement. The components and sequencing of ingestive responses appeared normal up to the point where food had to be mandibulated, or where liquids had to be taken into the mouth. Vigorous biting was readily elicited.

Sensitivity to bitter quinine solutions was markedly impaired in all six gustatory rats tested. Figure 24 presents the results of four representative rats. The data is plotted such that the detection threshold lies between those two adjacent molarities where relative QHCl intake is greater than 25%, and then less than 25% of the total fluid intake. Preoperative thresholds are indicated by a dotted horizontal line. Postoperatively, the rat determined which molarity was presented in the next four day interval, thus providing a continual psychophysical measure of sensitivity.

Insert Figure 24 Here

Note that since #78-56 remained at the top of the concentration scale, tracking was impossible. All subjects exhibited at least an order of magnitude increase in quinine aversion thresholds during the immediate postoperative period, with five of the six showing some recovery of function over the 50 days of testing. There were no obvious parallels between the severity of the threshold increase and the severity of the food and water intake deficits, within a given animal; nor was there an obvious relationship between the recovery of sensitivity and the recovery of ingestive behaviors.

Figure 25 describes the effects of gustatory deafferentation upon two measures of feeding efficiency.

Insert Figure 25 Here

The probability of ingesting solid food once it had been removed from the dish decreased significantly during the first 10 postop days, but subsequently returned to preoperative levels (day 1-10: $\underline{t}(13)=4.93$, $\underline{p} < .01$; day 11-20: $\underline{t}(13)=1.28$, $\underline{p} > .10$). Taste impairment also increased the amount of chewed uneaten crumbs found on the cage floor, an indication of a deficit in mandibulation. This deficit remained throughout the 50 days of observation and cannot be attributed to surgical artifacts since the effect was greater than that exhibited by sham controls ($\underline{t}(11)=5.12$, $\underline{p} < .01$). Prior work has shown that gustatory deafferentation does not affect the efficiency of ingesting semi-liquid foods (Jacquin and Zeigler, 1979).

A deficit in responsiveness to solid food is indicated in Figure 26, where the amount of rat chow pellets and moist and dry cat chow removed from the dish serves as a responsiveness measure.

Insert Figure 26 Here

By contrast with sham operates, deafferentation was followed by significant reductions through day 30 postop (day 11-20: $\underline{t}(13)=2.54$; $\underline{p} < .025$; day 21-30: $\underline{t}(13)=2.14$, $\underline{p} < .05$; day 31-40: $\underline{t}(11)=0.38$, $\underline{p} > .10$).

Decreased responsiveness to solid foods was paralleled by significant reductions in food and water intake, unattributable to surgical trauma, inadvertent damage to the hypoglossal nerve, or orosensorimotor impairment. Table 14 decribes the number of days of aphagia (intake of 1g or less) for each diet type, days of adipsia (intake of 1ml or less), the maximum weight loss, and the number of days required to regain preoperative weight in six rats offered the cafeteria diet.

Insert Table 14 Here

The following analyses represent comparisons with eight sham operates offered an identical diet. Though the mean days of adipsia was only 1.8, this is significantly longer than sham operates ($\underline{t}(12)=3.95$, $\underline{p} < .01$). Gustatory rats exhibited significant aphagias to rat chow pellets ($\underline{t}(12)=3.67$, $\underline{p} < .01$), dry cat chow ($\underline{t}(10)=4.54$, $\underline{p} < .01$), and moist cat chow ($\underline{t}(10)=3.10$, $\underline{p} < .01$); but did not differ from sham operates with respect to rat chow mash or pablum. These six rats lost a mean of 16.3% of their body weight, a significantly greater loss than the 5.3% exhibited by sham operates ($\underline{t}(12)=6.84$, $\underline{p} < .01$).

Once food and water intake returned, intake was insufficient to permit rapid recovery of body weight. By contrast with sham operates that required 11.4 days to regain ad-lib weight, gustatory rats required 34.2 days. This represents a significant difference ($t(12)=6.26$, $p < .01$).

Recovery of food intake was characterized by an orderly progression through the diet types: first pablum, then the liver-flavored moist and dry cat chows, and finally the rat chow pellets. The order of return suggests differential recovery of intake along a taste gradient; rat chow pellets were consumed last when compared to pablum ($t(10)=4.23$, $p < .01$), moist cat chow ($t(10)=2.19$, $p < .05$), or dry cat chow ($t(10)=2.98$, $p < .01$). Moreover, rat chow pellet intake returned as fast as rat chow mash ($t(10)=1.02$, $p > .10$) and dry cat chow intake returned as fast as moist cat chow ($t(10)=1.04$, $p > .10$); making it unlikely that diet texture and size variables made a significant contribution to aphagia. One would expect that if taste was the relevant variable in determining which diets were consumed, then pablum would be preferred over rat chow mash. This comparison, however, only approached statistical significance ($t(10)=1.40$, $p < .10$), in spite of the fact that rat chow mash was never consumed before pablum and four of the six animals ate pablum before rat chow mash.

Thus, deafferentation appears to have affected the "relative palatability" of the various diets by heightening the sensitivity to taste stimuli. A representative rat is plotted in Figure 27 to demonstrate the effects upon palatability. This characteristic progression through the diet types was not exhibited in any of the surgical controls.

Insert Figure 27 Here

Gustatory deafferentation also affected the "absolute palatability" of the available diets, as shown in Figure 28.

Insert Figure 28 Here

Differential effects upon food intake and body weight were not observed when rats were offered either rat chow pellets or rat chow mash in the single-choice situation; they all lost between 10-20% of their free-feeding weight and slowly recovered over a 31-40 day period. Food intake was significantly depressed in both groups and did not recover completely in the maximum 40 day observation period (rat chow mash, day 31-40: $t(16)=5.14$, $p < .01$; rat chow pellets, day 21-30: $t(27)=3.87$, $p < .01$, day 31-40: $t(26)=1.53$, $p < .10$). However, a striking difference was seen in rats offered pablum in a single-choice situation; normal intake returned during the 6-10 day period (day 1-5; $t(13)=6.08$, $p < .01$, day 6-10: $t(14)=0.57$, $p > .10$). This was followed by a hyperphagic trend (day 11-15: $t(13)=1.42$, $p < .10$). As a result, body weight quickly reached a level attained by sham operates (day 6-10) followed by striking weight gains. Thus, it was possible to obliterate the long-term effects of deafferentation upon intake control and weight regulation by providing unlimited "palatable" food.

To summarize, deafferentation reduced the "absolute palatability" of rat chow pellets and rat chow mash and possibly heightened the "absolute palatability" of pablum, making it likely that taste determined relative intake and the subsequent level of weight regulation in the single-choice situation. Note that all three groups exhibited equivalent preoperative weight gains.

The intake deficits were further analyzed with all experimental animals combined. These data are presented in Figure 29 and do not include data for the six rats offered only semi-liquid foods.

Insert Figure 29 Here

Following the initial 10-20% body weight loss, body weight consistently remained below control levels due to prolonged hypophagia and hypodipsia and the subsequent lack of compensatory overeating. Though normal solid food intake gradually recovered during the 41-50 day period (day 31-40: $\underline{t}(15)=1.90$, $\underline{p} < .05$; day 41-50: $\underline{t}(11)=1.20$, $\underline{p} > .10$), water intake remained significantly depressed (day 41-50: $\underline{t}(11)=3.40$, $\underline{p} < .01$). Indeed, the decreased water intake concomitant with normal solid food intake suggests a genuine long-term effect upon responsiveness to water. These deficits stand in contrast to the mild and transient effects of sham surgery. When compared to preop levels, sham operates showed no effect on total food intake (day 1-10: $\underline{t}(15)=1.25$, $\underline{p} > .10$), transient solid food intake deficits (day 1-10: $\underline{t}(15)=3.30$, $\underline{p} < .01$; day 11-20: $\underline{t}(12)=0.54$, $\underline{p} > .10$), and transient water intake deficits (day 11-20: $\underline{t}(8)=2.27$, $\underline{p} < .05$; day 21-30: $\underline{t}(3)=0.81$, $\underline{p} > .10$).

Metabolic or digestive deficiencies are likely not involved in the long-term effects upon intake and body weight for three reasons:

(1) Deafferented rats offered ad-lib pablum gained weight normally.

(2) Deafferented rats deprived of food or water for 24 hours did not differ from sham operates with respect to the amount of time required to regain lost body weight. These data also suggest that deafferented rats do regulate body weight and efficiently utilize nutrient intake

(see Table 15).

Insert Table 15 Here

---

(3) Body weight declines and remains at subnormal levels because deafferented rats maintain a lower ratio of ingested substances to body weight than was exhibited preoperatively (Table 16).

Insert Table 16 Here

The hypophagic-hypodipsic period was characterized by decreased F:BW ratios ($t(5)=6.81$, $p < .01$), W:BW ratios ($t(5)=4.21$, $p < .01$), and W:F ratios ($t(5)=2.56$, $p < .05$). Since these were not full-grown rats at the time of surgery, no change in the intake:BW ratios would have resulted in normal preoperative weight gains and rapid recovery of lost body weight. Chronically reduced body weight required that these ratios be lower than normal, as was the case with "yoked for food intake" controls (see Experiment 1).

Table 17 describes the effects of deafferentation upon the relationship between food and water intake.

Insert Table 17 Here

Solid food intake during 24 hour water deprivation did not differentiate gustatory from sham operates. However, deafferented rats drank substantially less than sham operates during 24 hour food deprivation ($t(40)=4.17$, $p < .01$), while their predeprivation intakes did not differ.

None of the above-described deficits are likely attributable to inadvertent hypoglossal nerve damage, though it may be partially responsible for the deafferented rat's apparent mandibulation deficit. Seven rats subjected to bilateral hypoglossal nerve sections manifested severe inefficiency in feeding and drinking. Up to 100g of crumbs were found daily on the cage floor and enormous amounts of time were spent in contact with the water tube and wallowing in the semi-liquid foods; all for minimal intake. These abnormalities were not observed after gustatory deafferentation.

DISCUSSION

In a recent review of taste neuropsychology, Pfaffmann, et al. (1979) stated: "We can expect many new developments on the CNS aspects of taste as the neural relations of the ventral taste pathways and its limbic projections are revealed. Increasingly here, as in the study of peripheral mechanisms, we can expect exciting new advances that will link gustatory function even more closely to appetite, food and fluid intake, preferences and aversions, and hedonic processes" (p.317). The present results have further strengthened this speculation by showing that interruption of the peripheral afferent flow of gustatory information disrupts ingestive behavior. Others have speculated that excitation of peripheral receptors (oral, gastric, splanchnic) and its concomitant CNS stimulation may be an important mechanism controlling quantitative aspects of ingestive behavior (e.g. Zeigler, 1976; Davis, et al., 1976; Emmers, 1977). Data presented here, as well as the results of the prior trigeminal work, indicate that this may very well be the case.

It has been known for some time that gustatory stimulation motivates and directs ingestive behavior, contributes to satiety, and the quantitative regulation of body weight in both vertebrates and invertebrates (e.g. Epstein, 1967; Dethier, 1967). These conclusions are largely based on indirect evidence: certain substances facilitate ingestion (e.g. sucrose) while others inhibit it (e.g. quinine). Although the present experiment did not succeed in producing an animal completely devoid of taste sensitivity, the relatively large sensory deficit produced by deafferentation was sufficient to genuinely impair responsiveness to food and water and consequently the long-term regulation of body weight; thus directly implicating gustation.

This experiment was designed to answer two questions: (1) Is peripheral gustatory input directly involved in the quantitative control of food and water intake? and (2) Can the changes in taste sensitivity following trigeminal orosensory deafferentation account for any or all of the components of the previously described trigeminal syndrome? The answer to the first question is yes. The following evidence substantiates the conclusion that gustatory deafferentation effects are a direct result of taste impairment: (1) QHCl aversion thresholds increased markedly over preoperative levels. (2) By providing a very sweet diet (pablum) I was able to largely obliterate the decreased intake observed when bland diets were offered. (3) Orosensorimotor impairment was minimal. (4) Sham operate and hypoglossal controls did not exhibit similar quantitative or qualitative changes. (5) Recovery of intake of the various diets progressed through a taste gradient suggesting that the original impairment was taste-specific. Thus, gustatory deafferentation diminishes the capacity of food and water related stimuli to support ingestion, producing hypophagia and hypodipsia. Highly palatable foods were required to overcome the deficits in perceiving orosensory stimuli, reminiscent of the hypothalamic recovery syndrome, where taste becomes a "psychic energizer" (Teitelbaum, 1955; Teitelbaum and Epstein, 1962; Wolgin and Teitelbaum, 1978).

Possible Sources of Confounding

Two possible variables in the present design may have confounded the results. Kratz and Levitsky (1978) found that intragastric intubation of 0.75g QHCl produced anorexia over a 24 hour period when paired with the consumption of a novel food. Six of the total 15 deafferented rats were ingesting appreciable quantities of QHCl solutions and denervation probably removed some of the cues that make for food familiarity. However, no differences in ingestive behavior were observed between these potentially confounded six rats and the remaining nine unexposed rats, therein eliminating the possible confounding by postingestive consequences.

Secondly, Stricker (1970) reported that chorda tympani nerve sections interfere with salivary secretion from the submaxillary glands. Since desalivation does not affect total food intake nor body weight regulation, only the patterning of meals and drinks (Kissileff, 1969), this is unlikely a confounding variable. Also, the body weight curves for deafferented rats on rat chow pellets vs. rat chow mash were nearly identical. Since these two foods require very different amounts of saliva for efficient ingestion, desalivation would be expected to produce differential effects in these two groups, which clearly did not occur.

Central vs. Peripheral Lesion Effects Upon Ingestive Behavior

Lesion effects upon ingestive behavior have now been evaluated at many points along the gustatory neuraxis. Though most studies have emphasized effects upon conditioned taste aversions, neophobia, and preference-aversion behavior; some attention has been paid to regulatory behavior at various neuronal levels. Exaggerated sucrose intake has been reported following parabrachial nucleus lesions (Nowlis, et al., 1977) and the amygdaloid projections of these third-order afferent gustatory neurons (Rolls and Rolls, 1973). Similarly, gustatory neocortical damage increases the preference for sucrose and weak salt solutions (Kiefer and Braun, 1977). If pablum can be considered similar to sucrose in its stimulatory properties, then the hyperphagic trend exhibited to pablum following gustatory deafferentation represents a similar finding.

A rather puzzling result was reported by Oakley (1965) using an operant lever pressing paradigm with varying concentrations of sucrose reinforcement. Lesions of the thalamic taste nucleus produced low response rates for saccharin and weak sucrose solutions, and only normal rates for strong sucrose. This is difficult to reconcile with the above-described hyperphagia exhibited when lesions were placed in other gustatory areas; unless, as Oakley points out, the lesions interfered with tactile sensitivity of the tongue. It's also possible that operant indices measure incentive value while consummatory indices measure preference. This work deserves mention on four other counts: (1) Taste-deficient rats pressed for water at a low rate that was unaffected by the addition of .002M QHCl, a concentration that was clearly avoided following peripheral gustatory deafferentation. (2) Lesioned rats exhibited a low rate of responding to distilled water when water deprived, leading Oakley to speculate that taste impairment affected sensitivity to water. He hypothesized that this was partly due to decreased lingual tactile sensitivity, though the present work showed that gustatory deafferentation did result in a decreased responsiveness to water. (3) Lesioned rats were described as thinner than controls, with one-stage bilateral lesions frequently resulting in aphagia to rat chow pellets and rat chow mash, findings similar to mine. (4) Lesioned rats became inefficient at drinking and eating, with piles of pellet crumbs collected on the cage floor. Again, I report similar effects on feeding efficiency, though no evidence exists for drinking inefficiency following peripheral deafferentation.

Many of Oakley's observations have since been substantiated and extended by Emmer's (1977) work on the role of the thalamic taste nucleus in food and water intake. After bilateral lesions rats decreased their hourly water intake to approximately 1/3 of their preoperative level in response to subcutaneous injection of NaCl, while partial lesions resulted in only a slight deficit. Interestingly, thalamic taste nucleus lesions concomitantly decreased the firing rate of hypothalamic neurons that responded positively to intravascular infusions of NaCl. These rats also showed massive reductions in food intake, both under normal conditions and in response to insulin administration. No quantitative intake data was provided, though the mean body weight at 21 days postop was 68% of ad-lib. These deficits are massive in comparison with those seen after peripheral gustatory deafferentation: weight loss to only 83.7% of ad-lib and a normal compensatory response to deprivation-induced water imbalance. These differences are likely attributable to the fact that thalamic taste neurons also monitor the concentration of glucose existing in the internal environment of the organism, via the splanchnic nerve ("intravascular taste", Bradley, 1973). This monitoring device remains available to the peripherally deafferented rat. However, the deafferented rat is not capable of normal monitoring of the concentration of internal substances via transcapillary filtration onto the taste bud itself (Emmers, 1977). Thus, cutting the afferent supply removes a potential source of coding internal chemical imbalances, such as salt deficiency (Contreras, 1977).

Ventral forebrain projections of pontine gustatory neurons have also been implicated in the control of ingestive behavior. Most striking are the aphagia, adipsia, feeding inefficiency, and reduced reactivity to sweet solutions produced by central amygdala lesions (Box and Mogenson, 1975). These findings have since been questioned by Kemble, et al. (1979) who found similar lesions to have no effect on recovery of postoperative body weight, food consumption levels, or feeding efficiency. They did, however, provide other data remarkably similar to that observed after peripheral deafferentation: mild but persistent hypodipsia, decreased water intake when food deprived, and continued quinine solution intake. These results suggest that the central amygdaloid nucleus processes peripherally supplied information which has a role in mediating the relationship between food and water intake and in some taste-mediated consummatory responses. Interestingly, the rostromedial zona incerta also seems to receive similar peripherally supplied gustatory information, since lesions there disrupt gustatory pathways (Emmers, 1977; Norgren and Leonard, 1973) and produce similar behavioral deficits (Evered and Mogenson, 1976; Rowland, et al., 1979). (See General Discussion for hypothalamic lesion effects and their relation to central gustatory processes.)

The deficits produced following lesions of the gustatory cortex seem to resemble, on a gross level, those following amygdala damage, but appear more specific to loss of taste rather than general decreased activation. Obviously further work is needed to delineate the actual neural pathways subserving taste sensitivity and their efferent instructions to various muscle groups. Only then will detailed behavioral analyses of lesion effects upon ingestive behavior illuminate the relative contributions of various levels of the gustatory neuraxis.

Central vs. Peripheral Lesion Effects Upon QHCl Sensitivity

Three-branch gustatory deafferentation raised QHCl aversion thresholds to .00005 - .00018M concentrations (mean of six rats between days 30-40 postop). This can be compared with Pfaffmann's (1952) report of QSO_4 aversion thresholds between .00006 - .00018M following two-branch deafferentation (mean of six rats between days 30-50 postop). The striking similarity between the two- and three-branch preparations suggests that the pharyngeal branch of the vagus nerve does not play a role in quinine sensitivity. This is not to say that deafferentation of pharyngeal taste buds did not contribute to the observed deficits in ingestive behavior, since they may be best-responsive to sour, sweet, or salt stimuli. Obviously, precise characterization of the sensitivity changes to these other stimulus qualities, as well as more precise control of the stimulus properties of the diets, will be required to understand the causal basis for the deficits in ingestive behavior produced by gustatory deafferentation.

The present work has shown that QHCl aversion thresholds rose approximately 1½ orders of concentration magnitude above preoperative level. Some degree of recovery took place in all animals tested over the 50 postop days. These data can be compared with QHCl thresholds following thalamic taste nucleus lesions and cortical ablation of the taste area. Thalamic taste nucleus lesions have been reported to produce 13-fold threshold increases, with only slight improvement seen over the five months of testing (Ables and Benjamin, 1960). These data are comparable to the present findings, yet recovery seemed more pronounced following peripheral deafferentation. Ablation of the cortical evoked potential area of the taste nerves, however, only resulted in a 6-fold threshold increase with normal discrimination returning by the second postoperative month (Benjamin, 1959; Benjamin and Akert, 1959).

I can only speculate as to the reasons for these differences. Cortical ablation of the taste area leaves small neurons scattered throughout the degenerated subnucleus which probably sends axons to other subcortical structures. Even complete decortication results in only transient discrimination deficits. The thalamic deficit is more severe, yet total removal of taste sensitivity has yet to be accomplished by any type of lesion. This is likely due to the other major gustatory pathway traversing the ventral forebrain (Norgren and Leonard, 1973; Norgren, 1976), though lesion studies in these areas have not systematically evaluated taste sensitivity.

Remaining taste sensitivity following three-branch gustatory deafferentation is particularly interesting in that an estimated 80% of the receptor population was eliminated (I. Miller, 1977). As Pfaffmann (1952) originally pointed out regarding preference-aversion behavior, the relatively large sensory deficit did not have a proportionately large effect on behavior; thus, a linear relation does not exist between the number of sensory elements removed and the behavioral effects. One could hypothesize that removal of the innervation of the remaining 20% of the taste buds would have a disproportionately large effect on QHCl sensitivity. It would be interesting to see the effects of sectioning the greater superficial petrossal and superior laryngeal nerves separately and in combination with the presently studied nerve sections.

Though not as extensive as that seen after trigeminal sections, behavioral variability was seen following gustatory deafferentation. Histological analyses of the tongue following identical denervations (Pfaffmann, 1952) revealed taste buds scattered around the tip of the tongue in most of the animals. The remaining buds were presumed to sustain innervation through fibers that reach the chorda tympani nerve through alternate pathways past the middle ear. These intact fibers, however, represent only 5% of the myelinated axons of the chorda tympani. Individual differences in possible alternate pathways may account for the observed variability in ingestive behavior.

Conclusions

The present results suggest that gustatory deafferentation genuinely affects the absolute and relative palatability of various foods and disrupts the intimate relationship between food and water intake (as evidenced by the decreased water intake during food deprivation), resulting in reduced food and water intake.

Further work is required to more precisely define the effect upon relative palatability. Short-term preference tests, or procedures which limit postingestive consequences, might be more appropriate than the 24 hour cafeteria paradigm in isolating the mechanisms responsible for the deafferented rat's preference behavior.

The effects upon absolute palatability deserve further mention. The hyperphagic trend in gustatory deafferented rats offered ad-lib pablum could represent the animal's attempt to compensate for the reduced flow of afferent input by "flooding" the remaining intact taste buds. Gentile (1968) has hypothesized that animals ingest to a point of maximum gustatory stimulation, where satiety occurs. If he were correct, animals would have to eat less of a strong, concentrated stimulus and more of a weak, diluted stimulus to acquire this set level of stimulation. Pablum might only be a weak, diluted stimulus to the deafferented rat and would require longer meals for satiety to occur. Further work on meal patterns using pablum is obviously required to test this speculation. In any event, this notion represents an interesting parallel to Contreras' (1977) receptor-action hypothesis for salt appetite. He found that salt deficiency resulted in a decreased firing rate in chorda tympani neurons to salt solutions applied to the tongue. Contreras hypothesized that more time and more drinking would be required for the taste nerve of a sodium deficient rat to accumulate a critical number of impulses necessary for satiety. Therefore, time spent drinking should increase with decreased salt concentration, since impulse frequency increases with concentration. A similar mechanism could account for the deafferented rat's unusual responsiveness to palatable food; a critical number of "pablum-driven" impulses might be necessary for satiety to occur.

Finally, the symptomatology produced by deafferenting 80% of the oropharyngeal taste buds is quantitatively and qualitatively different than that produced by complete trigeminal orosensory deafferentation. Table 18 summarizes the similarities and differences where equivalent measures are available.

Insert Table 18 Here

The wide array of differences leads me to reject the hypothesis that impaired taste sensitivity is totally responsible for the massive concatenation of deficits exhibited in the trigeminal preparation. However, it may partially contribute to the trigeminal rat's long-term retardation of body weight gain, feeding inefficiency, and decreased responsiveness to food and water. Further work is needed to determine the mechanisms responsible for "flavor". Somatosensory inputs may be necessary for efficient gustation. Flavor, as we know it, might be the result of an interaction of gustatory, tactile, thermal, pain, olfactory, proprioceptive, and gastric stimuli that summate to dictate the palatability of food, thus influencing the initiation, maintenance, and termination of ingestive behavior.

GENERAL DISCUSSION

Additional Contributions of Orosensory Systems to Ingestive Behavior

A. Control of Body Weight "Set Point"

Body weight loss is known to affect a variety of measures of hunger in vertebrates (Bolles, 1967; Collier, 1969; Zeigler, 1975a). Some metabolic correlate of body weight is likely monitored by rats and it is therefore conceiveable that deafferentation (trigeminal and/or gustatory) affects the level at which body weight is regulated. Thus, reduced intake might represent an adaptive response to a reduced "set point" for body weight (Keesey, 1973). It is indeed true that deafferented rats defend a reduced weight, as do trigeminally deafferented pigeons (Zeigler, 1975a); however, one would be hard pressed to pinpoint the mechanism by which a peripheral nerve section produces a lowered set point, even if we knew what and how a set point is achieved. The problem with this hypothesis is that it does not explain the mechanism by which intake is reduced to achieve a new weight level, rather it simply describes the performance of the animal. More fundamental analytical levels need to be addressed to explain the reduced intake.

B. Facilitation and Inhibition

The homeostatic model of intake control (LeMagnen and Tallon, 1966, 1968; Panksepp and Ritter, 1975) has delegated both facilitatory and inhibitory functions to orosensory factors (facilitation defined as a temporary nonlearned increase in strength of response as a result of the occurrence of a second stimulus or response; inhibition defined as any decrease in the strength of a response which is occasioned by positive stimulation). It has been shown that gustatory stimuli can facilitate intake (LeMagnen, 1971; Peck, 1978; Kratz and Levitsky; 1979; Mook, 1963; Davis, et al., 1975), as well as inhibit intake of the same substance, such as sucrose (Mook, 1974; Gentile, 1968). I have recently completed a series of experiments which clarify the respective roles of gustatory and trigeminal inputs in the facilitation and inhibition of food intake (Jacquin and Zeigler, 1979). By examining meal patterns in gustatory deafferented rats using semi-liquid rat chow mash, it's been shown that meal duration is significantly reduced below control levels, thus directly implicating gustation in the facilitation of intake. If gustatory inputs were involved in intake inhibition, then one would've expected meal duration to increase. In fact, this is precisely what occurred following trigeminal orosensory deafferentation, thus directly implicating trigeminal inputs in intake inhibition. However, the homeostatic model cannot account for the decreases in meal initiation produced by both deafferentation procedures. Orosensory factors must play a critical role in additional mechanisms responsible for the initiation of feeding behavior. Nor does the homeostatic model provide the mechanisms by which gustation and orosomatosensation facilitate and inhibit intake.

C. Reinforcement

As distinguished from facilitation, reinforcement refers to that which increases the probability of a response as a consequence of its presentation. Within various learning paradigms, it has been repeatedly demonstrated that orosensation, namely taste, is a powerful reinforcer of operant behavior (e.g. Sheffield and Roby, 1950; Guttman, 1953; Schlosberg and Pratt; 1956). Other work has shown that trigeminal inputs play a critical role in food or water reinforced lever pressing (Jacquin, 1978). The present results suggest that gustatory and trigeminal inputs are also potent reinforcers of eating and drinking behaviors, both in their initiation and in their maintenance. A similar conclusion has been reached by Snowdon (1969) in attempting to explain the reduced meal durations of intragastric feeding rats, as well as by Miller, et al. (1978) in attempting to explain the reduced meal frequency of trigeminal deafferented pigeons.

D. Incentive

As well as their role in reinforcing feeding and drinking, it is clear that orosensory stimuli have another function which is essentially motivational. The evidence for this statement comes from studies varying the quantity or quality of food reinforcement, particularly those studies in which the quantity or quality of reinforcement is changed during the course of a learning experiment (Crespi, 1944; Zeaman, 1949a,b; Guttman, 1953). These studies have shown that changes in these reinforcement parameters produces changes in performance which seem best described as the result of motivational (incentive) effects. It is also clear that stimuli present in the goal box or food magazine can acquire incentive properties and serve as secondary reinforcers (Estes, 1948).

The fact that a reinforcing stimulus can also function as an incentive poses certain theoretical problems. How do secondary reinforcing stimuli serve in these double and essentially opposite functions? How is experience with a reinforcer translated into incentive? How does experience which coincides with the termination of behavior come to contribute to the initiation of the response in a different situation?

In an attempt to reconcile these problems, both Seward (1950, 1951, 1952) and Spence (1956) have proposed that incentive motivation arises through the classical conditioning of a goal response, R_g, to the stimuli in the reinforcement situation. Thus, these theories contain the proposition that the operations for producing incentive motivation are the same as those for producing secondary reinforcement. In order to account for the functioning of incentives in places remote from the original conditioning situation, these theorists employed the concept of stimulus generalization. To the extent that the stimuli in the start situation are similar to those in the reinforcement situation, there is a tendency for the goal reaction (R_g) to be elicited. Since the primary reinforcer is absent, only a fractional component (r_g) of the complete goal response can occur. It is this fractional anticipatory goal reaction which is regarded as having motivational properties in initiating and maintaining the animal's behavior. Why r_g should have incentive properties remains a question (see Seward, 1956, Spence, 1956, and Hull, 1943, for possible mechanisms).

A growing body of evidence suggests that anticipatory responses and the stimuli they generate are indeed the immediate determinants of food-related incentive motivation (Jacquin, in preparation). In fact, these studies suggest that trigeminal orosensory deafferentation reduces or abolishes the flow of phasic sensory input that is a necessary accompaniment of food reinforced operant behavior. Fractional anticipatory goal responses, namely chewing and incisor bruxism, either might not occur, or the cutaneous feedback resulting from such activities are not experienced, resulting in an aborted operant sequence. These events may be necessary to bind the operant sequence together. These conclusions are based largely upon the fact that removing the ability to perform masticatory movement severely disrupts "scooping" patterns and food reinforced lever pressing.

Following trigeminal motor root sections, meal frequency and meal duration are drastically reduced in the "scooping" paradigm, despite impending starvation; while hypoglossal nerve sections do not disrupt meal patterns. When tested in a food reinforced lever pressing situation, trigeminal motor root animals perform at a very low level; in fact, usually below the level achieved by deafferented rats. Hypoglossal sections have no effect. It is important to note that neither "motor" animal ingest food or water, yet their response rates are strikingly different. How do these two preparations differ? The hypoglossal rat is capable of performing pre-feeding jaw movements, while the trigeminal motor root animal is not. The operant deficits seen after trigeminal motor root section may, therefore, reflect a functional deafferentation produced by removal of somatosensory inputs which normally occur as feedback from jaw-related prefeeding or fractional anticipatory goal responses.

Additional evidence provides support for a masticatory r_g and its concomitant somatosensory feedback as the basis for food incentive: (1) The similarities between the effects of deafferentation and motor root section suggests that they are mediated by disruptions of a common mechanism. (2) The operant findings are consistent with the frequent observation that oromotor responses (biting, licking, chewing) may play an important role in sustaining operant behaviors reinforced by intragastric self-injection procedures (Holman, 1969; Snowdon, 1969; Kissileff, 1973; Altar and Carlisle, 1979). (3) Masticatory movements do occur prior to feeding on solid food in the normal approach sequence of the adult rat. Similarly, developmental studies (Shuleikina, 1978, personal communication; Hall, 1979; Mateer, 1918, as cited by Wyrwicka, 1967) indicate that these mouthing movements occur prior to food contact in the rat, cat, and human neonate. Moreover, Shuleikina has found that chewing movements become classically conditioned to the food source prior to ingestion in the kitten. Recording EMG's from the masticatory muscles, she has shown that in development pre-feeding chewing movements occur farther and farther away from the food source until they become preparatory to lever pressing. It may be that these movements and their concomitant somatosensory feedback become the necessary component of the lever pressing sequence, especially since Ellison and Konorski (1964) have shown that conditioned salivation is not necessary for the initiation and maintenance of food reinforced lever pressing.

I would therefore hypothesize that feeding and drinking first appear in development as operant behavior (see Johanson and Hall, 1979), but later become classically conditioned to stimuli coincident with ingestion. These conditioned stimuli gradually assume necessary functions in maintaining the approach sequence to food and water (such as taste, olfactory, and tactile cues). Operant lever pressing, in the adult, could therefore represent a similar developmental sequence where conditioned stimuli serve to bind the sequence together. Jaw movement-produced somatosensory feedback must be considered a likely candidate. Data presented by Konorski (1967) supports this hypothesis. In two groups of dogs conditioned responses (CR) were established by reinforcing a conditioned stimulus (CS), by either presenting the bowl with diluted milk, or introducing this fluid directly into the mouth through a hole made in the cheek. It was found that whereas in the first instance the CR consisted mainly of the posture of expectation, in the second instance the vigorous mouthing movements and even swallowing movements were observed in response to the CS. The CR became so similar to the UR that by observation of the behavior of the animal it was impossible to tell at which moment the fluid was introduced into the mouth. Our lever may represent a similar CS. Obviously, the mode of reinforcement delivery, the temporal contiguity, and the amount of experience in a given ingestive situation will determine the necessity of certain CS's in operant and consummatory behavior. (For additional experiments suggesting a role for oromotor produced feedback in ingestive behavior see Wyrwicka, 1967; Rodgers, et al., 1965; Castro, 1972; Morgane, 1969; Sclafani, et al., 1973; Levine, 1977; Robins, 1977; Patten and Rudy, 1967.)

In any event, the oromotor nerve section data suggests certain testable hypotheses which, if borne out, will show that food and water are not prepotent reinforcers, but provide incentive via masticatory r_g's. Further research might document that trigeminal deafferentation reduces intake by eliminating factors necessary for incentive motivation.

E. Food Conditioning

A disruption in the "oral metering" of intake could account for the changes in intake patterns of deafferented rats. If oral factors do act as conditioned stimuli which allow for adjustments of meal size and frequency to postabsorptive consequences (LeMagnen, 1971; Booth, et al., 1972, 1976; Rozin and Kalat, 1971; Snowdon, 1969; Miller, et al., 1978), then severing the link would disrupt meal patterns, presumably increasing meal duration and subsequently decreasing meal frequency. In fact, Miller, et al. have shown that trigeminal deafferentation in the pigeon decreases meal frequency and increases meal duration. They hypothesize that the removal of trigeminal orosensory stimuli:

(1) decreases the incentive value of food which results in fewer meals initiated; and (2) disrupts the link between oral stimulation and delayed systemic effects which normally terminate the meal, switching the termination controls from conditioned oral cues to crop distension. Similar changes in meal patterns are seen in the trigeminal deafferented rat (Jacquin and Zeigler, 1979) and could be explained by a similar hypothesis.

Powley (1977) has recently reviewed the evidence suggesting that gustatory and olfactory stimulation triggers immediate systemic effects (cephalic reflexes), that could provide the contiguity necessary for food conditioning. Gustatory stimuli may therefore serve as "releasers" of cephalic reflexes, such as insulin release, thereby explaining the intake deficits produced by gustatory deafferentation. Powley has hypothesized that oral stimuli act on hypersensitive cephalic reflex chains to produce ventromedial hypothalamic obesity (but see Sclafani, et al., 1979). It is conceiveable that gustatory deafferentation produces the opposite effect upon visceral responses, resulting in decreased intake.

F. General "Activation"

The present results could also be interpreted as the result of decreased responsiveness to all external stimulation, if orosensory stimulation does serve a tonic activating function. This has been suggested by Wolgin and Teitelbaum (1978) in attempting to explain the anorexia of hypothalamic cats. Recent experiments suggest that this may indeed be the case; orosensory deafferentation effects may not be specific to ingestive behavior (Jacquin, Olazabal, and Zeigler, in preparation). A group of trigeminal deafferented rats provided data on the frequency of grooming and rearing bouts during the first hour after being placed in an observation cage and the first hour after the lights went out. Significant decreases in both of these noningestive behaviors was observed. A second group of animals were tested for activity deficits. Trigeminal deafferentation resulted in striking reductions in wheel running throughout the 50 days of postoperative testing. Interestingly, gustatory deafferentation also produced marked reductions in activity, unattributable to surgical artifacts. The extent of these reductions is even more astounding in view of the fact that similar weight losses had a facilitatory effect on wheel running in a separate control group. However, these data may be confounded by the possibility that activity and the incentives to ingest are interrelated.

Thus, deafferentation may reduce or abolish a tonic flow of sensory input crucial for general "activation". Zeigler (1975a) has suggested that the deafferented pigeon's reduced food intake is due to a "reduction in the tonic trigeminal sensory input that normally reaches the central nervous system during the act of eating" (p.835). However, this hypothesis is only applicable to situations where some intake is achieved; e.g. with semi-liquid foods where tonic inputs could play an important role. What it cannot do is account for the lack of responsiveness to solid foods that are not taken into the mouth. As Zeigler points out, this may be indicative of a general loss of excitability in the sensorimotor systems underlying ingestion or it may reflect the disruption of processes specific to the neural control of ingestion. The data presented in this experiment, as well as anatomical considerations, suggest the former. Unlike the pigeon, the trigeminal deafferented rat exhibits its most profound reductions in food intake coincident with disruptions in other behaviors, such as activity, drinking, grooming, rearing, biting attack, licking, gnawing, taste sensitivity, and undoubtedly others I haven't looked at. The behavioral lack of specificity, in conjunction with the massive removal of brainstem reticular formation inputs (Darien-Smith, 1973) and transynaptic degeneration into brainstem trigeminal nuclei (Grant and Arvidson, 1975) make it likely that trigeminal orosensory deafferentation produces effects upon ingestive behavior, at least in part, by reducing the excitability of the interneurons and motoneurons that normally participate in all oromotor activity. The specificity of the behavioral deficits produced by gustatory deafferentation remain to be explored.

Orality Reconsidered

From the time of Bernard (1878) many workers have been attracted to the notion of internal constancy, i.e. independence from external stimuli. Because of its parsimonious nature, the "internal homeostatic model" grew to incorporate ingestive behavior. The nature of the internal changes responsible for the initiation of nutrient intake usually were considered as part of the problem of "motivation". In time, "motivation" came to refer to a concrete mechanism underlying behavior, thus the advent of "drive theory". Animals were believed to respond to food and water because an internal deficit signal produced a state of "drive", or "central exitatory state", which predisposed the organism to respond more vigorously to external stimuli (Lashley, 1938; Stellar, 1954; Dethier, et al., 1965). At the extreme, Hull (1943) believed that "drive reduction" was the essence of reinforcement, thus increasing the probability that the behavioral sequence would be repeated.

Formidable support for the "drive" notion came from studies of CNS lesion effects upon ingestive behavior; destruction of the lateral hypothalamus produced aphagia and adipsia while destruction of the ventromedial hypothalamus produced hyperphagia (Anand and Brobeck, 1951; Teitelbaum, 1955). The categorization of these behavioral deficits generalized to the embodiment of causal mechanisms within the CNS; the LH turned on feeding and the VMH turned it off. Orosensory inputs were discounted as a contributing factor to the quantitative control of ingestive behavior in view of the following: peripheral orosensory nerve sections produced "no effect" upon water intake in dogs (Bellows and VanWagenen, 1939); normal nutrient intake was achieved when rats pressed a lever to inject food or water directly into the stomach (Epstein, 1960; Epstein and Teitelbaum, 1962); and animals continued to regulate despite adulteration of the taste and caloric properties of the diet (Teitelbaum, 1955; Teitelbaum and Epstein, 1962). The prominent theory in the 1960's was, therefore, an internal homeostatic one, with orosensation believed to contribute little to hypothalamic monitoring of internal deficit signals and quantitative intake control (Epstein, 1967). However, in their zeal to repudiate the "peripheralists", they may have "thrown out the baby with the bath water" (Blass and Hall, 1976).

Evidence in support of the "centralist" position has since come under close scrutiny. Bellows, a physiologist, was so earnest in his attempts to discredit Cannon's "dry mouth" theory of thirst that he ignored his own data: a significant depression in food and water intake following trigeminal deafferentation (Bellows and VanWagenen, 1939). In addition, reexamination of the intragastric self-injection phenomenon has revealed a powerful orosensory component (Holman, 1969; Snowdon, 1969; Kissileff, 1973; Altar and Carlisle, 1979). Interestingly, the effects upon ingestive behavior produced by gustatory deafferentation resemble in degree and kind the effects upon lever pressing seen when rats are shifted from oral to intragastric reinforcement: reduced food intake to about 75% of normal levels and smaller meals. This similarity is not surprising since the intragastric procedure constitutes a reversible deafferentation of gustatory receptors.

Similarly, it is becoming increasingly clear that no unitary interpretation of the LH or VMH syndromes is likely to be satisfactory because neither syndrome reflects a unitary phenomenon (Epstein, 1971; Zeigler, 1976; Powley, 1977). In fact, reexamination of the anatomical, physiological, and behavioral aspects of the LH syndrome has revealed a significant orosensorimotor denervation. Pontine gustatory neurons traverse the LH (Norgren, 1976; Norgren and Leonard, 1973), as do trigeminal lemniscal fibers (Smith, 1973), as do neurons with olfactory input in the piriform cortex and olfactory tubercle (Scott and Chafin, 1975; Scott and Leonard, 1971). LH lesions produce degeneration in gustatory and trigeminal sensory and motor nerve nuclei (Mufson, et al., 1976; Mufson and Riss, 1977). Neurophysiological evidence indicates that both olfactory and gustatory neurons influence LH neurons (Norgren, 1970; Scott and Pfaffmann, 1967, 1972), and that pontine neurons which respond to orosomatosensory stimuli have direct pathways to the LH (Norgren 1974). Moreover, many studies have physiologically demonstrated alveolar inputs passing through the LH (Wyrwicka, 1969; Takaori, et al., 1968; Wyrwicka and Chase, 1970). It is not surprising, therefore, that neurobehavioral studies have implicated orosensorimotor dysfunction as a crucial component of the LH syndrome (Marshall, et al., 1971; Turner, 1973; Marshall and Teitelbaum, 1974; Marshall, et al., 1974; Wolgin and Teitelbaum, 1978; Stricker and Zigmond, 1976; O'Laughlin and Feldman, 1976; Wyrwicka, et al., 1975; Zeigler and Karten, 1974). Furthermore, since the lower brainstem has been shown to be independently capable of controlling the patterning and integration of ingestive behavior (Woods, 1964; Lovick, 1972; Grill and Norgren, 1978; Berntson and Micco, 1976), "the critical role of the hypothalamus may not be so much the establishment of basic response patterns, nor even the integration among such patterns, but rather the more refined development and elaboration of primitive behaviors and the establishment of additional sources of control over such responses" (Berntson and Micco, 1976, p.477). Thus, central behavioral systems do not directly activate rigid motor sequences, but rather facilitate complex sensorimotor mechanisms which are highly sensitive to stimulus cues of the environment and available goal objects, and generate responses appropriate to the stimulus situation.

The presently accepted viewpoint, therefore, is that gustatory stimulation does play a crucial role in intake control, though only when diet choices must be made (LeMagnen, 1971; Booth, et al., 1976), when incentives are required to elicit ingestion (Davis and Levine, 1977; Kissileff, 1973), and when the performance of the behaviors leading to food and water must be aroused and sustained (Teitelbaum and Epstein, 1962; Wolgin and Teitelbaum, 1978). The present work provides <u>direct</u> evidence suggesting that gustatory stimuli do not act alone in determining diet choice, incentive, and arousal; trigeminal orosensory inputs make a substantial contribution to the qualitative and quantitative control of intake. Specifically, both gustation and orosomatosensation are important in the <u>initiation</u>, maintenance, and termination of the meal, water intake, reinforcement processes, and the long-term regulation of body weight. The present findings suggest that we have seriously underestimated the significance of peripheral orosensory contributions to the quantitative control of hunger and thirst.

In fact, the historical emphasis placed upon taste in determining "palatability" may be unjustified, since the magnitude of the effects of trigeminal deafferentation upon the quantitative control of ingestive behavior is far greater than that produced by gustatory deafferentation. Thus, the "palatability" of food may reflect not only chemosensory properties, but somatosensory properties related to texture, viscosity, size, or even the simple fact that the diet can be ingested by licking rather than grasping and biting (Zeigler, 1981). To this day workers in the field of intake control insist that gustation represents the major source of exogenous stimulation. In discussing the mechanisms responsible for intake in the blowfly, rat, and human infant, Davis and Levine (1977) stressed that "*the* behavior responsible for getting food into the body is activated by chemoreceptors and can be driven at a rate which is proportional to the concentration of the stimulating substance" (p.381). The present data, as well as Miller's (1977, 1978b, 1979), suggest a reevaluation of the relative importance of these two sensory systems in determining intake in the rat.

Conclusions: Brain Mechanisms, Sensorimotor Processes, and the Problem of Motivation

Various dichotomous formulations have been used to describe motivational states and their causal basis. Harlow (1953) has spoken of "interoceptive" and "exteroceptive" controls, while Milner (1970) distinguished between "regulatory" and "nonregulatory" motivational variables. With regard to ingestive behavior, most writers insist on a firm distinction between "homeostatic" and "nonhomeostatic" factors (Falk, 1961; Adolph, et al., 1954; Kissileff, 1973). Pfaffmann (1961) has distinguished between the "sensory" and "motivating" properties of the sense of taste. Teitelbaum (1967) advanced the conceptual dichotomy between sensorimotor and motivational mechanisms in the control of behavior, which is best described by the following: "Clearly, when an act is a completely automatic consequence of a stimulus we need not speak of motivation. As long as a fixed, built-in relation exists between a stimulus and a response we have no justification for inferring the existence of a motivational state underlying the response to the stimulus...To infer motivation, we must break the fixed connection between stimulus and response. The(se) characteristics of the learned act - the arbitrary, essentially interchangeable nature of the act and of the stimulus that elicits it, as well as the measure of control the animal exerts over the response - distinguish it as a voluntary act...If an operant occurs motivation exists" (p.58). (Teitelbaum, though, has recently reversed his position on this issue; 1977.)

Unfortunately, dichotomous formulations have been used to explain behavior. While one may legitimately categorize behaviors along a continuum of complexity, it is unlikely that such schemes will provide insight into causal mechanisms. As Zeigler (1976, p.379) has pointed out: "the deficits in behavior seen after brain lesions can only be the result of a disruption in the normal mechanisms controlling that behavior. Exactly how 'higher-level' motivational deficits are presumed to be causally mediated - other than by the disruption of the normal spatiotemporal organization of eating behavior - was never satisfactorily explained."

Moreover, the peripheral approach to the study of ingestive behavior has not received its due attention largely because of the tenaciously held belief that sensorimotor and motivational mechanisms are embodied in separate neural structures; peripheral = "low level" sensorimotor processes, central = "high level" motivational processes. The present results do not verify this assumption, rather they point to the utility of a sensorimotor-reflex analysis as the key to understanding motivated behavior (Lashley, 1938). Zeigler (1981) has hypothesized that the mechanisms responsible for ingestive behavior are <u>isomorphic</u> with the sensorimotor processes involved. Our data support this interpretation. Trigeminal deafferentation, and to a lesser extent gustatory deafferentation, do produce effects which may be dissociated into sensorimotor or motivational deficits by appropriate behavioral techniques. However, deafferentation invariably produces both types of deficit.

An examination of CNS lesion studies and ingestive behavior in the rat reveals some interesting parallels between reported motivational disruptions and accompanying deficits in the consummatory response sequence (Box and Mogenson, 1975; Braun, 1975; Evered and Mogenson, 1976; Kolb and Nonneman, 1975; Kolb, et al., 1977; Levine, et al., 1971 ; Lyon, et al., 1968; Marshall, et al., 1974; Oakley, 1965; Parker and Feldman, 1967; Zigmond and Stricker, 1976; Wolf and DiCara, 1974; Wyrwicka, et al., 1975; Zeigler and Karten, 1974). In all of these cases, food or water intake deficits are reported which, at first glance, might be considered due to decreased hunger or thirst. However, remarkably similar sensorimotor deficits are also observed. While intraoral delivery of food or water always elicited lapping, chewing, and swallowing, food or water placed on the lip or perioral area failed to elicit mouth opening and/or tongue extension. All of these studies report particular difficulties in the rat's ability to grasp and manipulate rat chow pellets. Similarly, drinking from a sipper tube represents a difficult task. Many of these investigators also report the development of alternative modes of ingestive behavior, such as drinking in a contorted position, licking yet failing to make contact with the sipper tube, "scooping", "shoveling", or "cornering" of a food pellet. If intake is achieved, most authors report excessive spillage of water or food (crumbs). As you recall, all of these symptoms also occur following peripheral deafferentation, suggesting that these reports of reduced intake reflect similar disruptions of orosensory information at various levels of the neuraxis.

Our experiments suggest that a careful analysis of the sensorimotor capacities of neurologically damaged animals may provide insight into the causes of reduced food and water intake. Others have performed such refined analyses in centrally-lesioned rats exhibiting reduced food or water intake. As an example of the possibly subtle nature of the consummatory response deficit, and its concomitant reduced food intake, Evered and Mogenson (1977) clarified the deficits mediating reduced water intake of rats with zona incerta lesions. The zona incerta is part of an intricate network receiving neural connections from the substantia nigra, globus pallidus, the principal trigeminal sensory nucleus, and the gustatory parabrachial nucleus (Huang and Mogenson, 1972; Lidsky, et al., 1975; Smith, 1973; Norgren and Leonard, 1973).

Rats with zona incerta lesions drink normally following intracellular or extracellular dehydration, yet exhibit reductions in daily water intake, suggesting a specific impairment in secondary drinking. A microanalysis of drinking patterns indicated that these rats made as many or more laps at the drinking tube as controls, but obtained less liquid per lap. Evered and Mogenson concluded that the lesions impaired the sensorimotor control of drinking and the subsequent reduction in drinking efficiency was the cause of the attenuated water intake. Thus, what looked like a motivational deficit was mediated by subtle impairments in the act of lapping; the zona incerta may participate in the control of oromotor activity by integrating various sources of orosensory inputs. Similarly, the basal ganglia appear to be involved in the proper orientation of the head with respect to food and water and coordinated oromotor activity (Levine, et al., 1971; Lidsky, et al., 1978). Thus, the CNS appears to be hierarchically organized to handle various aspects of neurosensory inputs and modulate outputs of increasing orders of complexity; i.e. the mechanisms underlying sensorimotor and motivational processes do not require different neural structures. This notion has been repeatedly emphasized by Zeigler (1976, 1981).

Despite widespread adherence to a sensorimotor vs. motivational dichotomy, some workers are beginning to take note of the inadequacies of such an approach. For example, Mook (1974) found that while saccharin-sweetened water is preferred to plain water, saccharin-sweetened food is rarely preferred to bland food. He hypothesized that when sweetness is a redundant cue in food or water recognition, it is ignored; thus, the sensorimotor vs. motivational distinction cannot hold in explaining intake. "What seems to be a hedonic or motivating aspect of the sweet taste may actually reduce to its sensory (or discriminative, or releasing) aspect" (p.485). Fitzsimons (1972) has gone as far as to say that oropharyngeal factors enable the animal to anticipate its future water requirements and, therefore, must be considered a critical regulatory, or homeostatic, mechanism. Obviously, the magnitude of the deficits produced by orosensory deafferentation suggest a reevaluation of the commonly accepted notion of orosensation as a non-homeostatic mechanism.

Findings such as these suggest the need for a careful analysis of peripheral and central interactions in the control of vertebrate ingestive behavior. Future physiological and behavioral research must address the question of how particular sensory messages are converted into potent determinants of behavior.

FIGURE 1

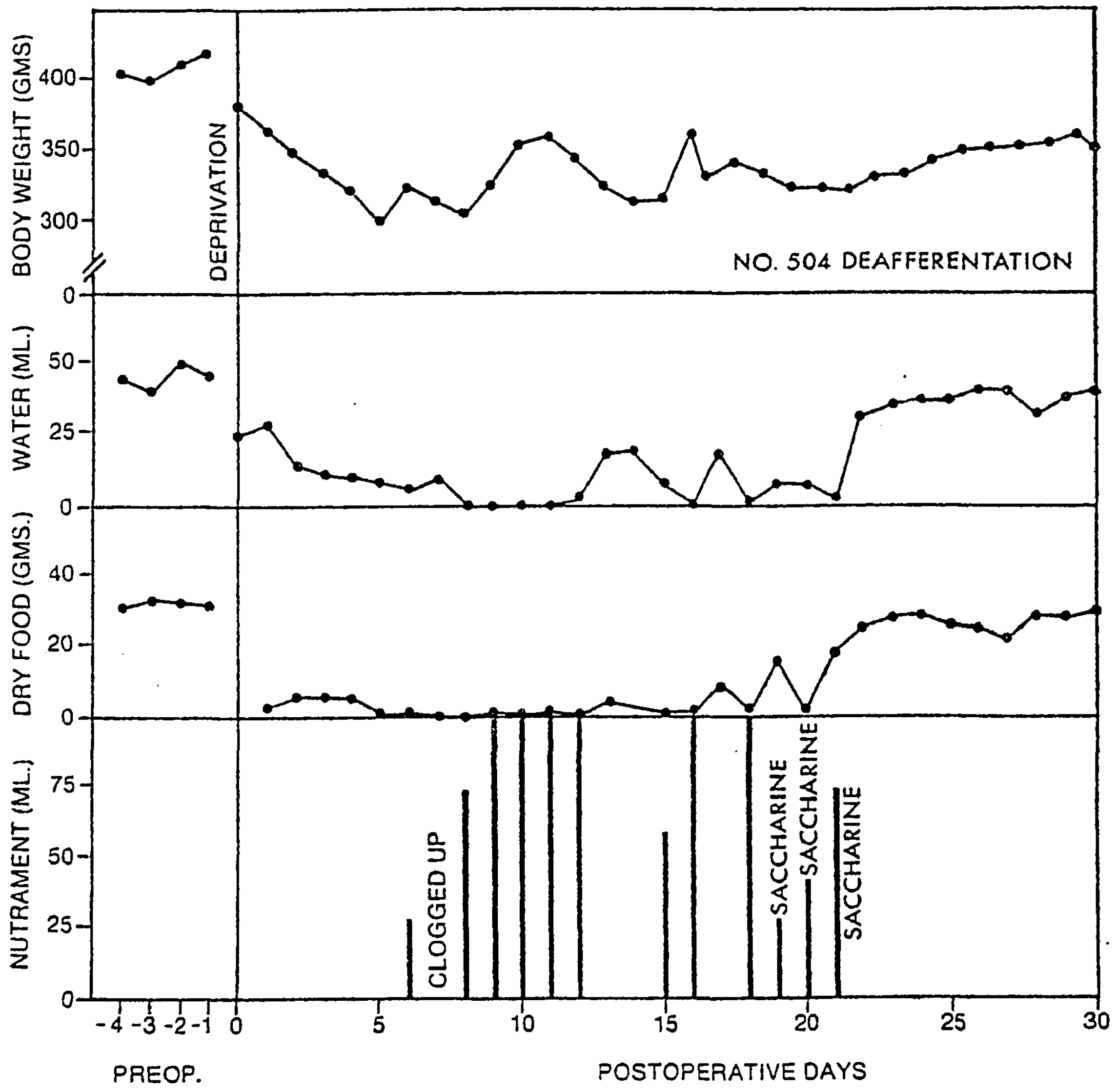
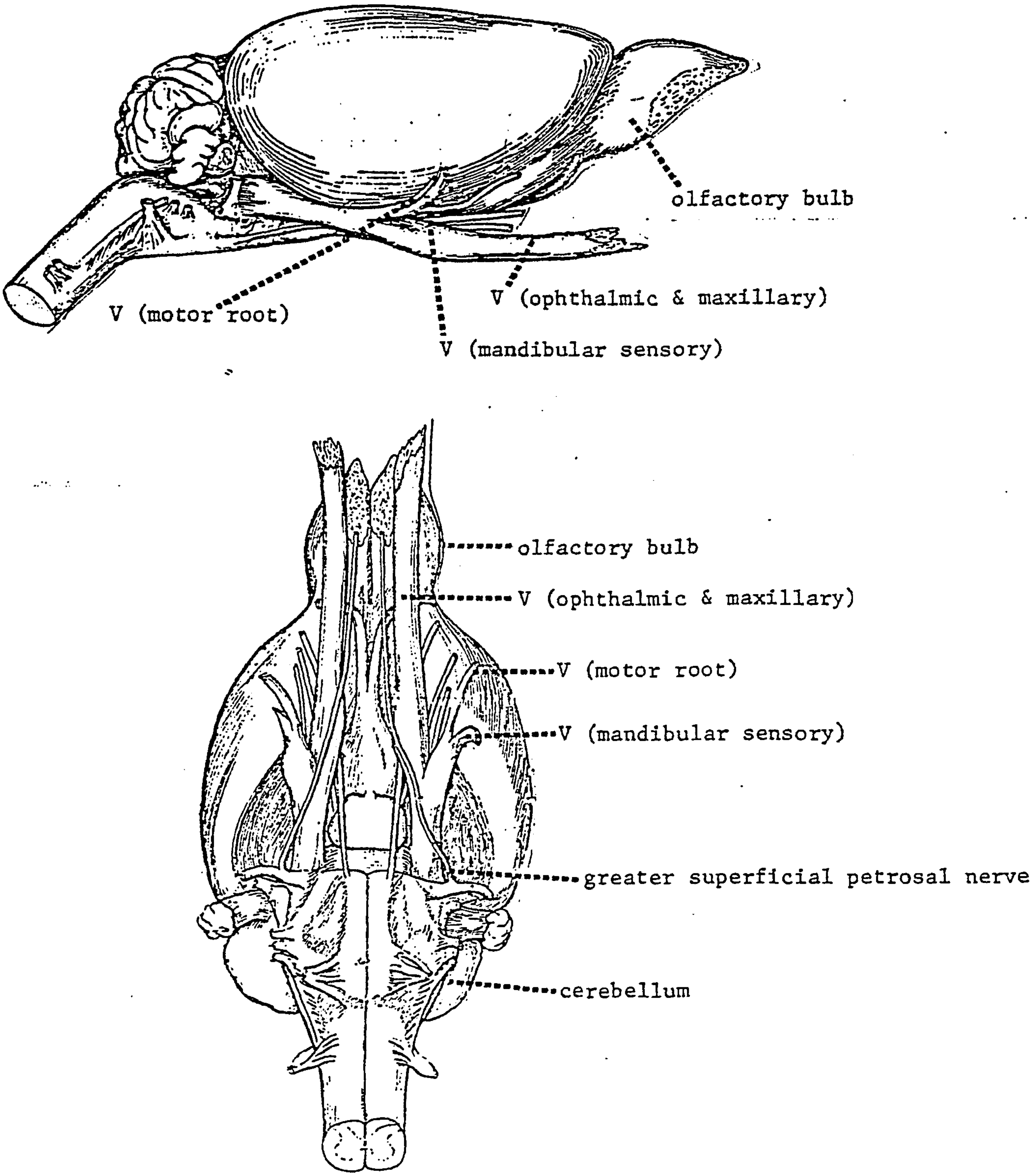

BODY WEIGHT (GMS)
400
350
300
0
WATER (ML.)
50
25
0
DRY FOOD (GMS.)
40
20
0
NUTRAMENT (ML.)
75
50
25
0
DEPRIVATION
NO. 504 DEAFFERENTATION
CLOGGED UP
SACCHARINE
SACCHARINE
SACCHARINE
-4 -3 -2 -1 0
5
10
15
20
25
30
PREOP.
POSTOPERATIVE DAYS

FIGURE 2


olfactory bulb
V (motor root)
V (ophthalmic & maxillary)
V (mandibular sensory)
olfactory bulb
V (ophthalmic & maxillary)
V (motor root)
V (mandibular sensory)
greater superficial petrosal nerve
cerebellum

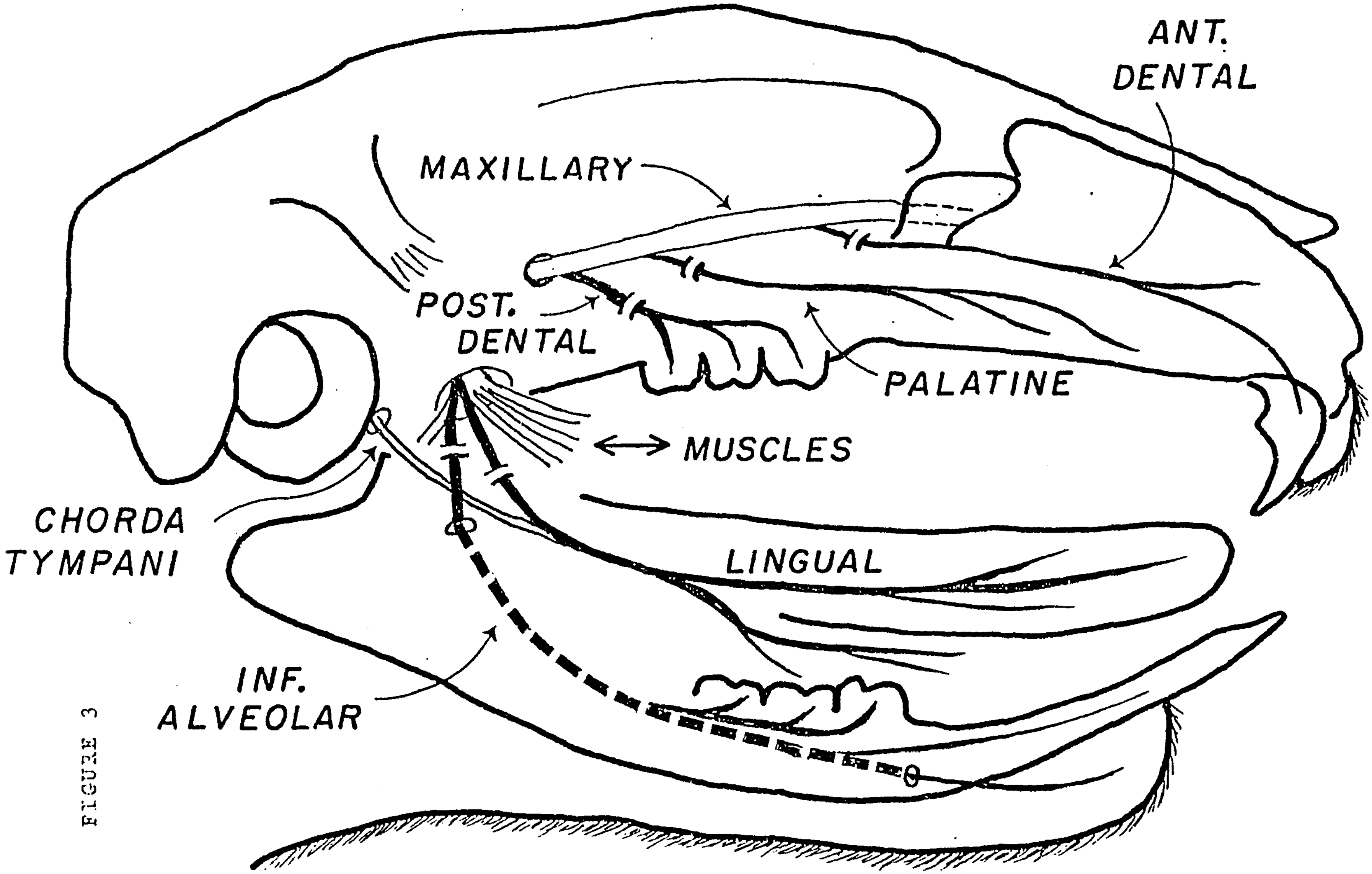

ANT. DENTAL
MAXILLARY
POST. DENTAL
PALATINE
MUSCLES
CHORDA TYMPANI
LINGUAL
INF. ALVEOLAR

FIGURE 3

FIGURE 4

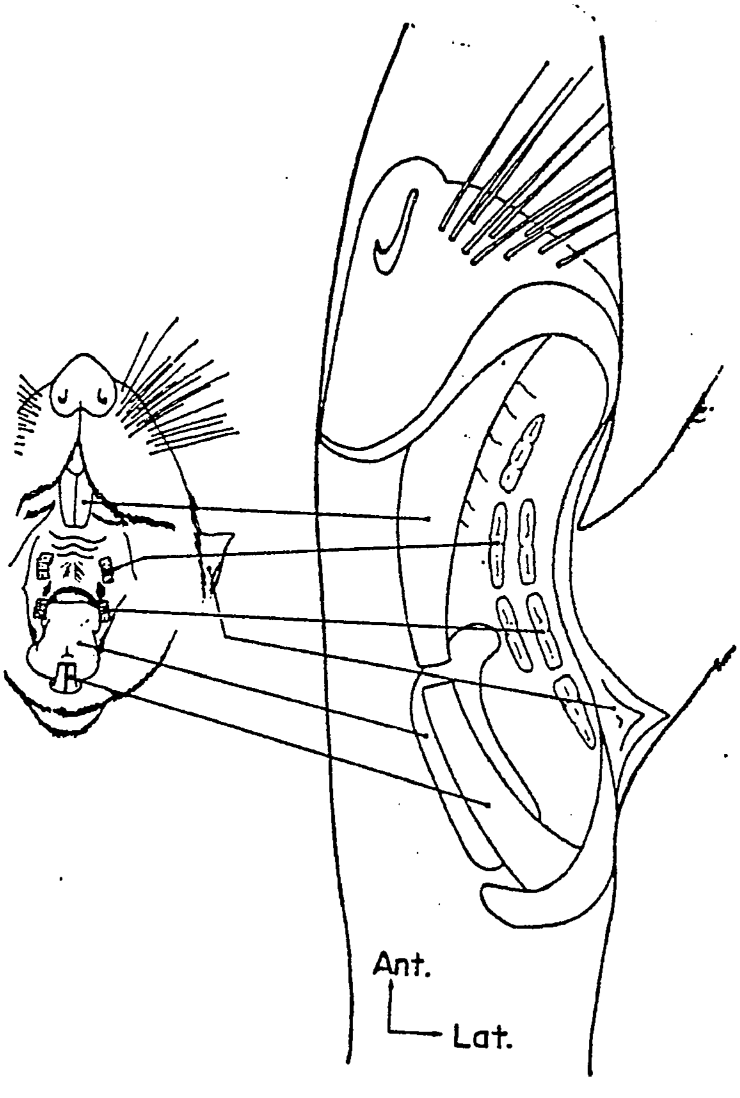


FIGURE 5

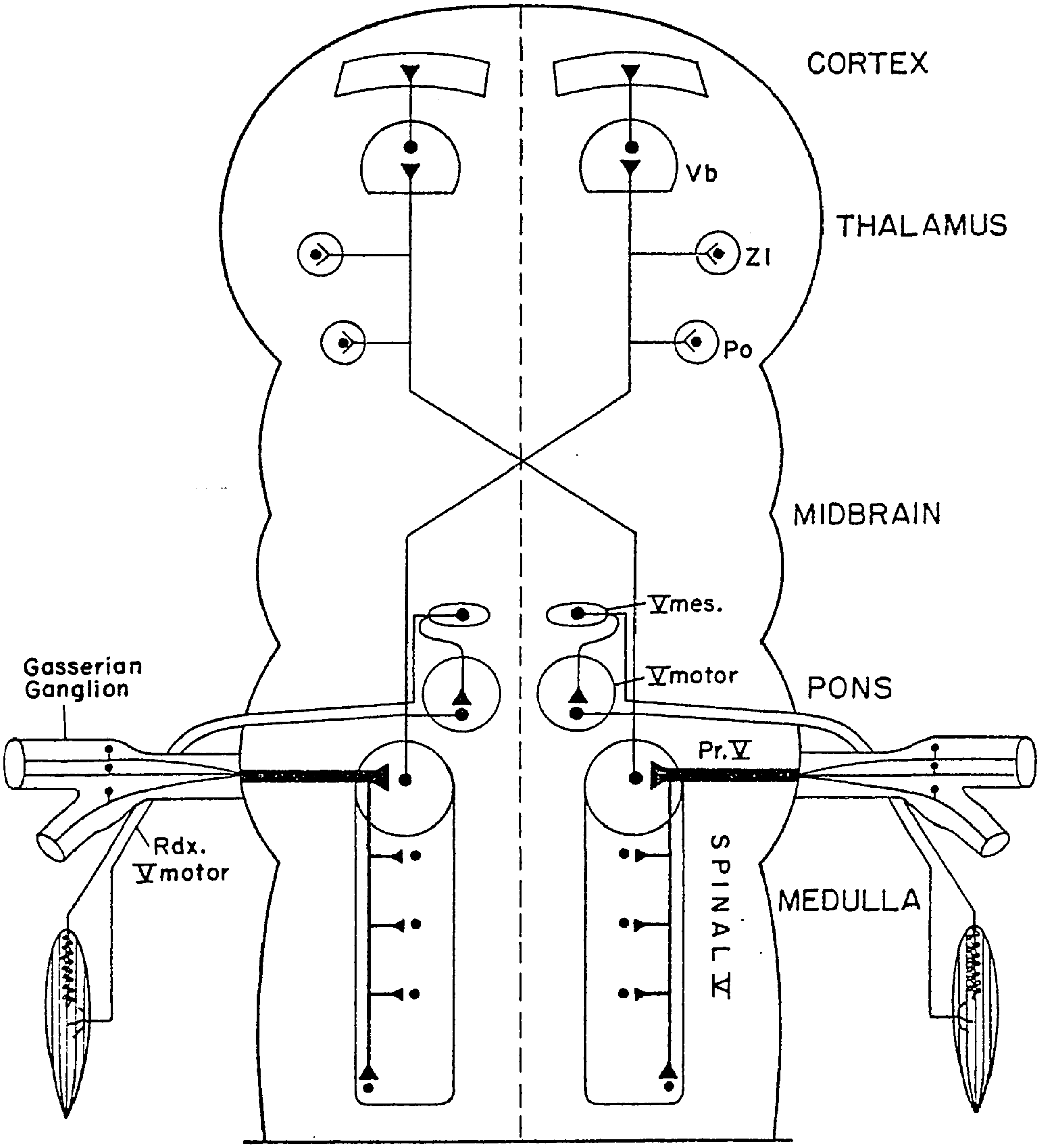

CORTEX
Vb
THALAMUS
ZI
Po
MIDBRAIN
Ṿmes.
Gasserian Ganglion
Ṿmotor
PONS
Pr.Ṿ
Rdx. Ṿmotor
SPINAL Ṿ
MEDULLA

FIGURE 6

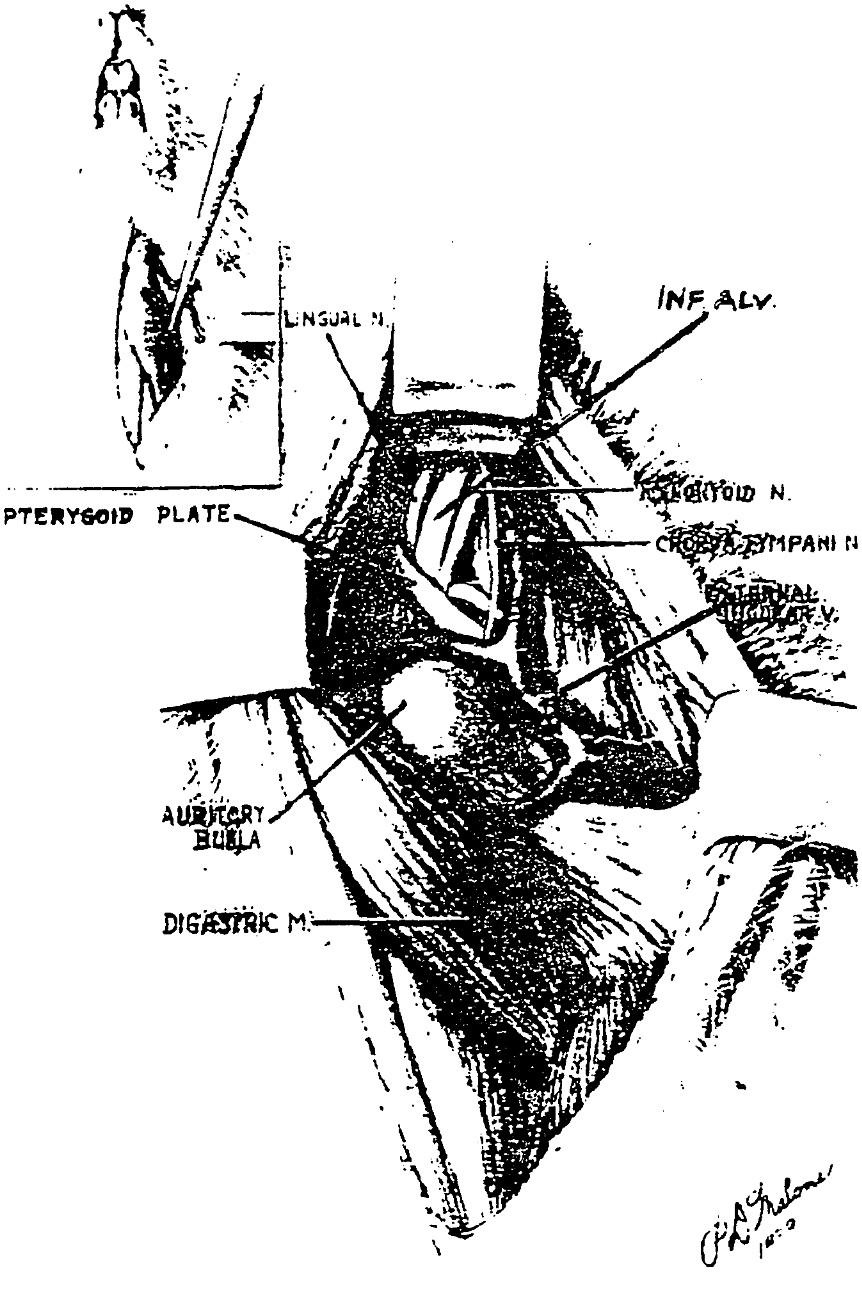
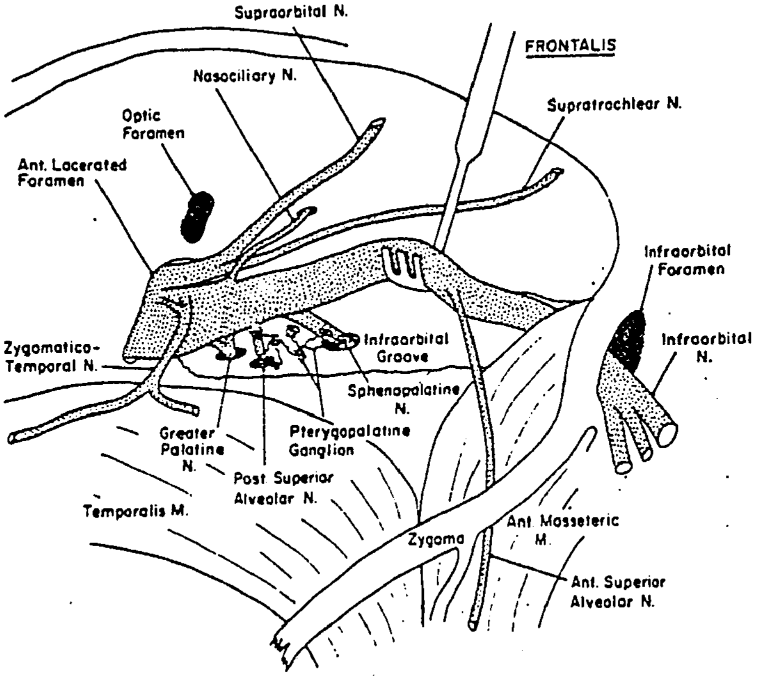

LINGUAL N.
INF. ALV.
MYLOHYOID N.
PTERYGOID PLATE
CHORDA TYMPANI N
EXTERNAL JUGULAR V.
AUDITORY BULLA
DIGASTRIC M.

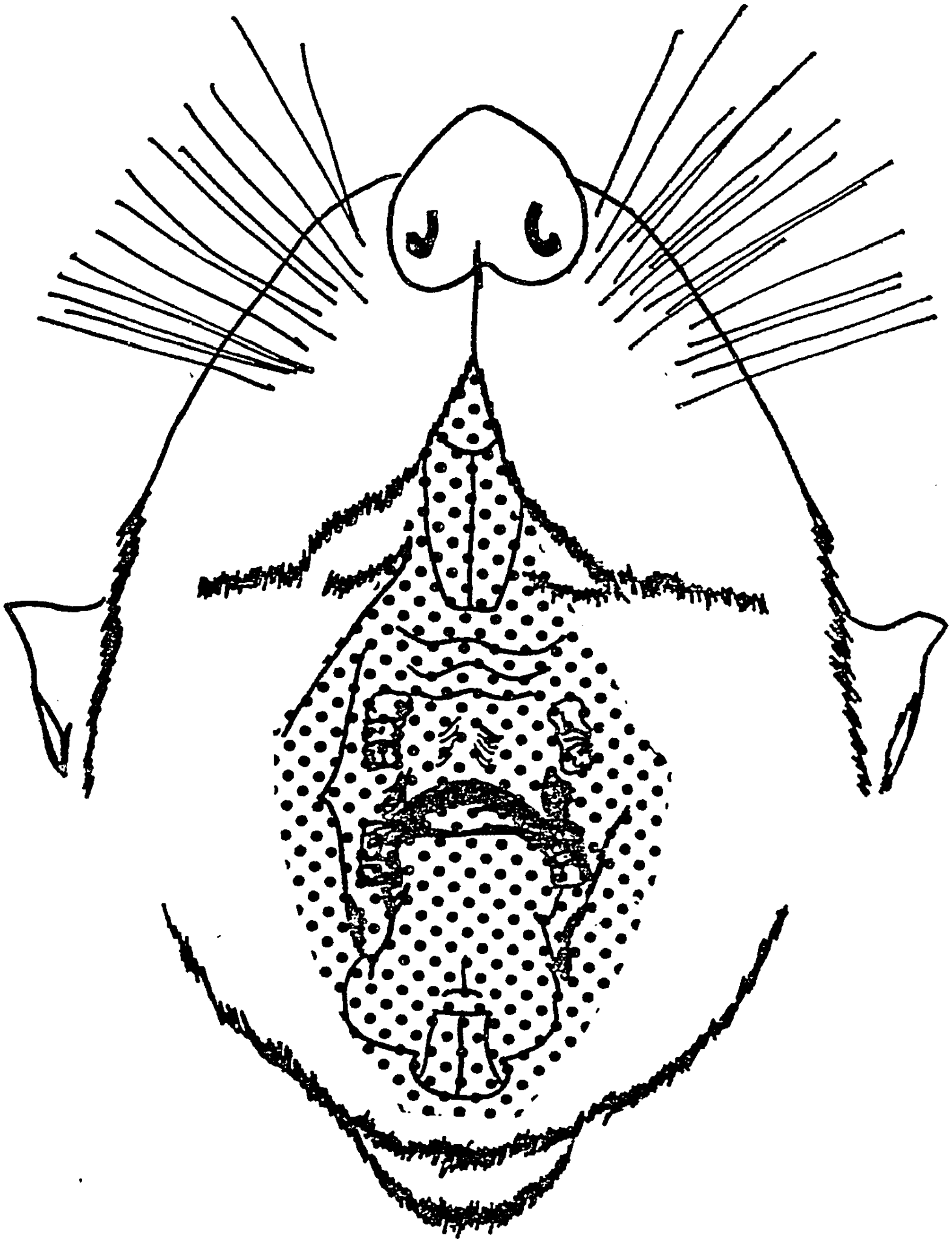
FIGURE 7



Exposed regions after surgical procedure.

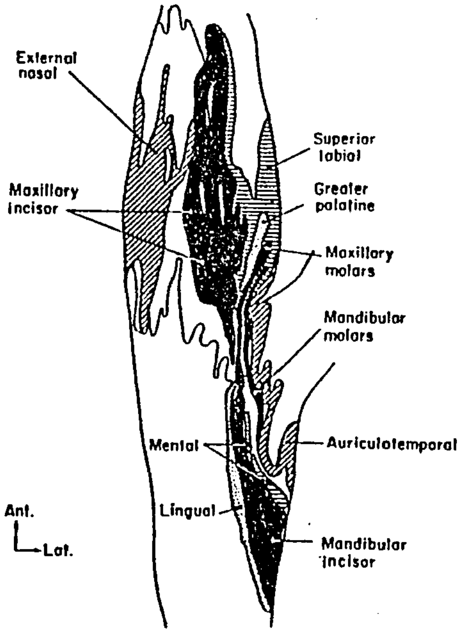
J Dent Res March–April 1973, Vol 52 No. 2

FIGURE 8



CHROMATOLYTIC CELLS

(Gregg & Dixon, 1973)



HRP

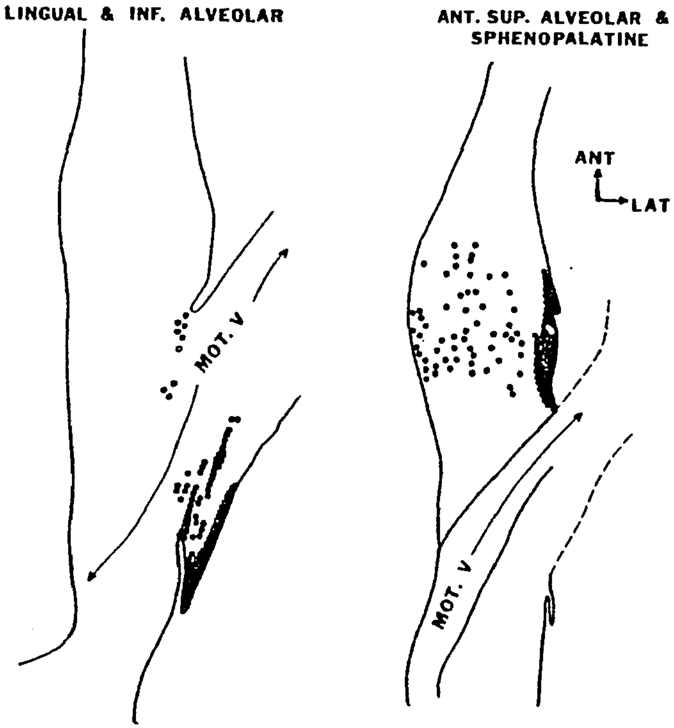
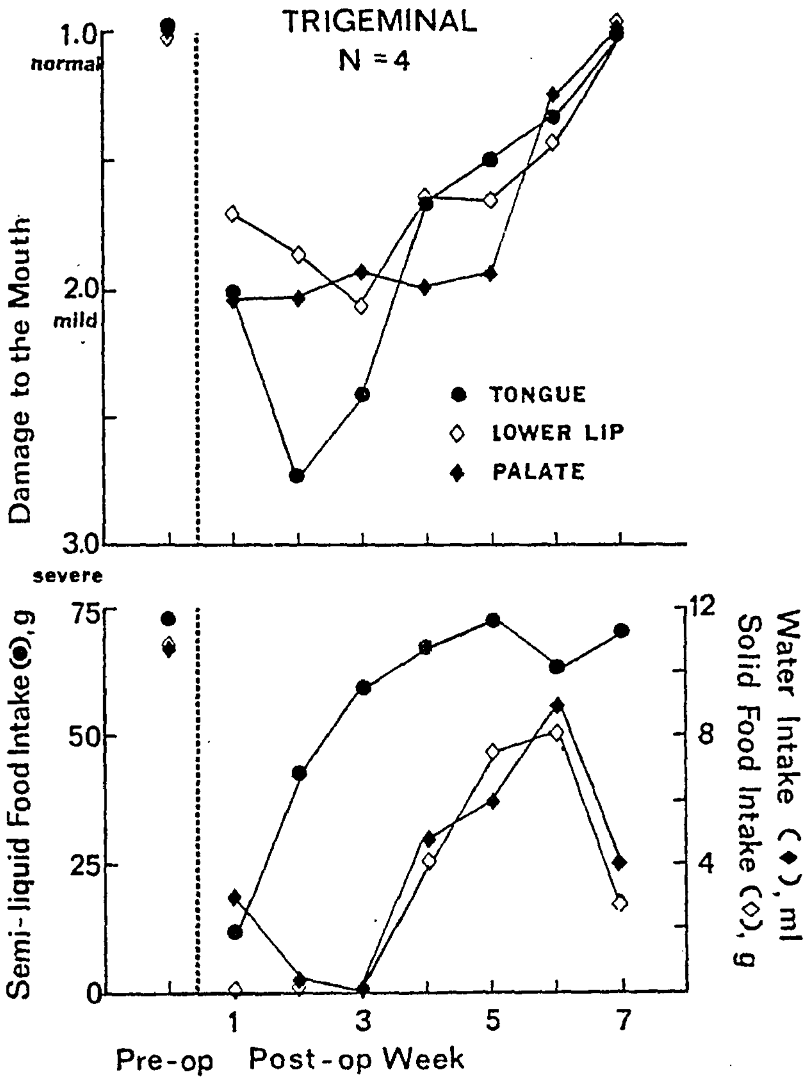


FIGURE 9

FIGURE 10


TRIGEMINAL
N = 4
Damage to the Mouth
1.0
normal
2.0
mild
3.0
severe
● TONGUE
◇ LOWER LIP
◆ PALATE
Semi-liquid Food Intake (●), g
75
50
25
0
12
8
4
Water Intake (◆), ml
Solid Food Intake (◇), g
1
3
5
7
Pre-op
Post-op Week

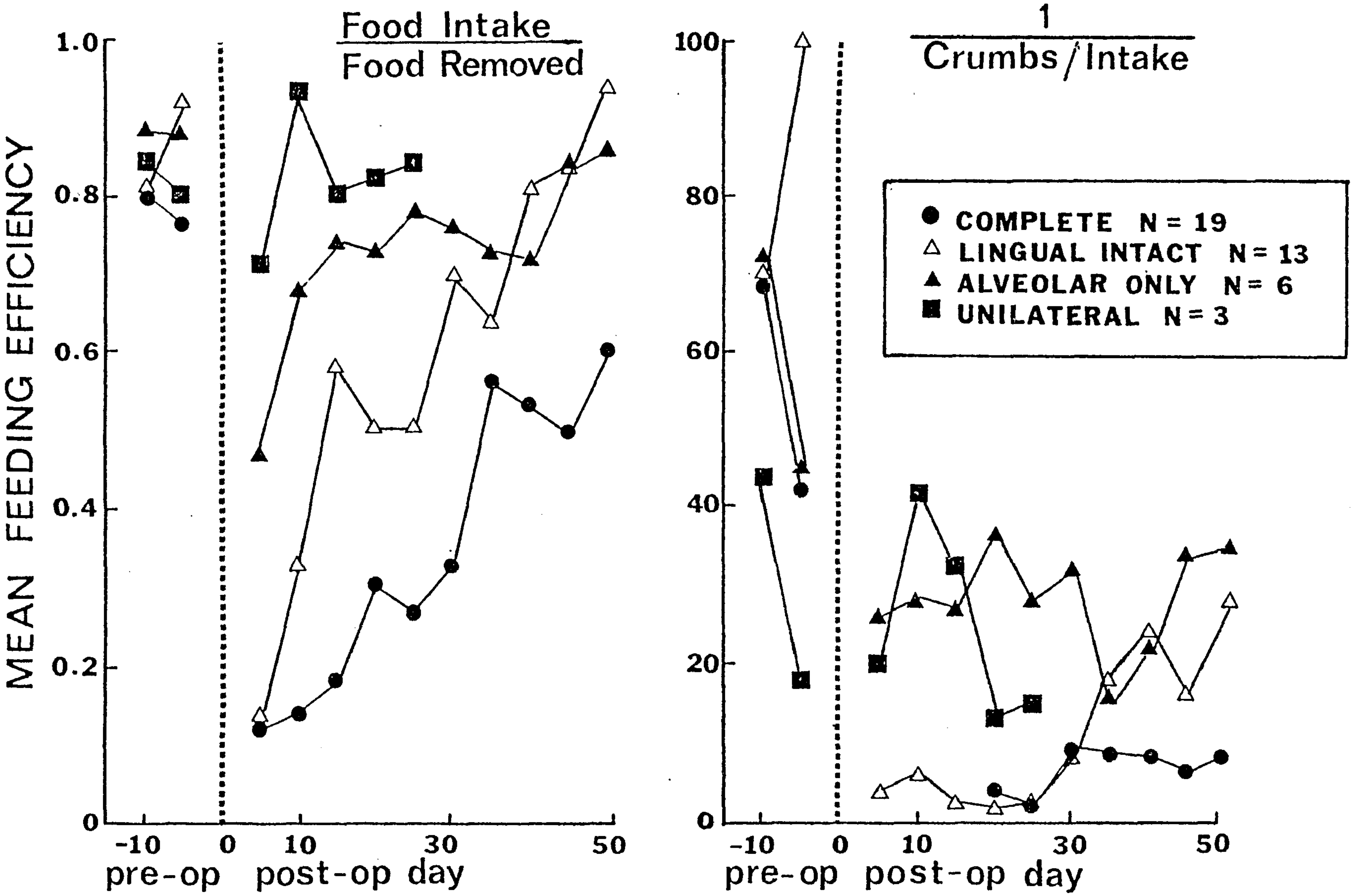

MEAN FEEDING EFFICIENCY
Food Intake / Food Removed
1.0
0.8
0.6
0.4
0.2
0
-10
0
10
30
50
pre-op post-op day
1 / Crumbs/Intake
100
80
60
40
20
0
-10
0
10
30
50
pre-op post-op day
● COMPLETE N = 19
△ LINGUAL INTACT N = 13
▲ ALVEOLAR ONLY N = 6
■ UNILATERAL N = 3

FIGURE 11

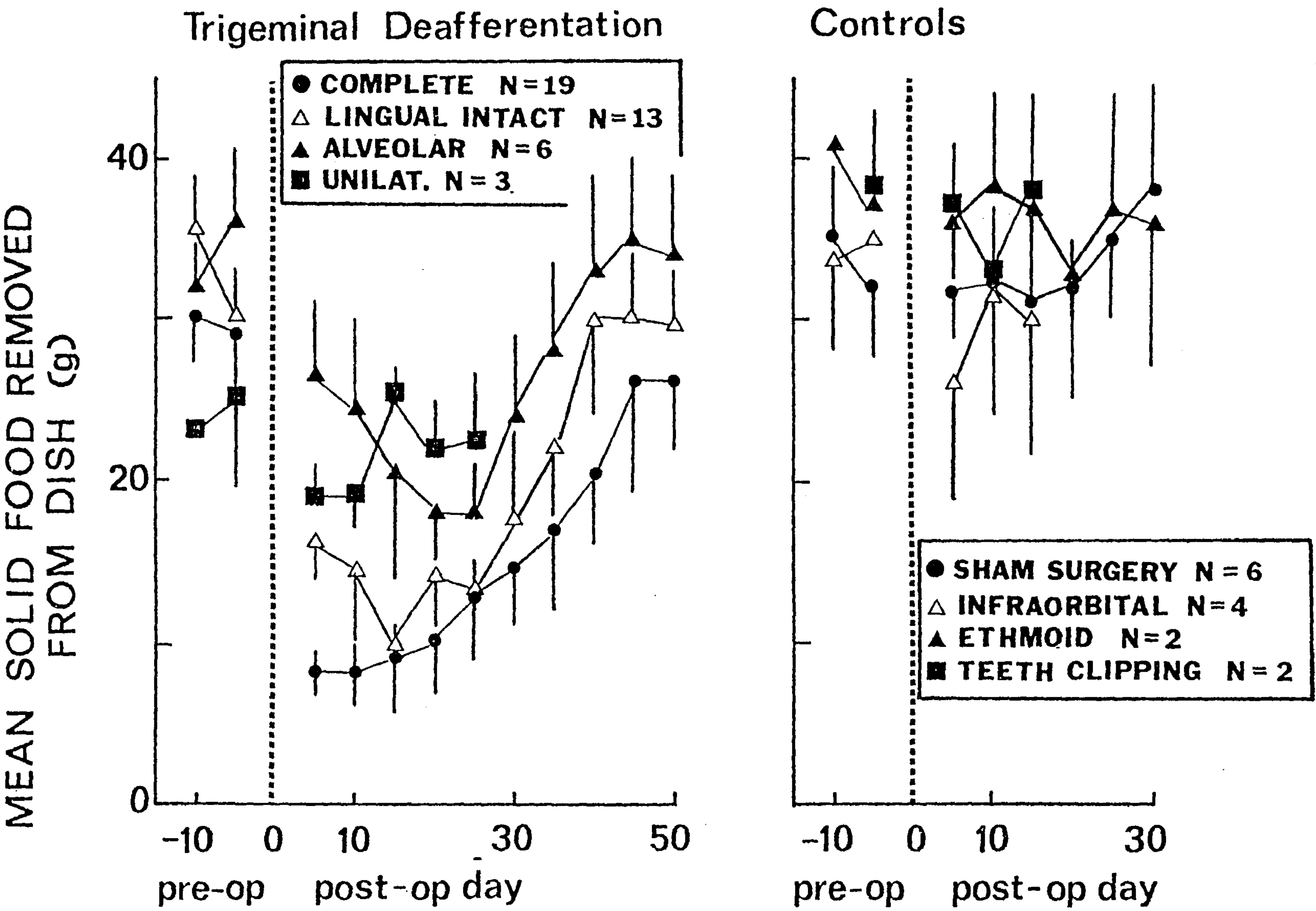

Trigeminal Deafferentation
Controls
● COMPLETE N=19
△ LINGUAL INTACT N=13
▲ ALVEOLAR N=6
■ UNILAT. N=3
● SHAM SURGERY N=6
△ INFRAORBITAL N=4
▲ ETHMOID N=2
■ TEETH CLIPPING N=2
MEAN SOLID FOOD REMOVED FROM DISH (g)
40
20
0
-10
0
10
30
50
pre-op
post-op day
-10
0
10
30
pre-op
post-op day

FIGURE 12

FIGURE 13

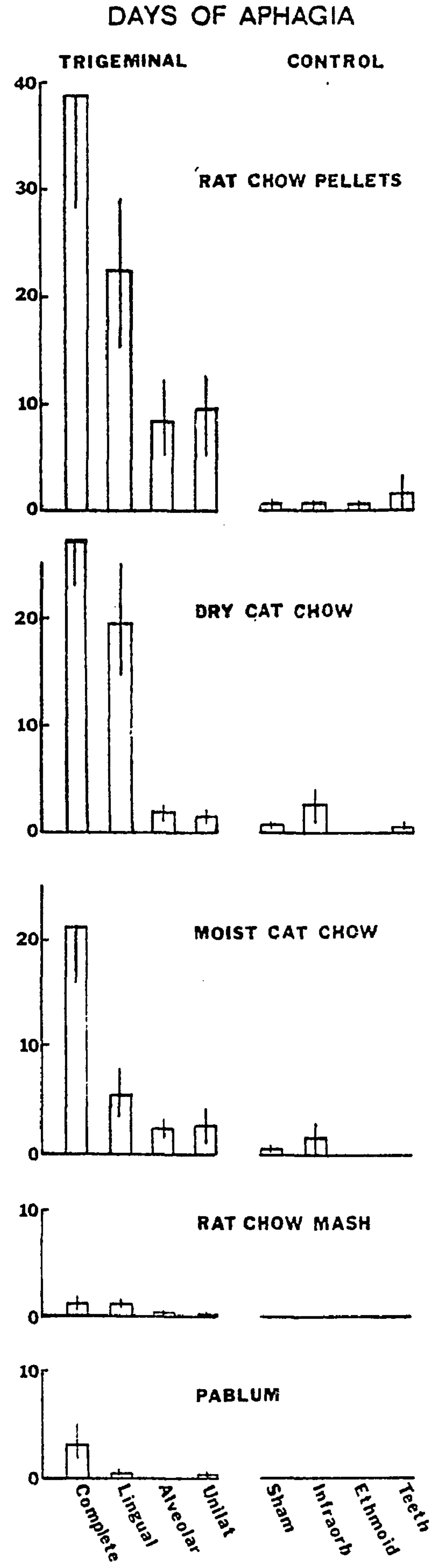
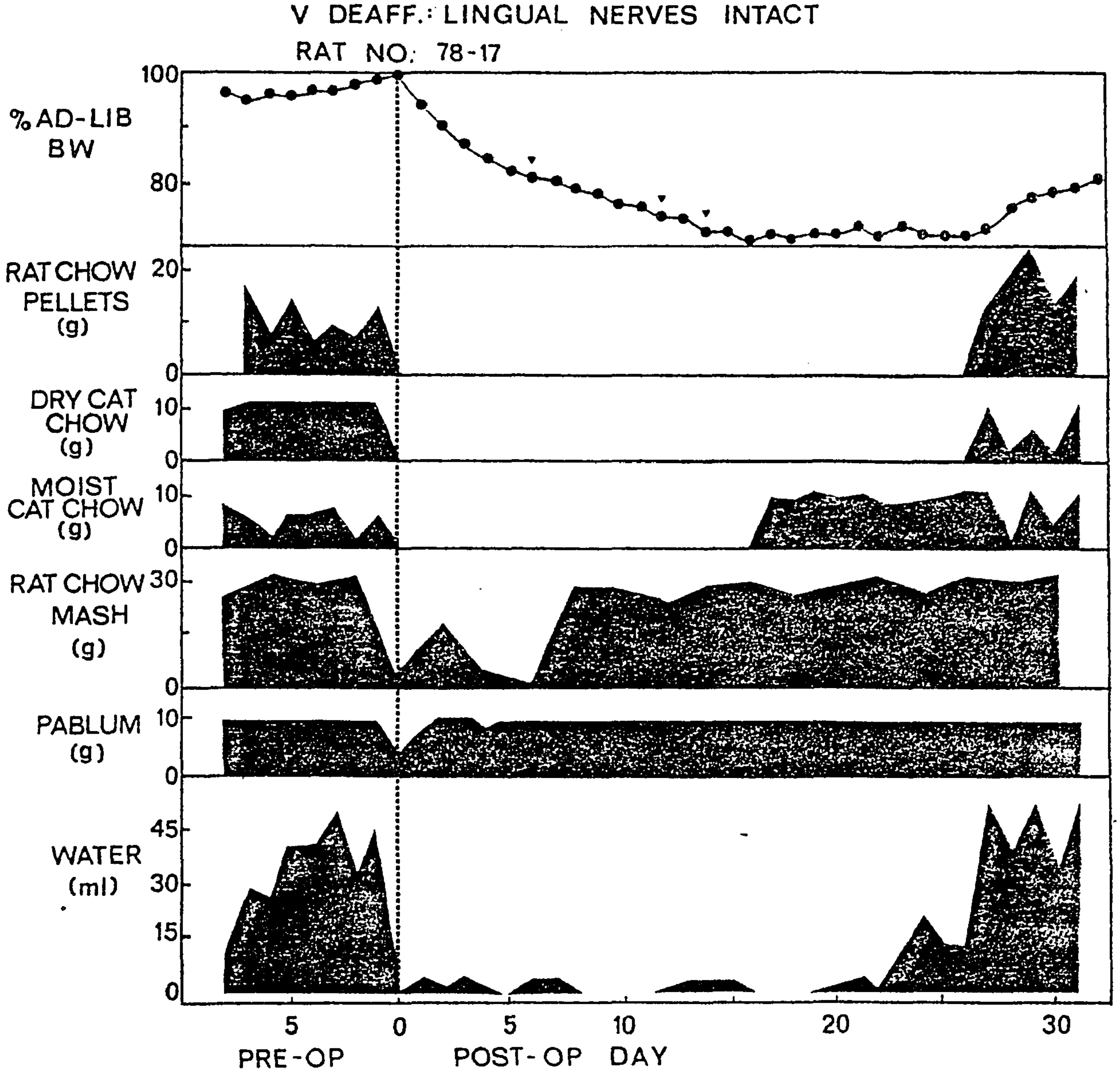

DAYS OF APHAGIA
TRIGEMINAL
CONTROL
RAT CHOW PELLETS
DRY CAT CHOW
MOIST CAT CHOW
RAT CHOW MASH
PABLUM
40
30
20
10
0
Complete
Lingual
Alveolar
Unilat
Sham
Infraorb
Ethmoid
Teeth

FIGURE 14


V DEAFF.: LINGUAL NERVES INTACT
RAT NO: 78-17
100
% AD-LIB BW
80
RAT CHOW PELLETS (g)
20
0
DRY CAT CHOW (g)
10
0
MOIST CAT CHOW (g)
10
0
RAT CHOW MASH (g)
30
0
PABLUM (g)
10
0
WATER (ml)
45
30
15
0
5
0
5
10
20
30
PRE-OP
POST-OP DAY

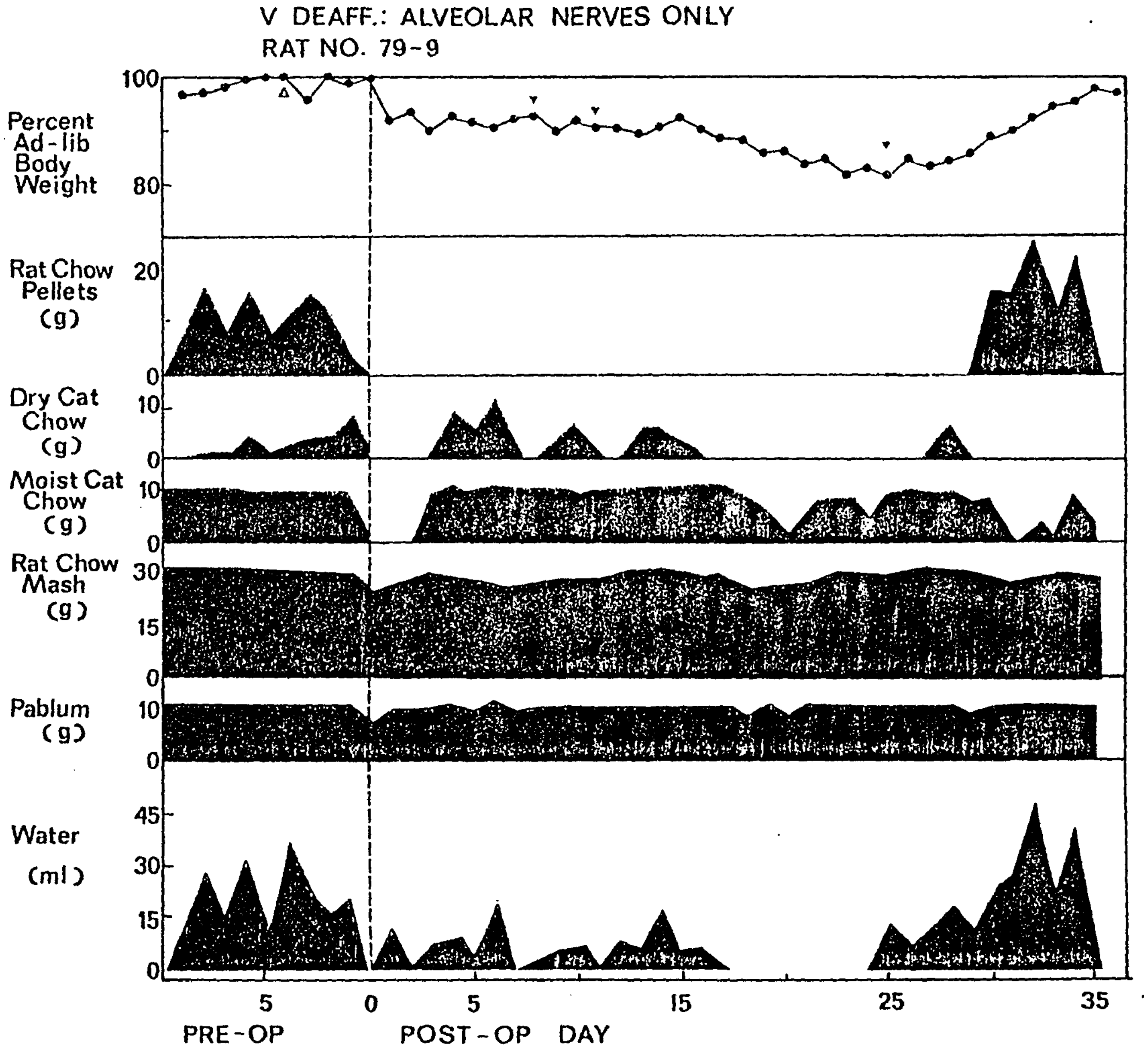

V DEAFF.: ALVEOLAR NERVES ONLY
RAT NO. 79-9
Percent Ad-lib Body Weight
100
80
Rat Chow Pellets (g)
20
0
Dry Cat Chow (g)
10
0
Moist Cat Chow (g)
10
0
Rat Chow Mash (g)
30
15
0
Pablum (g)
10
0
Water (ml)
45
30
15
0
5
0
5
15
25
35
PRE-OP
POST-OP DAY

FIGURE 15

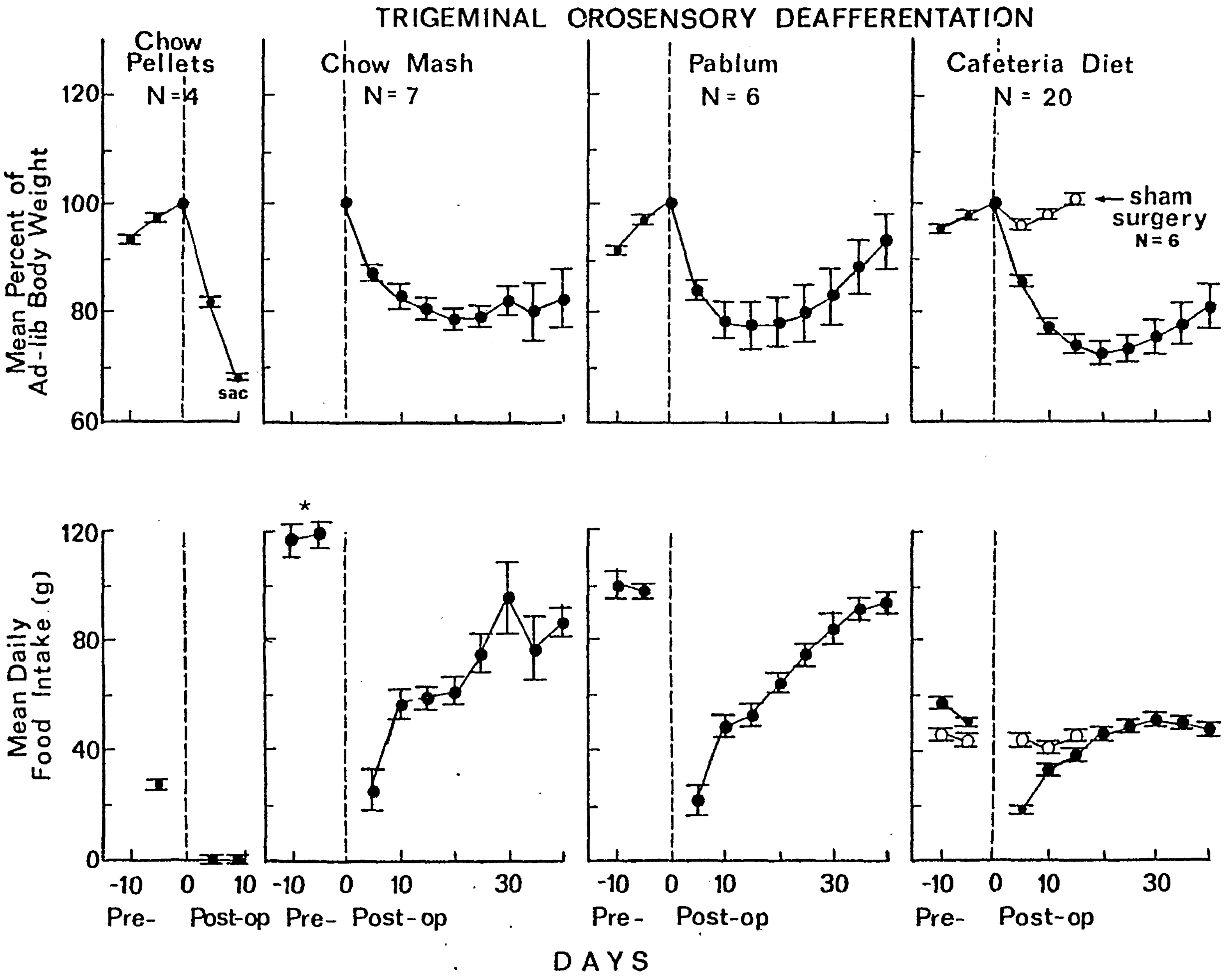

TRIGEMINAL OROSENSORY DEAFFERENTATION
Chow Pellets
N = 4
Chow Mash
N = 7
Pablum
N = 6
Cafeteria Diet
N = 20
sham surgery
N = 6
sac
*
Mean Percent of Ad-lib Body Weight
Mean Daily Food Intake (g)
120
100
80
60
120
80
40
0
-10
0
10
-10
0
10
30
-10
0
10
30
-10
0
10
30
Pre-
Post-op
Pre-
Post-op
Pre-
Post-op
Pre-
Post-op
DAYS

FIGURE 16

FIGURE 17

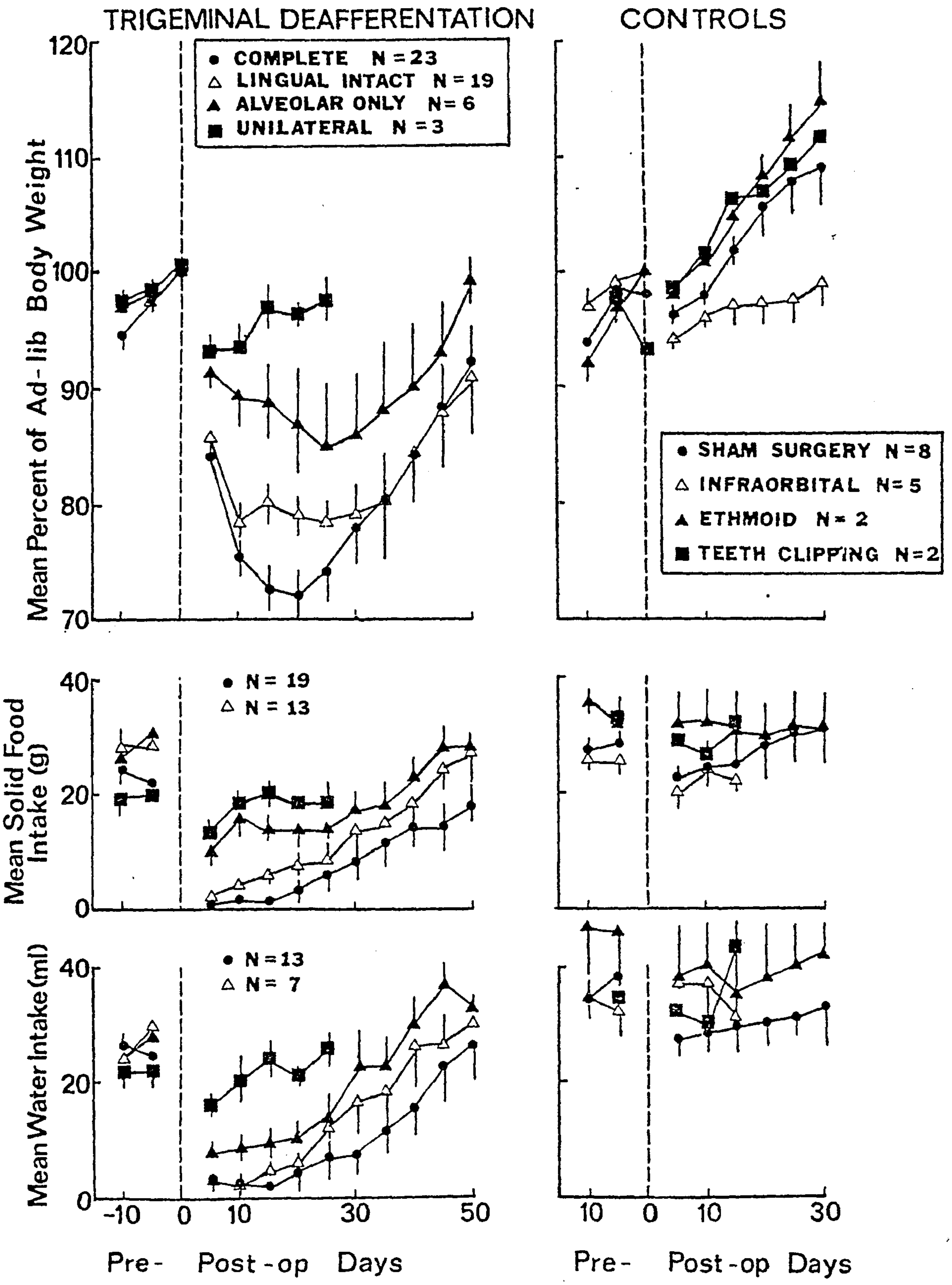

TRIGEMINAL DEAFFERENTATION
CONTROLS
● COMPLETE N = 23
△ LINGUAL INTACT N = 19
▲ ALVEOLAR ONLY N = 6
■ UNILATERAL N = 3
● SHAM SURGERY N = 8
△ INFRAORBITAL N = 5
▲ ETHMOID N = 2
■ TEETH CLIPPING N = 2
Mean Percent of Ad-lib Body Weight
120
110
100
90
80
70
Mean Solid Food Intake (g)
40
20
0
● N = 19
△ N = 13
Mean Water Intake (ml)
40
20
0
● N = 13
△ N = 7
-10
0
10
30
50
10
0
10
30
Pre- Post-op Days
Pre- Post-op Days

FIGURE 18

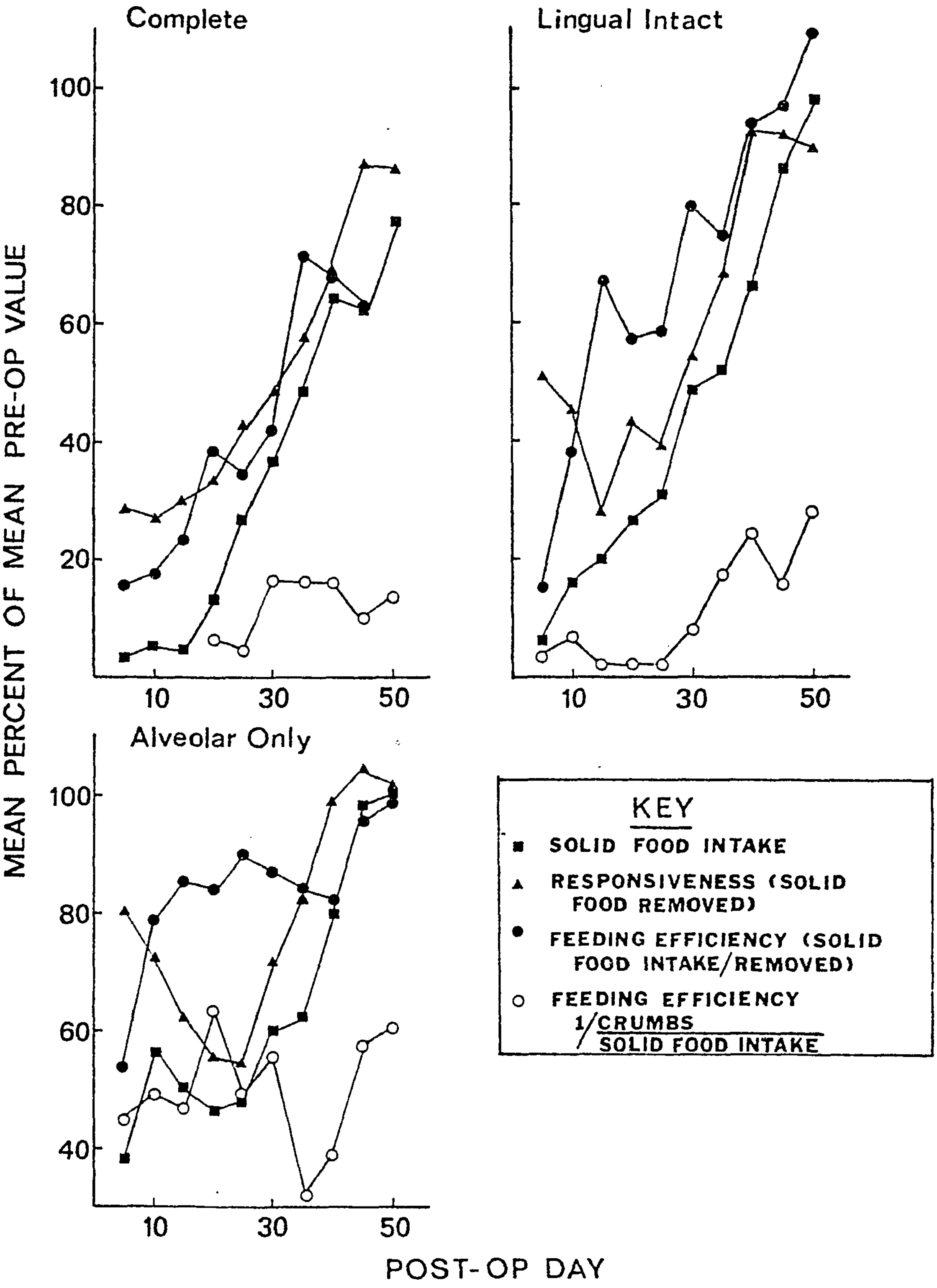

Complete
Lingual Intact
Alveolar Only
MEAN PERCENT OF MEAN PRE-OP VALUE
POST-OP DAY
100
80
60
40
20
10
30
50
KEY
■ SOLID FOOD INTAKE
▲ RESPONSIVENESS (SOLID FOOD REMOVED)
● FEEDING EFFICIENCY (SOLID FOOD INTAKE/REMOVED)
○ FEEDING EFFICIENCY 1/CRUMBS/SOLID FOOD INTAKE

FIGURE 19

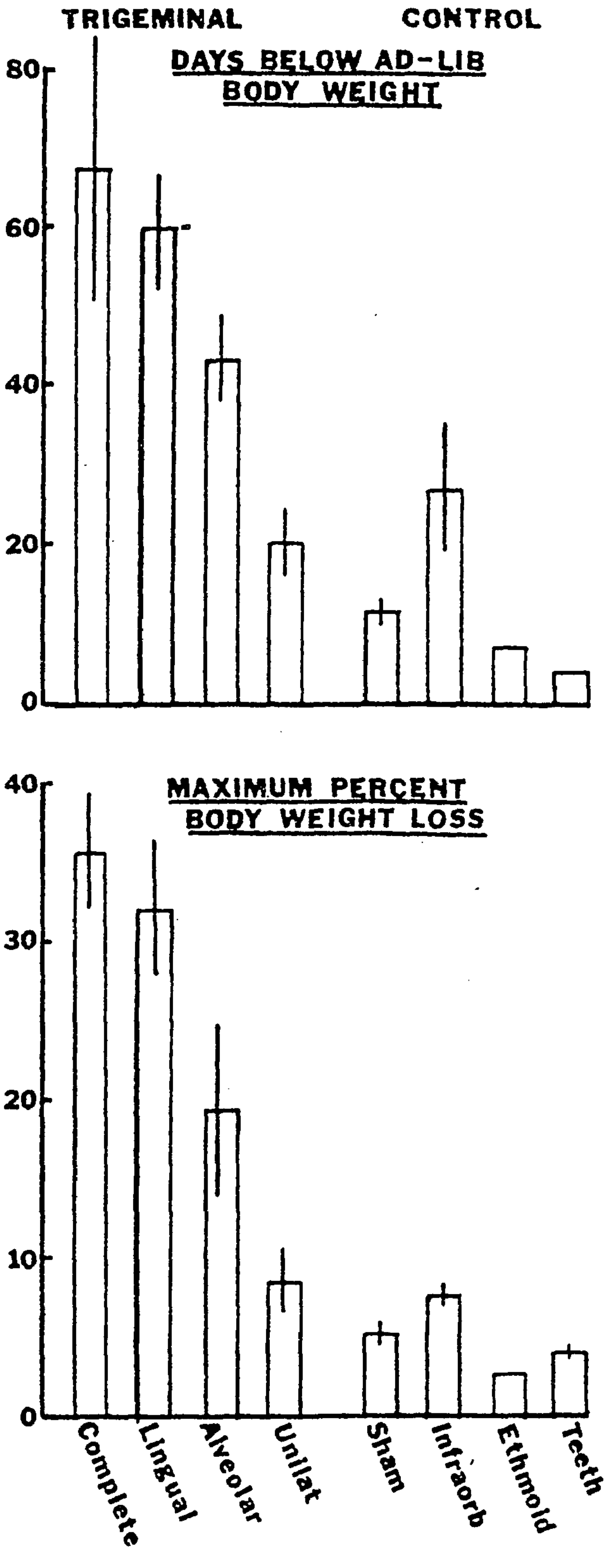
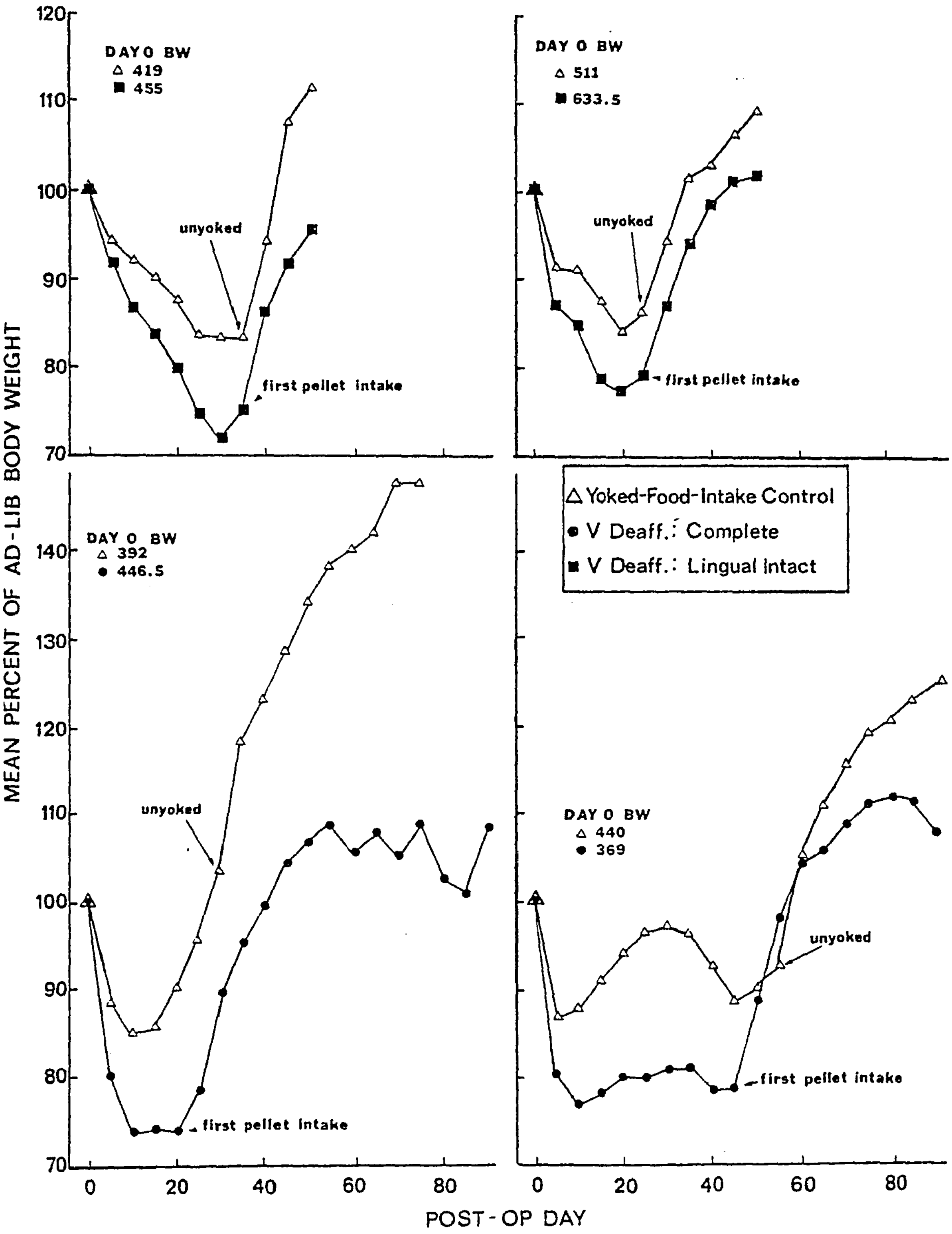

TRIGEMINAL
CONTROL
DAYS BELOW AD-LIB BODY WEIGHT
80
60
40
20
0
MAXIMUM PERCENT BODY WEIGHT LOSS
40
30
20
10
0
Complete
Lingual
Alveolar
Unilat
Sham
Infraorb
Ethmoid
Teeth

FIGURE 20


MEAN PERCENT OF AD-LIB BODY WEIGHT
POST-OP DAY
DAY 0 BW
△ 419
■ 455
unyoked
first pellet intake
DAY 0 BW
△ 511
■ 633.5
unyoked
first pellet intake
DAY 0 BW
△ 392
● 446.5
unyoked
first pellet intake
△ Yoked-Food-Intake Control
● V Deaff.: Complete
■ V Deaff.: Lingual Intact
DAY 0 BW
△ 440
● 369
unyoked
first pellet intake
120
110
100
90
80
70
140
130
120
110
100
90
80
70
0
20
40
60
80
0
20
40
60
80

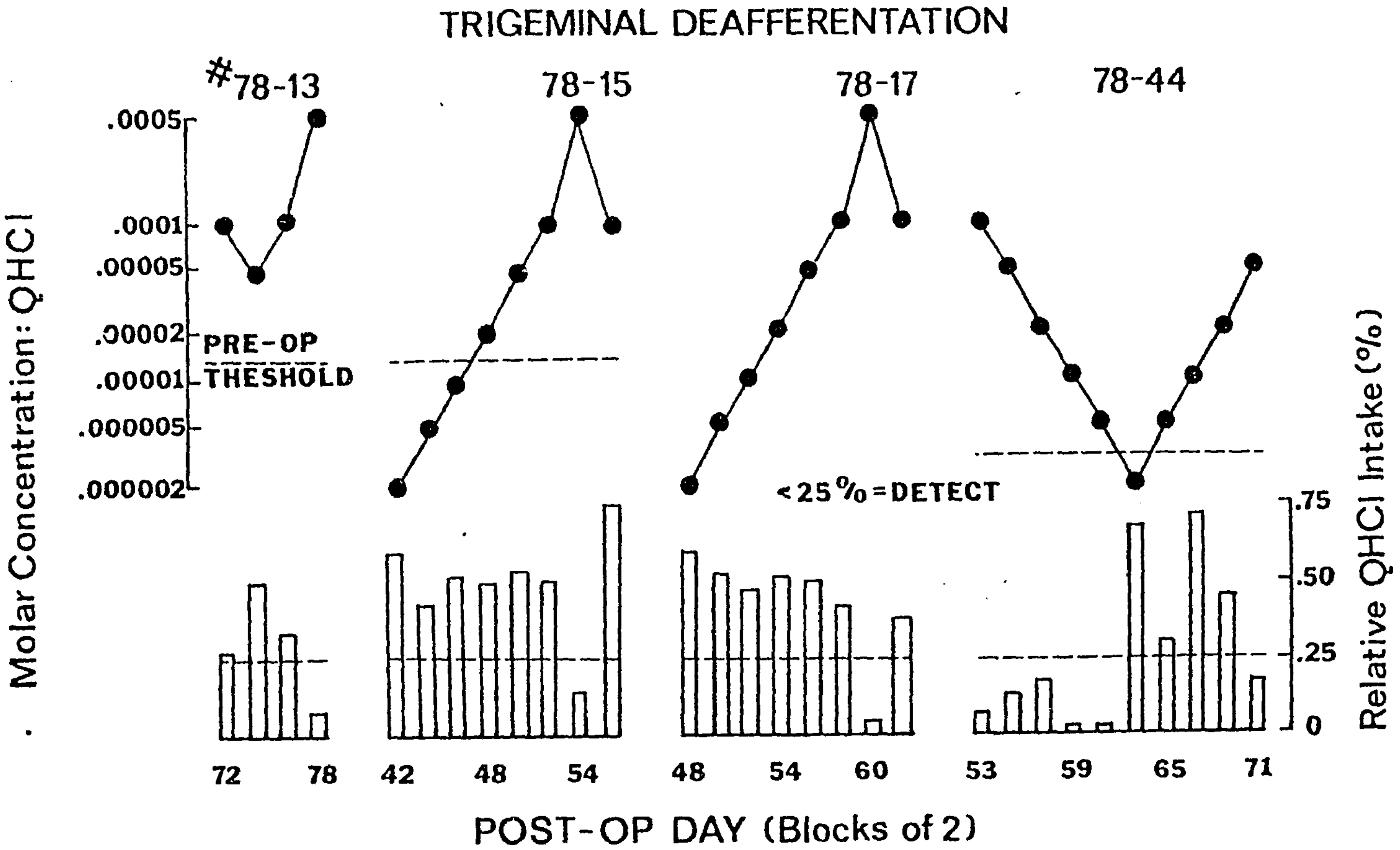

TRIGEMINAL DEAFFERENTATION
#78-13
78-15
78-17
78-44
Molar Concentration: QHCl
.0005
.0001
.00005
.00002
.00001
.000005
.000002
PRE-OP
THESHOLD
<25%=DETECT
Relative QHCl Intake (%)
.75
.50
.25
0
72
78
42
48
54
48
54
60
53
59
65
71
POST-OP DAY (Blocks of 2)

FIGURE 21

FIGURE 22

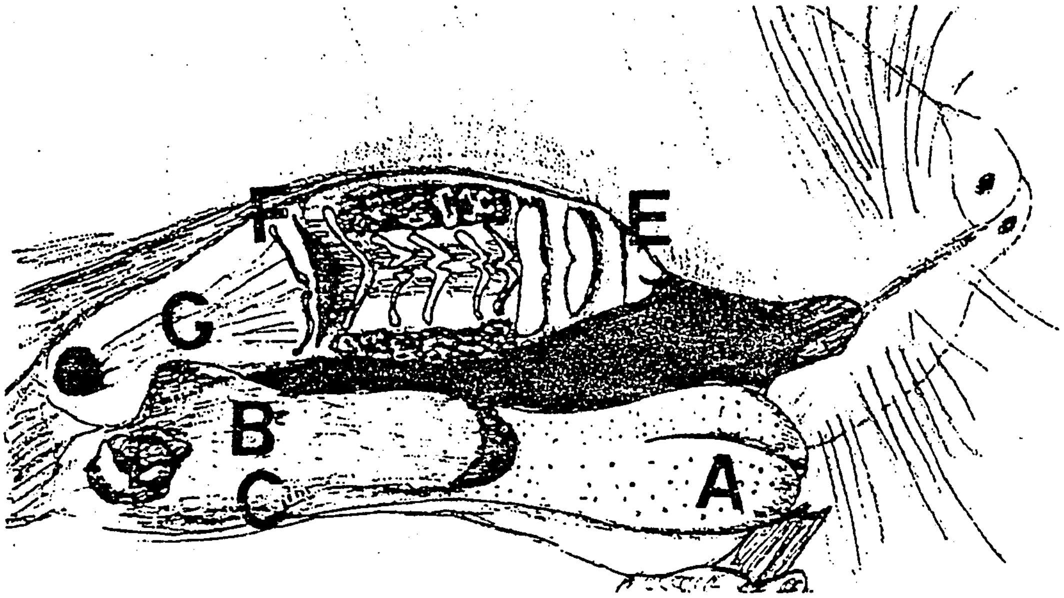


Fig. 5. Diagram of oropharyngeal taste bud distribution by region. A, fungiform papillae; B, circumvallate papillae; C, foliate papillae; D, epiglottis; E, NID; F, GS; G, PPF.

FIGURE 23

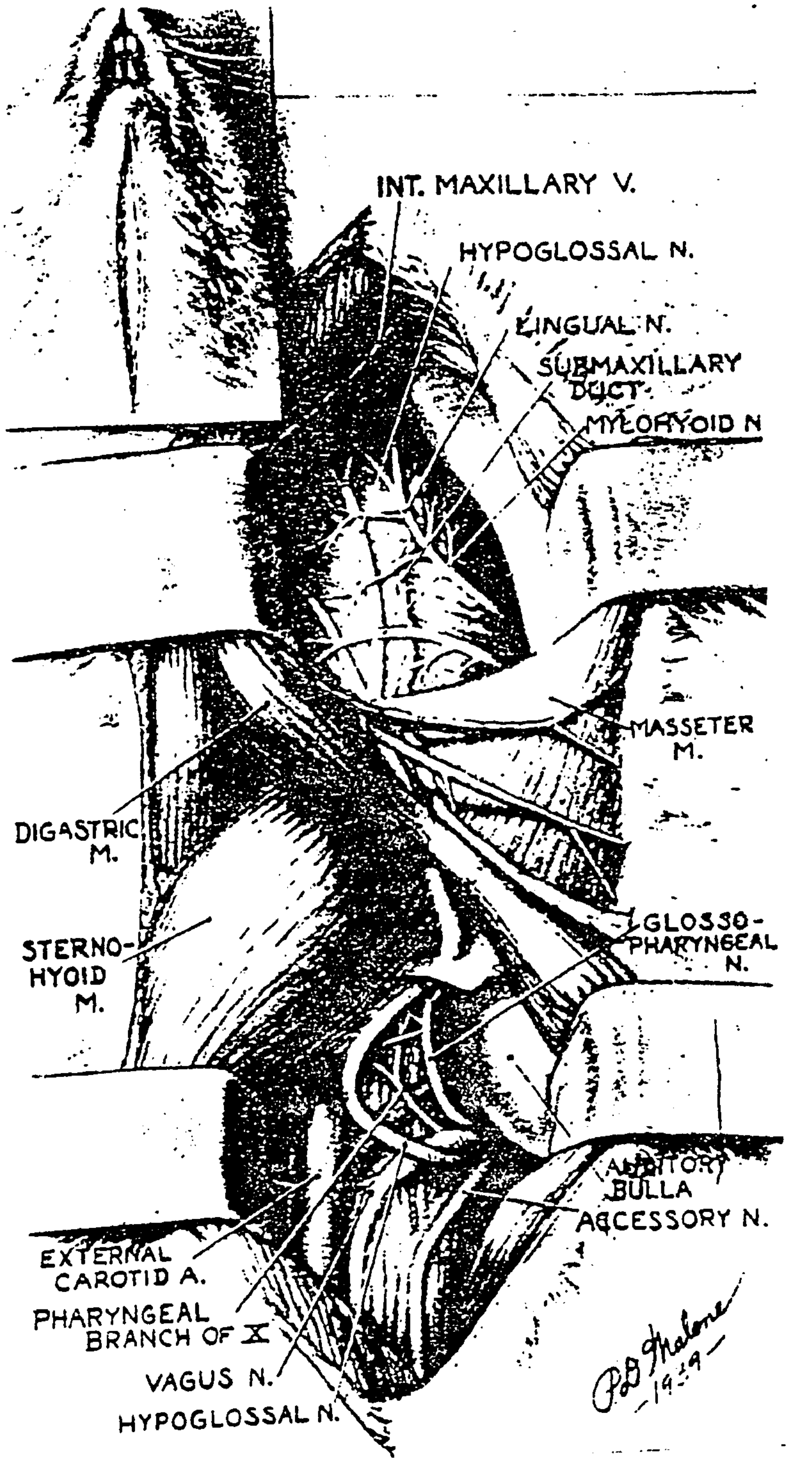


Fig. 31. — Drawing showing the operative technique used in avulsing the lingua and glossopharyngeal nerves and the pharyngeal branch of the 10 th nerve.

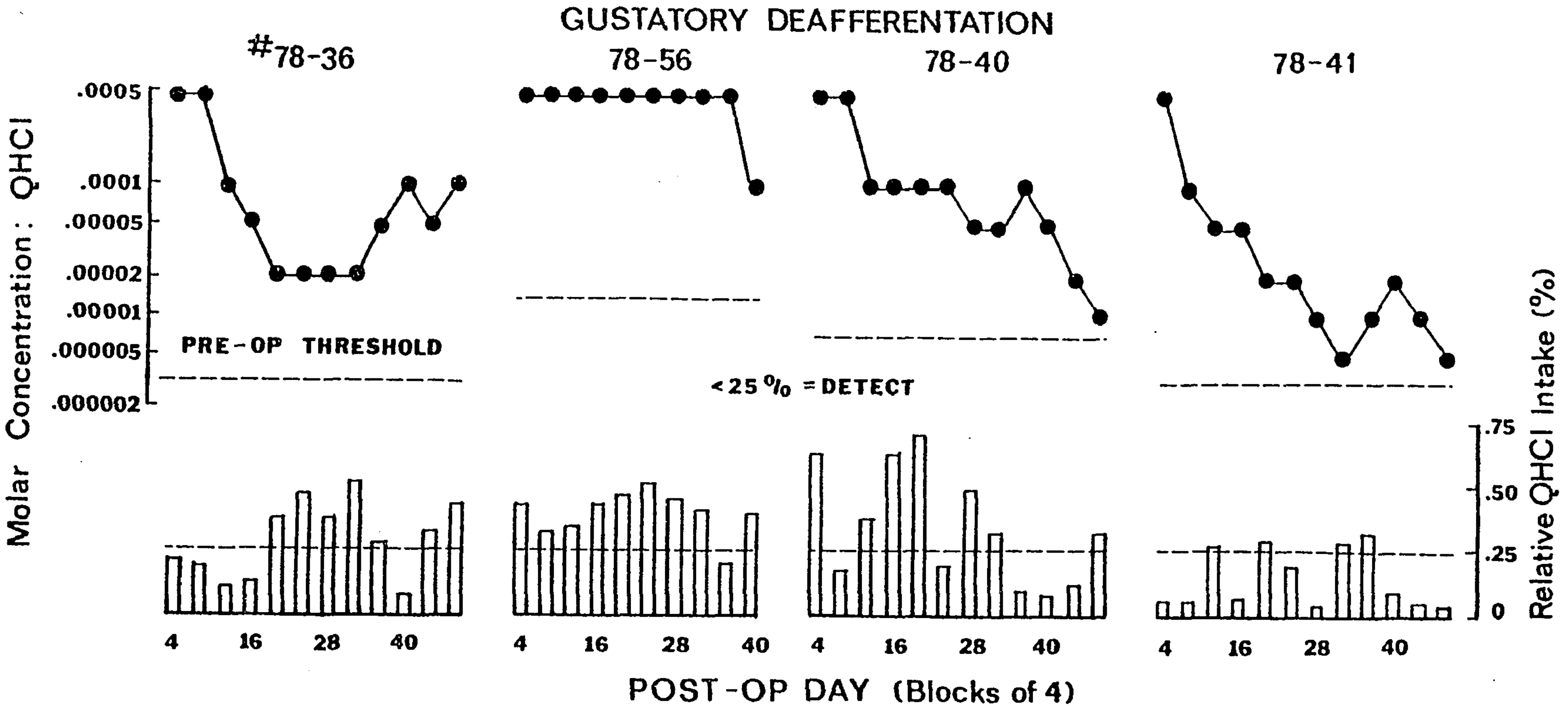

GUSTATORY DEAFFERENTATION
#78-36
78-56
78-40
78-41
Molar Concentration: QHCl
.0005
.0001
.00005
.00002
.00001
.000005
.000002
PRE-OP THRESHOLD
<25 % = DETECT
Relative QHCl Intake (%)
.75
.50
.25
0
4
16
28
40
POST-OP DAY (Blocks of 4)

FIGURE 24

FIGURE 25

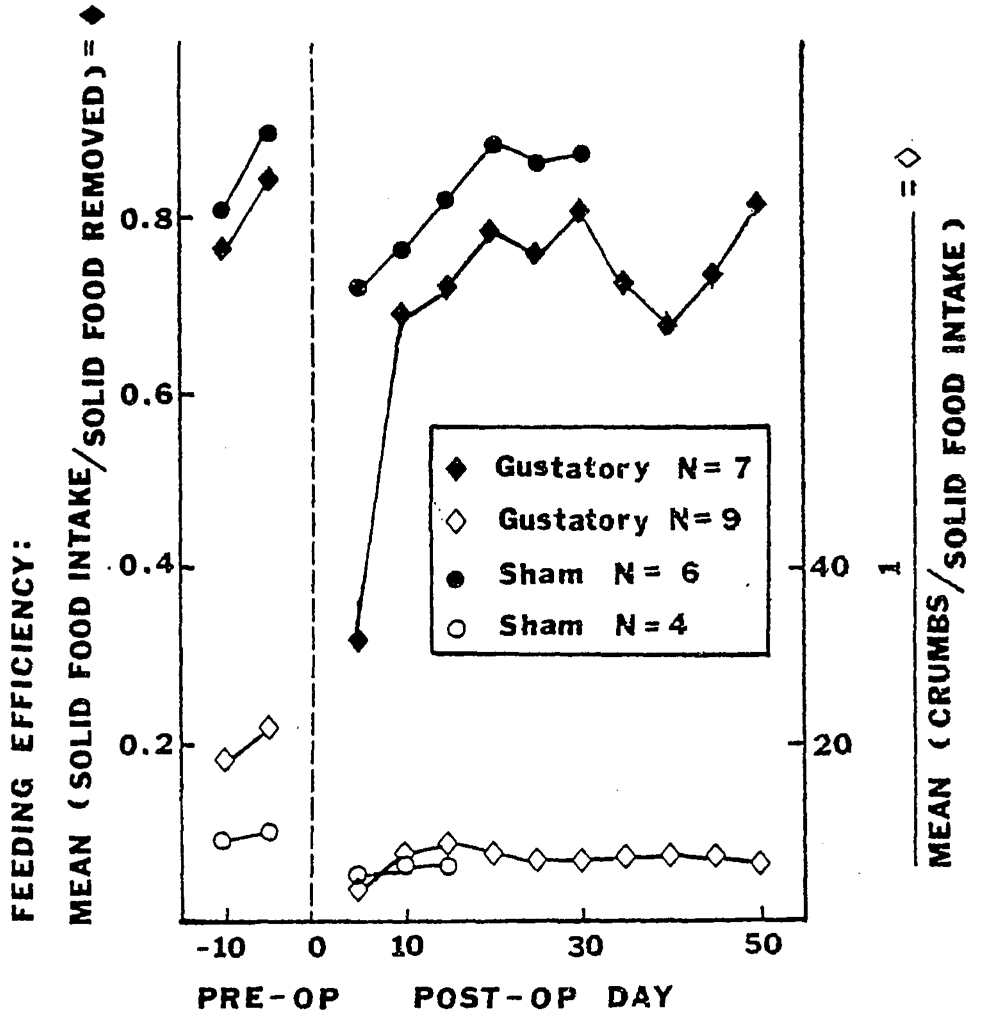
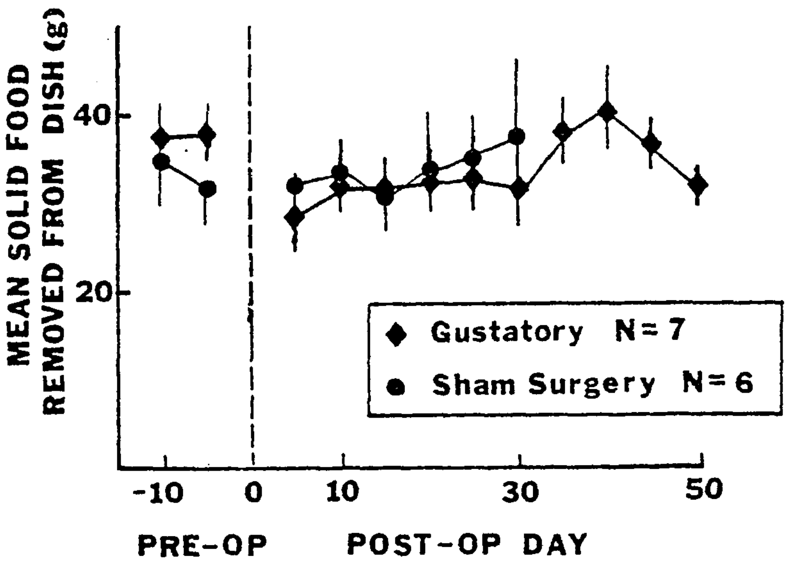


FIGURE 26



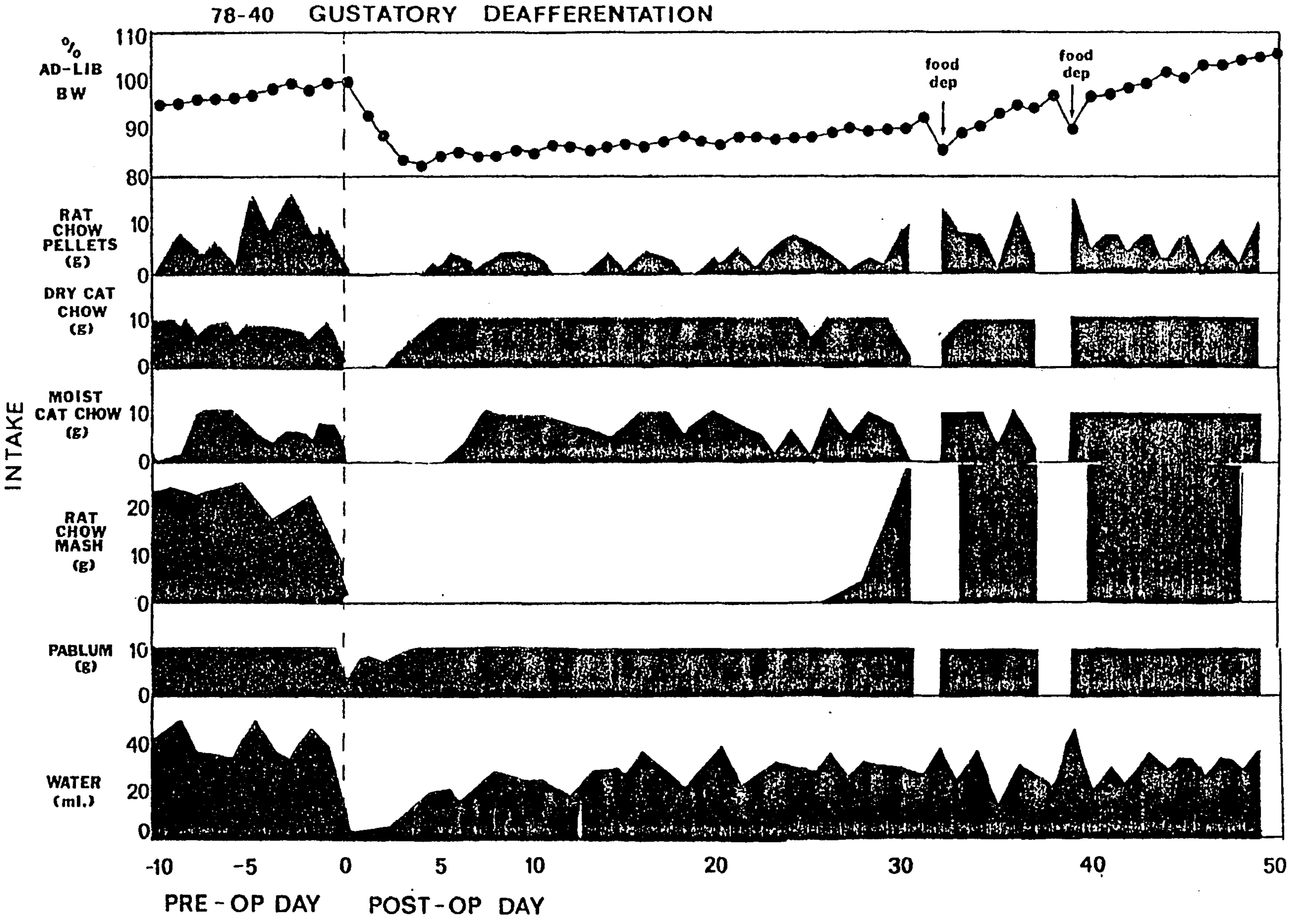

78-40 GUSTATORY DEAFFERENTATION
% AD-LIB BW
110
100
90
80
food dep
food dep
INTAKE
RAT CHOW PELLETS (g)
10
0
DRY CAT CHOW (g)
10
0
MOIST CAT CHOW (g)
10
0
RAT CHOW MASH (g)
20
10
0
PABLUM (g)
10
0
WATER (ml.)
40
20
0
-10
-5
0
5
10
20
30
40
50
PRE-OP DAY
POST-OP DAY

FIGURE 27

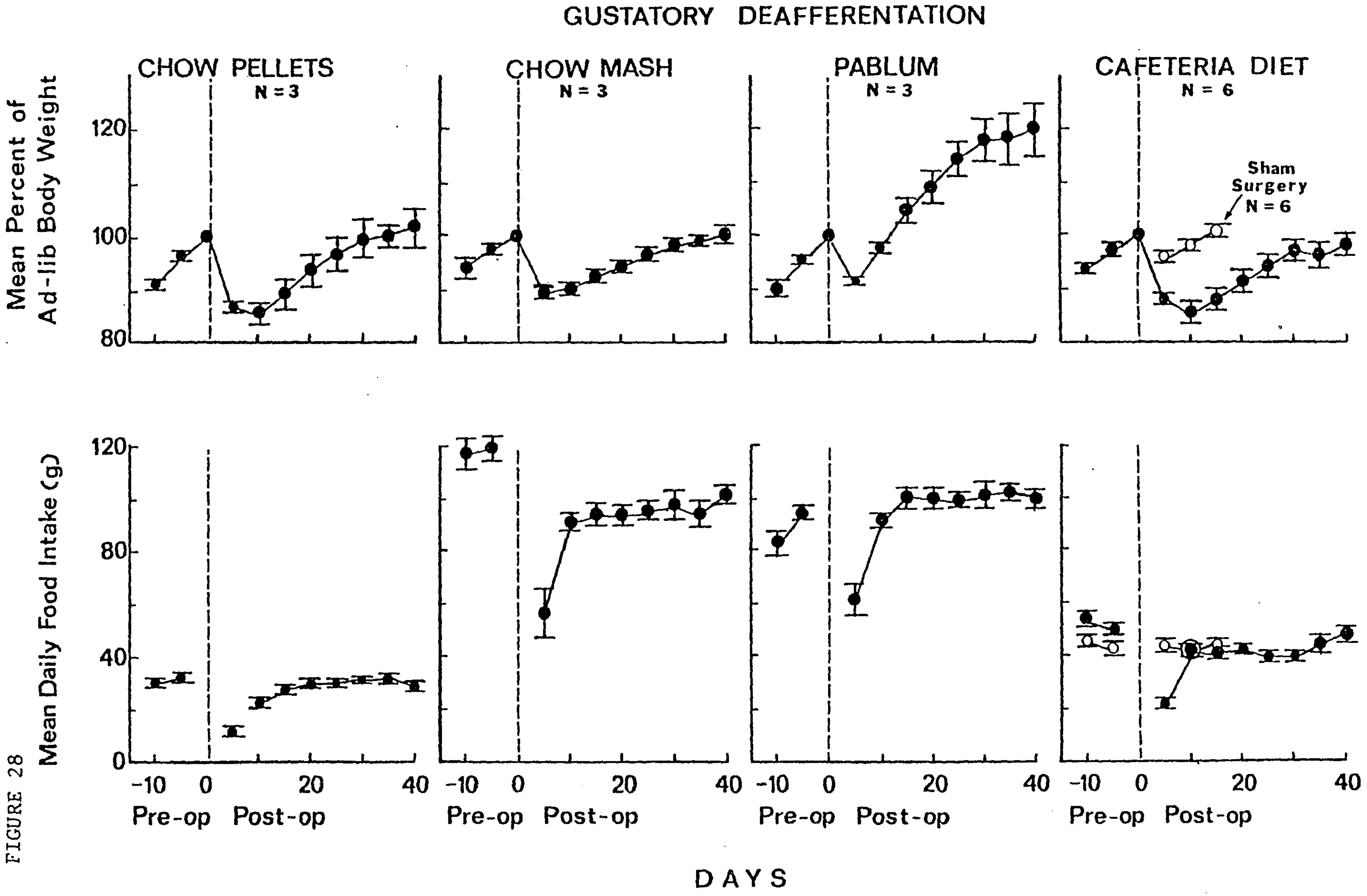

GUSTATORY DEAFFERENTATION
CHOW PELLETS
N = 3
CHOW MASH
N = 3
PABLUM
N = 3
CAFETERIA DIET
N = 6
Sham Surgery N = 6
Mean Percent of Ad-lib Body Weight
80
100
120
Mean Daily Food Intake (g)
0
40
80
120
-10
0
20
40
Pre-op
Post-op
DAYS

FIGURE 28

FIGURE 29

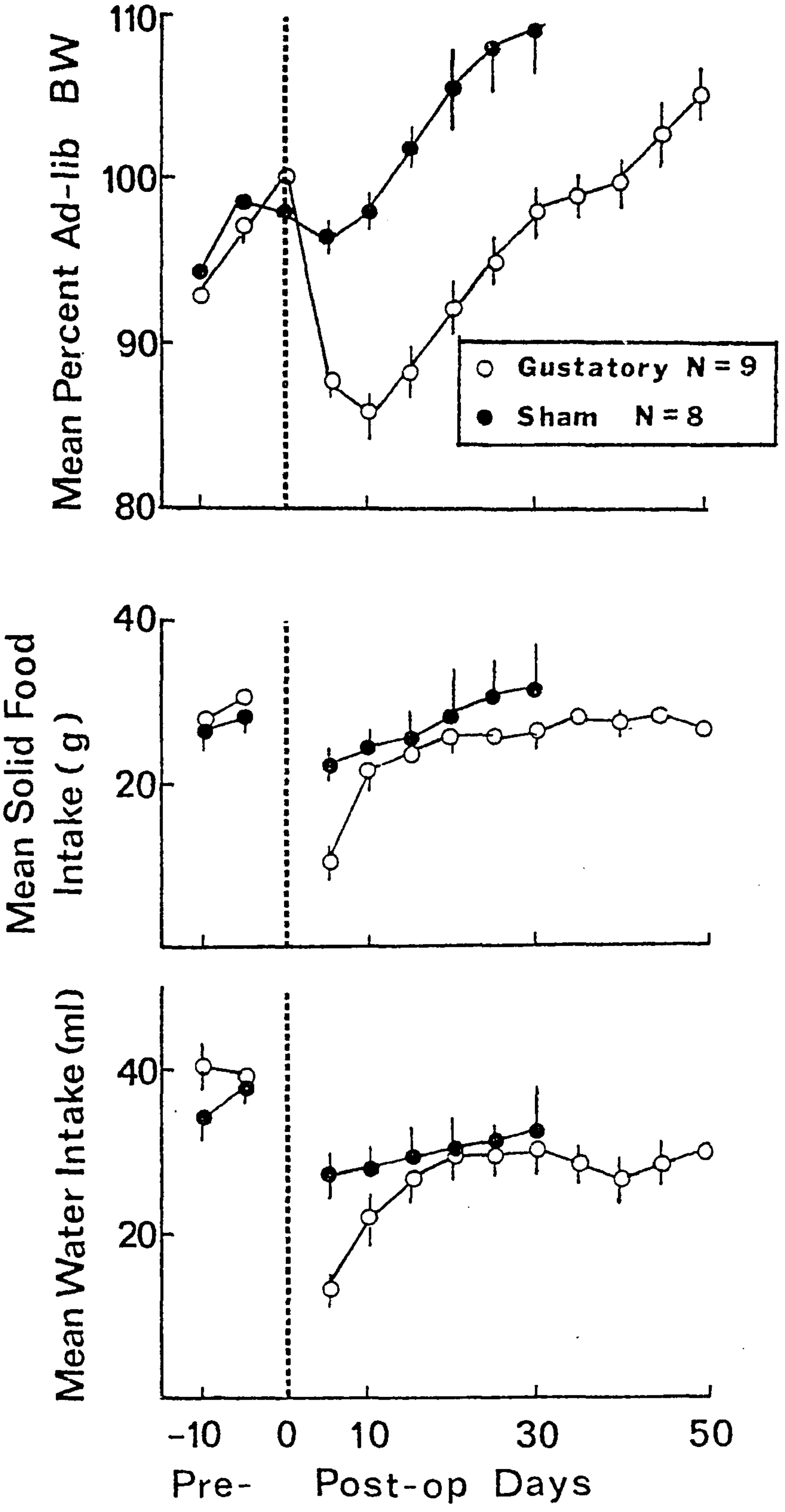

Mean Percent Ad-lib BW
110
100
90
80
○ Gustatory N = 9
● Sham N = 8
Mean Solid Food Intake (g)
40
20
Mean Water Intake (ml)
40
20
-10
0
10
30
50
Pre-
Post-op Days

TABLE 1 - DEAFFERENTATION EFFECTS UPON THE CONDITION OF THE INCISORS

SURGICAL GROUP	INCISORS[1]			
COMPLETE (N=4)	78-42	78-44	79-6	79-7
Preop. Week 1	12,12	14,14	12,12	11,11
Postop. Week 1	16,15	17,17 *	15,15 *	15,15 *
2	22,20 *	15,15	18,18 *	14,14 *
3	15,15 *	17,17 *	15,15 *	15,15 *
LINGUAL INTACT (N=3)	78-45	79-13	79-14	
Preop. Week 1	13,13	11,11	12,12	
Postop. Week 1	16,16 *	15,15	14,14	
2	16,11 *	22,23 *	19,21 *	
ALVEOLAR (N=3)	79-8	79-9	79-24	
Preop. Week 1	11,11	15,15	11,11	
Postop. Week 1	16,16	16,16	16,15	
2	16,16	20,20 *	15,17 *	
INFRAORBITAL (N=3)	79-4	79-5		
Preop. Week 1	11,11	13,13		
Postop. Week 1	13,13	13,13		

1. Total length (upper + lower) of right and left incisors before filing.

* Incisors were filed during this week.

TABLE 2 - DEAFFERENTATION EFFECTS UPON THE CONDITION OF THE MOUTH

SURGICAL GROUP	TONGUE[1]				LOWER LIP[2]				PALATE[2]			
COMPLETE (N=4)	78-42	78-44	79-6	79-7	78-42	78-44	79-6	79-7	78-42	78-44	79-6	79-7
Preop. Week 1	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Postop. Week 1	1.6	2.0	2.0	2.5	1.4	1.9	1.5	2.0	2.0	2.6	1.5	2.0
2	2.3	1.7	3.0	4.0	2.0	2.0	2.5	1.0	2.1	2.0	2.0	2.0
3	3.0	1.0	1.7	4.0	2.3	2.0	2.0	2.0	2.0	3.0	1.7	1.0
LINGUAL INTACT (N=3)	78-45	79-13	79-14		78-45	79-13	79-14		78-45	79-13	79-14	
Preop. Week 1	1.0	1.0	1.0		1.0	1.0	1.0		1.0	1.0	1.0	
Postop. Week 1	1.0	1.0	1.0		2.1	2.0	2.0		2.3	2.0	2.0	
2	1.5	1.0	1.0		2.2	1.0	1.0		2.5	1.0	1.0	
ALVEOLAR (N=3)	79-8	79-9	79-24		79-8	79-9	79-24		79-8	79-9	79-24	
Preop. Week 1	1.0	1.0	1.0		1.0	1.0	1.0		1.0	1.0	1.0	
Postop. Week 1	1.0	1.0	1.0		1.0	1.0	2.0		1.0	1.0	1.0	
2	1.0	1.0	1.0		2.0	2.5	2.0		1.5	2.0	1.0	
INFRAORBITAL (N=2)	79-4	79-5			79-4	79-5			79-4	79-5		
Preop. Week 1	1.0	1.0			1.0	1.0			1.0	1.0		
Postop. Week 1	1.0	1.0			1.0	1.0			1.0	1.0		

1. Amount of damage: 1 = normal; 2 = mild abrasions; 3 = severe abrasions; 4 = tip bitten off.
2. Amount of damage: 1 = normal; 2 = mild abrasions; 3 = severe abrasions.

TABLE 3 - Body weight, rat chow pellet intake (g), water intake (ml), and two measures of feeding efficiency in two rats with naturally occurring bite malocclusions and subsequent incisor overgrowth.

Day	Body Weight	Pellet Intake	Water Intake	$\frac{\text{Food Intake}}{\text{Food Removed}}$	$1 / \frac{\text{Crumbs}}{\text{Food Intake}}$
1	616	36.5	53	.99	73.0
2	625	39	49	.97	39.0
3	629	30	46	.94	60.0
4	637	42	50	.98	42.0
5	640	31	49	.95	31.0
1*	408	16	36	.91	16.0
2	406	26	53	.96	25.9
3	414	23	41	.96	23.0
4	420	22.5	38	.98	45.0
5	432	29.5	44	.98	59.2

* Incisors clipped 1 cm on this day

TABLE 4 - DEAFFERENTATION EFFECTS UPON OROMOTOR RESPONSES

SURGICAL GROUPS	ORAL STIMULI		EXTRAORAL STIMULI	
COMPLETE (N=4)	NUTRIMENT[1]	Q-TIP[2]	PAW PINCH[3]	TAIL PINCH[3]
Preop. Week 1	94/ 94/ 94	93/ 93	100/ 98/100/ 94	100/ 60/ 90/ 50
Postop. Week 1	100/100/100	79/ 51	93/ 69/ 74/ 55	92/ 87/ 85/ 51
2	89/ 89/ 89	59/ 39	100/ 87/ 91/ 51	94/ 89/ 94/ 28
3	100/100/100	69/ 65	98/ 87/ 91/ 55	100/ 89/ 96/ 45
4	100/100/100	100/100	100/100/100/ 91	100/100/ 66/ 50
LINGUAL INTACT (N=3)				
Preop. Week 1	78/ 78/ 78	100/ 99	100/ 93/100/ 93	100/ 94/ 97/ 92
Postop. Week 1	76/ 71/ 71	99/ 53	98/ 97/ 69/ 66	100/100/ 89/ 75
2	67/ 67/ 67	89/ 69	100/100/ 98/ 87	100/100/100/ 72
ALVEOLAR (N=3)				
Preop. Week 1	100/100/100	93/ 87	100/100/100/ 78	100/ 72/100/ 61
Postop. Week 1	100/100/100	98/ 98	100/ 97/ 94/ 78	100/ 87/100/ 87
2	100/100/100	98/ 94	100/100/100/100	100/100/100/ 94
INFRAORBITAL (N=2)				
Preop. Week 1	100/100/100	95/ 78	95/ 83/ 95/ 75	100/100/100/ 84
Postop. Week 1	100/100/100	85/ 83	95/ 83/ 94/ 64	100/ 78/ 89/ 62
2	100/100/100	100/100	100/100/100/100	100/100/100/100

1. Mean % : mouth open / lick / swallow
2. Mean % : mouth open / lick or bite
3. Mean % : head turn / mouth contact / mouth open / bite

TABLE 5 - Deafferentation effects upon non-oromotor responses. Data represent the mean percentage of the total stimulus presentations where an appropriate orienting response occurred.

	Limb Use	Odor	Corneal Reflex	Whisker Touch
COMPLETE (N = 4)				
Preop week 1	100	85	100	72
Postop week 1	95	66	100	46
2	81	71	100	33
3	100	78	100	65
4	100	50	100	50
LINGUAL INTACT (N = 3)				
Preop week 1	100	83	100	78
Postop week 1	97	74	100	67
2	98	69	100	67
ALVEOLAR ONLY (N = 3)				
Preop week 1	100	100	100	64
Postop week 1	100	100	100	58
2	100	100	100	100
INFRAORBITAL CONTROL (N = 2)				
Preop week 1	100	100	100	75
Postop week 1	100	67	100	41
2	100	0	100	17
3	100	100	100	37
4	100	100	100	100

TABLE 6 - Order of recovery through the five diet types in 17 bilateral orosensory deafferented rats that resumed eating each of the diets. Data represent the percentage of the total cases in which intake of that diet recovered 1st, 2nd, 3rd, etc.

	ORDER OF RECOVERY				
	1st	2nd	3rd	4th	5th
Pablum	88	12	0	0	0
Rat Chow Mash	65	24	6	6	0
Moist Cat Chow	6	12	65	12	6
Dry Cat Chow	6	0	24	53	18
Rat Chow Pellets	0	0	18	24	59

TABLE 7 - Effects of trigeminal deafferentation upon water intake in rats offered the cafeteria diet. Adipsia is defined as intake of 1ml or less. Sample sizes as in Figure 13.

	Days to First Intake		Subsequent Days of Adipsia*	
	$\overline{M}$	SE	$\overline{M}$	SE
Trigeminal:				
Complete	5.4	2.3	11.9	4.7
Lingual Intact	3.3	1.8	12.4	4.6
Alveolar Only	0.7	0.2	8.6	3.7
Unilateral	0.3	0.3	0	0
Control:				
Sham	0.1	0.1	0	0
Infraorbital	0.4	0.2	0	0
Ethmoid	0	0	0	0
Teeth	0	0	0	0

*Total days of adipsia following the first instance of intake until either death or recovery of preoperative water intake.

TABLE 8 - Pearson product moment correlations among measures of intake, responsiveness, and efficiency (#), with respect to solid food, in three experimental groups over the first 50 postoperative days.

	Complete	Lingual Intact	Alveolar Only
Responsiveness + Intake	.97 *	.882*	.846*
Efficiency A + Intake	.951*	.916*	.687*
Efficiency B + Intake	.574	.865*	.214
Efficiency A + Responsiveness	.963*	.705*	.211
Efficiency B + Responsiveness	.382	.914*	.869*

* $p < .05$

\# responsiveness to solid food = amount of food removed from dish

efficiency A = solid food intake/solid food removed

efficiency B = $1 \Big/ \frac{\text{Uneaten crumbs}}{\text{Solid food intake}}$

TABLE 9 - Rate of weight loss in trigeminal (N=9) and sham operates (N=7), both aphagic and adipsic for the first five postop days.

	Trigeminal		Sham Operate	
Postop Day	$\overline{M}$ % Ad-lib BW	SE	$\overline{M}$ % Ad-lib BW	SE
0	100	0	100	0
1	91.18	0.51	91.83	0.57
2	85.69	0.57	87.04	0.67
3	81.63	0.67	83.28	0.83
4	78.13	0.76	79.48	0.83
5	75.16	0.85	76.31	0.79

TABLE 10 - Number of days required to regain lost body weight following 24 hour food or water deprivation in "recovered" V and sham operate rats.

	FOOD DEP.: Days to Regain BW			WATER DEP.: Days to Regain BW		
	N	$\overline{M}$	SE	N	$\overline{M}$	SE
V	19	3.95	0.65	12	2.17	0.37
Sham	24	4.21	0.88	9	1.78	0.28

TABLE 11 - Effects of trigeminal deafferentation upon the relation between mean daily food intake (g), water intake (ml), and body weight (g) over a 10 day period in hypophagic rats on the cafeteria diet.

	PREOPERATIVE DATA						POSTOPERATIVE DATA					
Group	Food Intake	Water Intake	Body Weight	Ratio W:F	Ratio F:BW	Ratio W:BW	Food Intake	Water Intake	Body Weight	Ratio W:F	Ratio F:BW	Ratio W:BW
Complete												
77-12	52.5	36.0	441.7	0.698	0.117	0.082	27.4	23.8	385.6	0.869	0.071	0.062
77-13	42.3	34.9	469.6	0.826	0.090	0.074	18.0	39.0	419.7	2.161	0.043	0.093
78-15	46.4	24.6	585.0	0.530	0.079	0.042	21.3	2.5	435.9	0.117	0.049	0.006
Lingual Intact												
78-13	44.8	26.2	556.2	0.585	0.081	0.047	34.8	16.5	308.7	0.473	0.113	0.053
78-16	43.0	26.7	563.4	0.662	0.076	0.047	31.0	7.7	512.2	0.248	0.061	0.015
78-17	50.2	30.5	631.6	0.607	0.079	0.048	31.8	5.3	456.8	0.167	0.070	0.012
Alveolar Only												
79-8	49.5	23.6	488.6	0.477	0.101	0.048	37.6	13.2	479.7	0.352	0.078	0.028
79-9	48.1	18.0	431.5	0.374	0.111	0.042	33.8	6.9	399.8	0.205	0.085	0.017
79-24	42.2	19.8	426.2	0.470	0.099	0.046	34.6	9.3	400.7	0.270	0.086	0.034
Mean Ratios				0.577	0.093	0.053				0.540	0.073	0.034

TABLE 12 - "Yoked for food intake" control group: Effects upon the relation between mean daily food intake (g), water intake (ml), and body weight.

	PREOPERATIVE DATA						POSTOPERATIVE DATA					
Rat #	Food Intake	Water Intake	Body Weight	Ratio W:F	Ratio F:BW	Ratio W:BW	Food Intake	Water Intake	Body Weight	Ratio W:F	Ratio F:BW	Ratio W:BW
78-11	44.3	23.0	445.3	.519	.099	.052	37.7	22.3	490.3	.592	.077	.045
78-14	41.5	25.6	451.0	.617	.092	.057	31.9	13.6	390.2	.426	.082	.035
78-15	52.9	27.5	502.5	.520	.105	.055	46.9	25.9	462.9	.552	.101	.056
78-16	63.8	17.7	427.7	.277	.149	.041	45.0	11.5	382.8	.256	.118	.030
Mean Ratios				.483	.111	.051				.456	.094	.041

TABLE 13 - Effect of trigeminal deafferentation upon the relation between food and water intake.

		WATER INTAKE			
		Pre-Food-Dep.		During Food-Dep.	
	N	$\overline{M}$	SE	$\overline{M}$	SE
V	19	29.56	3.82	20.21	1.85
Sham	23	33.07	3.17	22.61	2.36

		FOOD INTAKE			
		Pre-Water-Dep.		During Water-Dep.	
	N	$\overline{M}$	SE	$\overline{M}$	SE
V	12	26.02	4.39	14.92	1.15
Sham	9	30.24	5.81	19.44	2.53

TABLE 14 - Effects of gustatory deafferentation (N=6) and sham surgery (N=8) upon intake and body weight (g) in rats maintained on the cafeteria diet.

	DAYS BEFORE FIRST INTAKE															
	Rat Chow Pellets		Dry Cat Chow		Moist Cat Chow		Rat Chow Mash		Pablum		Water		Maximum % BW Loss		Days Below Ad-lib BW	
	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE
GUST.	11.2	2.6	3.2	0.5	4.7	1.4	5.8	4.5	0	0	1.8	0.5	16.3	1.6	34.2	3.8
SHAM	2.1	0.8	0.5	0.3	0.3	0.3	0	0	0	0	0.1	0.1	5.3	0.7	11.4	1.5

TABLE 15 - Number of days required to regain lost body weight following 24 hour food or water deprivation in gustatory and sham operate rats.

	FOOD DEP.: Days to Regain BW			WATER DEP.: Days to Regain BW		
	N	$\overline{M}$	SE	N	$\overline{M}$	SE
Gust.	30	3.63	0.28	4	1.75	0.48
Sham	24	4.21	0.88	9	1.78	0.28

TABLE 16 - Effects of gustatory deafferentation upon the relation between mean daily food intake (g), water intake (ml), and body weight (g) over a 10 day period in hypophagic rats on the cafeteria diet.

	PREOPERATIVE DATA						POSTOPERATIVE DATA					
Rat #	Food Intake	Water Intake	Body Weight	Ratio W:F	Ratio F:BW	Ratio W:BW	Food Intake	Water Intake	Body Weight	Ratio W:F	Ratio F:BW	Ratio W:BW
78-7	52.9	44.5	482.5	0.840	0.110	0.092	40.2	18.7	415.1	0.465	0.097	0.045
78-8	48.3	32.8	515.6	0.679	0.094	0.064	39.2	18.9	457.6	0.483	0.086	0.041
78-40	43.5	39.7	502.9	0.911	0.087	0.079	29.6	22.8	439.7	0.770	0.067	0.052
78-41	52.0	37.5	636.5	0.721	0.082	0.059	43.4	32.9	606.7	0.757	0.072	0.054
78-52	63.9	22.2	427.1	0.347	0.150	0.052	55.2	12.1	413.3	0.219	0.134	0.029
78-54	57.3	26.5	389.8	0.462	0.147	0.068	42.3	16.9	334.5	0.400	0.126	0.051
Mean Ratios				0.660	0.112	0.069				0.516	0.097	0.045

TABLE 17 - Effect of gustatory deafferentation upon the relation between food and water intake.

		WATER INTAKE			
		Pre-Food-Dep.		During Food-Dep.	
	N	$\overline{M}$	SE	$\overline{M}$	SE
Gust.	19	30.56	2.88	10.21	1.59
Sham	23	33.07	3.17	22.61	2.36
		FOOD INTAKE			
		Pre-Water-Dep.		During Water-Dep.	
	N	$\overline{M}$	SE	$\overline{M}$	SE
Gust.	4	28.98	3.13	17.75	0.25
Sham	9	30.24	5.81	19.44	2.53

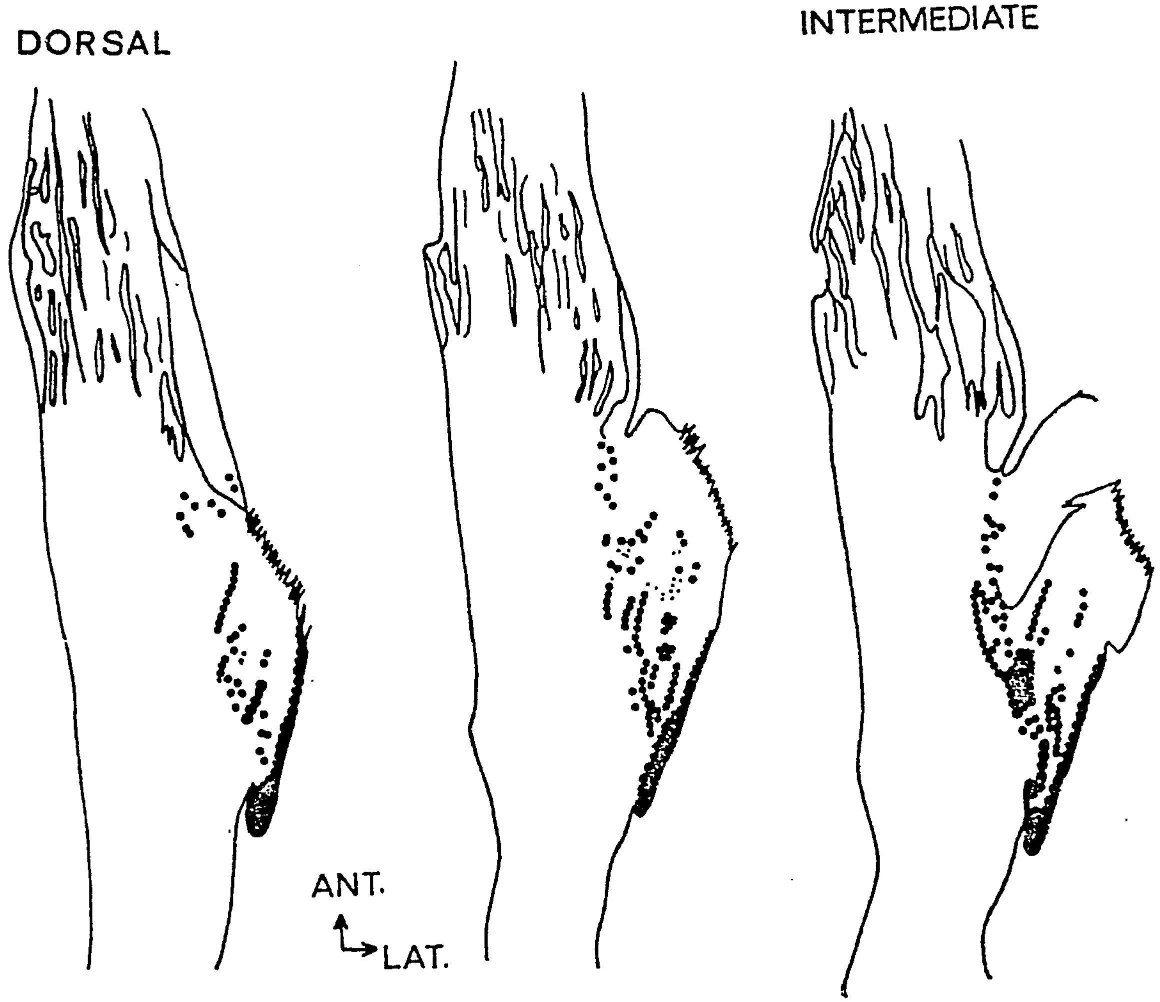
TABLE 18 - Similarities and differences in the trigeminal and gustatory preparations.

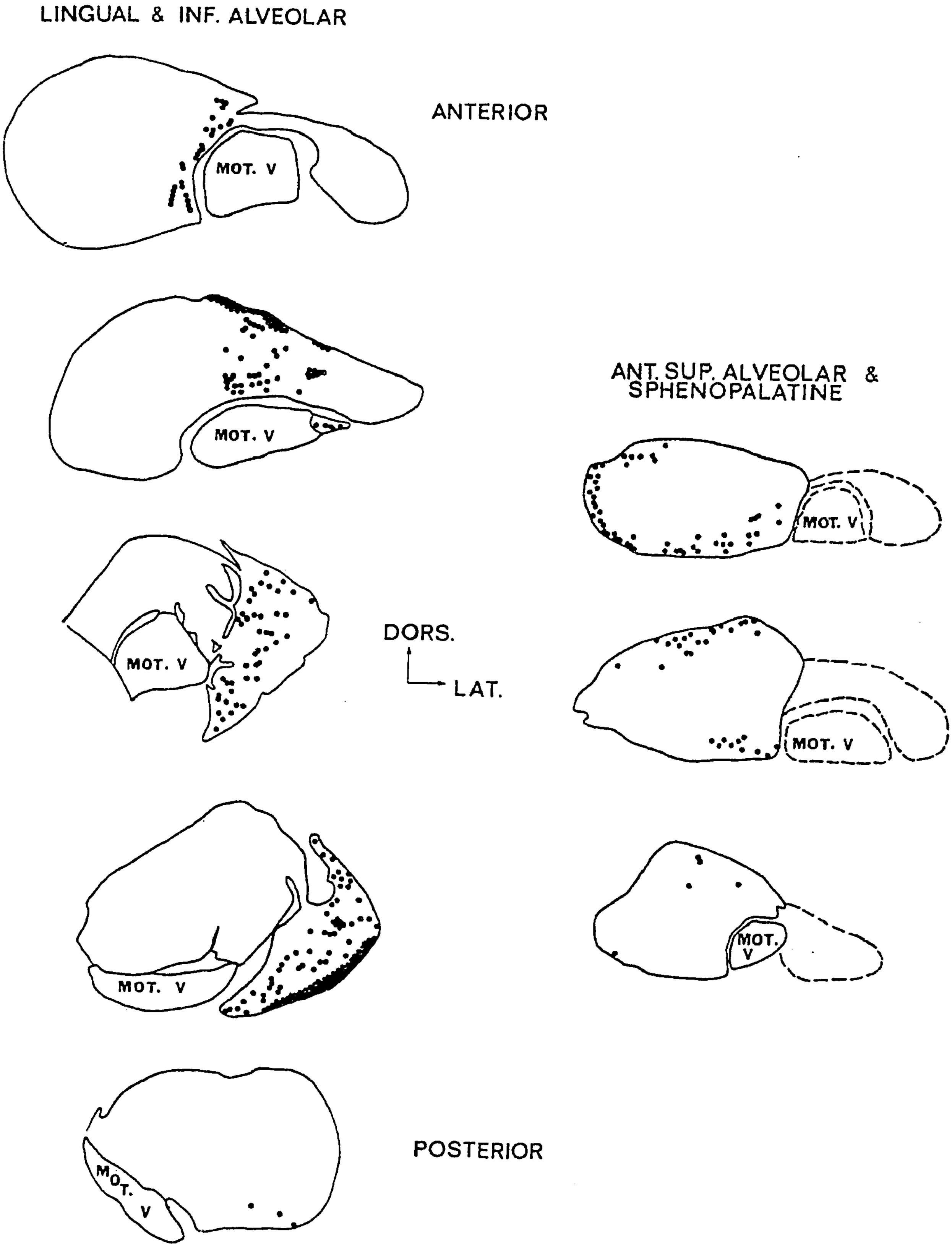
TRIGEMINAL	GUSTATORY
1. Orosensorimotor impairment	1. No effect
2. Consummatory response components intact	2. Same
3. Consummatory response sequence disrupted	3. Only mandibulation
4. ↓ food intake/food removed ratios	4. Mild and transient
5. ↑ crumbs/food intake ratios	5. Same
6. Severe ↓ responsiveness to solid foods, recovers by day 41-50	6. Mild ↓ responsiveness, recovers by day 31-40
7. ↑ thresholds for QHCl aversion: 10-20 fold	7. Same
8. Severe solid food aphagia: a. rat chow pellets - 38.5 days b. dry cat chow - 27.0 days c. moist cat chow - 21.1 days	8. Mild: a. rat chow pellets - 11.2 days b. dry cat chow - 3.2 days c. moist cat chow - 4.7 days
9. Mild mash aphagia: a. rat chow mash - 1.9 days b. pablum - 3.6 days	9. None to mild: a. rat chow mash - 5.8 days b. pablum - 0 days
10. Mild adipsia: 5.4 days	10. Mild: 1.8 days
11. Severe maximum weight loss: 35.6%	11. Mild: 16.3%
12. Severe retardation in recovery of lost weight: 67.1 days	12. Mild: 34.2 days
13. "Finicky": palatability determined by texture, and possibly taste and/or size a. rat chow pellets - starvation b. rat chow mash - hypophagia c. pablum - hypophagia with rapid recovery	13. "Finicky": palatability determined by taste of food: a. hypophagia b. hypophagia c. hyperphagic trend
14. ↓ F:BW, W:BW, W:F ratios during hypophagic period	14. Same
15. Water intake recovers completely with solid food intake (day 41-50)	15. Hypodipsia remains despite complete recovery of solid food intake (day 41-50)
16. ↓ solid food intake during water dep.	16. ↓ water intake during food dep.

APPENDIX

A Labeled cell bodies at representative dorsal and intermediate ganglion levels following lingual and inferior alveolar HRP treatment. Also shown are the HRP-labeled cell bodies in the coronal plane. Dotted lines indicate that these areas became detached in processing the nerves. Separate examination of these tissues indicated no HRP uptake.

LINGUAL & INF. ALVEOLAR (Horizontal)




LINGUAL & INF. ALVEOLAR
ANTERIOR
MOT. V
MOT. V
ANT. SUP. ALVEOLAR & SPHENOPALATINE
MOT. V
MOT. V
DORS.
LAT.
MOT. V
MOT. V
MOT. V
MOT. V
POSTERIOR
MOT. V

References

Abd-el-malek, S. A contribution to the study of the movements of the tongue in animals, with special reference to the cat. J. Anat., 1939, 73, 15-31.

Ables, M., & Benjamin, R.M. Thalamic relay nucleus for taste in albino rats. J. Neurophysiol., 1960, 23, 376-382.

Adolph, E.F. Urges to eat and drink in rats. Am. J. Physiol., 1947, 151, 110-125.

Adolph, E.F., Barker, J.P., & Hoy, P.A. Multiple factors in thirst. Am. J. Physiol., 1954, 178, 538-562.

Albert, D.J., Storlien, L.H., Wood, D.J., & Ehman, G.K. Further evidence for a complex system controlling feeding behavior. Physiol. Behav., 1970, 5, 1075-1082.

Allen, J.D., Stein, G.W., & Long, C.J. The effect of food deprivation on responding for food odor in the rat. Learn. Motiv., 1972, 3(1), 101-107.

Altar, A., & Carlisle, H.J. Intragastric drinking in the rat: Evidence for a role of oropharyngeal stimulation. Physiol. Behav., 1979, 22, 1221-1225.

Alvarado-Mallart, M.R., Batini, C., Buisseret-Delmas, C., & Corvisier, J. Trigeminal representations of the masticatory and extraocular proprioceptors as revealed by horseradish peroxidase retrograde transport. Exp. Brain Res., 1975, 23, 167-179.

Amerine, M.A., Pangborn, R.M., & Roessler, E.B. Principles of Sensory Evaluation of Food. New York: Academic Press, 1965.

Anand, B.K., & Brobeck, J.R. Hypothalamic control of food intake in rats and cats. Yale J. Biol. Med., 1951, 24, 123-140.

Balagura, S., & Coscina, D.V. Periodicity of food intake in the rat as measured by an operant response. *Physiol. Behav.*, 1968, *3*, 641-643.

Bellows, R.T. Time factors in water drinking in dogs. *Am. J. Physiol.*, 1939, *125*, 87-97.

Bellows, R.T. & vanWagenen, W.P. The effect of resection of the olfactory, gustatory, and trigeminal nerves on water drinking in dogs with and without diabetes insipidus. *Am. J. Physiol.*, 1939, *126*, 13-19.

Benjamin, R.M. Absence of deficits in taste discrimination following cortical lesions as a function of the amount of preoperative practice. *J. Comp. Physiol. Psychol.*, 1959, *52*, 255-258.

Benjamin, R.M. Some thalamic and cortical mechanisms of taste. In Y. Zotterman (Ed.), *Olfaction and Taste*. Oxford: Pergamon Press, 1963, 309-329.

Benjamin, R.M., & Akert, K. Cortical and thalamic areas involved in taste discrimination in the albino rat. *J. Comp. Neurol.*, 1959, *111*, 231-260.

Bernard, C. *Lecons sur les Phènomenes de la Vie Communs aux Animaux et aux Vegetaux*. Paris: Bailliere et Fils, 1878, *1*, 111-124.

Berntson, G.G., & Hughes, H.C. Medullary mechanisms for eating and grooming behaviors in the cat. *Exp. Neurol.*, 1974, *44*, 255-265.

Berntson, G.G. & Micco, D.J. Organization of brainstem behavioral systems. *Brain Res. Bull.*, 1976, *1*, 471-483.

Blass, E.M., & Hall, W.G. Drinking termination: Interactions among hydrational, orogastric, and behavioral controls in rats. *Psychol. Rev.*, 1976, *83*(5), 356-374.

Blatt, B., & Lyon, M. The interrelationship of forebrain and midbrain structures involved in feeding behavior. *Acta Neurol. Scand.*, 1968, *44*, 576-595.

Blom, S. Afferent influences on tongue muscle activity. A morphological and physiological study in the cat. Acta Physiol. Scand., 1960, Suppl. 170, 1-97.

Bolles, R.C. The interaction of hunger and thirst in the rat. J. Comp. Physiol. Psychol., 1961, 54, 580-584.

Bolles, R.C. Theory of Motivation. New York: Harper and Row, 1967.

Booth, D.A. Conditioned satiety in the rat. J. Comp. Physiol. Psychol., 1972, 81, 457-471.

Booth, D.A., Toates, F.M., & Platt, S.V. Control system of hunger and its implications in animals and man. In D. Novin, W. Wyrwicka, & G. Bray (Eds.), Hunger: Basic Mechanisms and Clinical Implications. New York: Raven Press, 1976.

Box, B.M., & Mogenson, G.J. Alterations in ingestive behaviors after bilateral lesions of the amygdala in the rat. Physiol. Behav., 1975, 15, 679-688.

Bradley, R.M. Electrophysiological investigations of intravascular taste using perfused rat tongue. Am. J. Physiol., 1973, 224, 300-304.

Braun, J.J. The neocortex and feeding behavior in the rat. J. Comp. Physiol. Psychol., 1975, 89, 507-522.

Brightman, V. Disordered oral sensation and appetite. In The Chemical Senses and Nutrition. New York: Academic Press, 1977.

Brobeck, J.R. Food intake as a mechanism of temperature regulation. Yale J. Biol. Med., 1948, 20, 545-552.

Brobeck, J.R. Energy exchange. In J.F. Fulton (Ed.), Textbook of Physiology (17th Ed.). Philadelphia: Saunders, 1955.

Cabanac, M., Minaire, Y., & Adair, E.R. Influence of internal factors on the pleasantness of a gustative sweet sensation. Communs Behav. Biol., 1968, Part A, 1, 77-82.

Cannon, W.B. The physiological basis of thirst. Proc. Roy. Soc. Lond., 1918, Ser. B, 90, 283-301.

Castro, A.J. The effects of cortical ablations on tongue usage in the rat. Brain Res., 1972, 45, 251-253.

Collier, G. Body weight loss as a measure of motivation in hunger and thirst. Ann. N.Y. Acad. Sci., 1969, 157, 594-609.

Collier, G., Hirsch, E., & Hamlin, P. The ecological determinants of reinforcement in the rat. Physiol. Behav., 1972, 9, 705-716.

Collings, V.B. Human taste response as a function of locus of stimulation on the tongue and soft palate. Perc. Psychophys., 1974, 16, 69-74.

Contreras, R.J. Changes in gustatory nerve discharges with sodium deficiency: A single-unit analysis. Brain Res., 1977, 121, 373-378.

Cooper, S. Muscle spindles in the intrinsic muscles of the human tongue. J. Physiol., 1953, 122, 193-202.

Corbit, J.D. Hyperphagic hyperreactivity to adulteration of drinking water with QHCl. J. Comp. Physiol. Psychol., 1965, 60, 123-124.

Crespi, L.P. Amount of reinforcement and level of performance. Psychol. Rev., 1944, 51, 341-357.

Darian-Smith, I. The trigeminal system. In A. Iggo (Ed.), Handbook of Sensory Physiology, Vol. II, Somatosensory Systems. New York: Springer-Verlag, 1973.

Daunton, N.G. Sensory components of the bite-force response in the rat. J. Comp. Physiol. Psychol., 1977, 91, 203-220.

Davis, J.D., Collins, B.J., & Levine, M.W. Peripheral control of drinking: Gastrointestinal filling as a negative feedback signal, a theoretical and experimental analysis. J. Comp. Physiol. Psychol., 1975, 89, 985-1002.

Davis, J.D., Collins, B.J., & Levine, M.W. Peripheral control of meal size: Interaction of gustatory stimulation and postingestional feedback. In D. Novin, W. Wyrwicka, & G. Bray (Eds.), *Hunger: Basic Mechanisms and Clinical Implications*. New York: Raven Press, 1976.

Davis, J.D., & Levine, M.W. A model for the control of ingestion. *Psychol. Rev.*, 1977, *84*, 379-412.

Dellow, P.G., & Lund, J.P. Evidence for central timing of rhythmical mastication. *J. Physiol. (Lond.)*, 1971, *215*, 1-13.

Dethier, V.G. Feeding and drinking behavior of invertebrates. In C.E. Code (Ed.), *Handbook of Physiology*, sect. 6: *Alimentary Canal*, vol. 1: *Control of Food and Water Intake*. Washington, D.C.: Amer. Physiol. Soc., 1967.

Dethier, V.G., Solomon, R.L., & Turner, L.H. Sensory input and central excitation and inhibition in the blowfly. *J. Comp. Physiol. Psychol.*, 1965, *60*, 303-313.

Doty, R.W., & Bosma, J.F. An electromyographic analysis of reflex deglutition. *J. Neurophysiol.*, 1956, *19*, 44-60.

Dubner, R., Sessle, B.J., & Storey, A.T. *The Neural Basis of Oral and Facial Function*. New York: Plenum Press, 1978.

Eisenman, J., Landgren, S., & Novin, D. Functional organization in the main sensory trigeminal nucleus and in the rostral subdivision of the nucleus of the spinal trigeminal tract in the cat. *Acta Physiol. Scand.*, 1963, *59*, *Suppl. 214*.

Ellison, G.D., & Konorski, J. Separation of the salivary and motor responses in instrumental conditioning. *Science*, 1964, *146*, 1071-1072.

Ellison, G.D., Sorenson, C.A., & Jacobs, B.L. Two feeding syndromes following surgical isolation of the hypothalamus in rats. *J. Comp. Physiol. Psychol.*, 1970, *70*, 173-188.

Emmers, R. Tonic control of water intake via the thalamic taste nucleus. *Ann. N.Y. Acad. Sci.*, 1977, *290*, 124-138.

Emmers, R. Interaction of neural systems which control nutritional balance. *Brain Res.*, 1979, *161*, 411-429.

Epstein, A.N. Water intake without the act of drinking. *Science*, 1960, *131*, 497-498.

Epstein, A.N. Oropharyngeal factors in feeding and drinking. In C.E. Code (Ed.), *Handbook of Physiology*, sect. 6: *Alimentary Canal*, vol. 1: *Control of Food and Water Intake*. Washington, D.C.: Amer. Physiol. Soc., 1967, 197-218.

Epstein, A.N. The lateral hypothalamic syndrome: Its implications for the physiological psychology of hunger and thirst. In E. Stellar & J.M. Sprague (Eds.), *Progr. Physiol. Psychol.*, 1971, *4*. New York: Academic Press.

Epstein, A.N., & Teitelbaum, P. Regulation of food intake in the absence of taste, smell, and other oropharyngeal sensations. *J. Comp. Physiol. Psychol.*, 1962, *55*, 753-759.

Estes, W.K. Discrimination conditioning. II. Effects of a Pavlovian conditioned stimulus upon a subsequently established operant response. *J. Exp. Psychol.*, 1948, *38*, 173-177.

Evered, M.D., & Mogenson, G.J. Regulatory and secondary water intake in rats with lesions of the zona incerta. *Am. J. Physiol.*, 1976, *230*, 1049-1057.

Evered, M.D., & Mogenson, G.J. Impairment in fluid ingestion in rats with lesions of the zona incerta. *Am. J. Physiol.*, 1977, *233*, R53-R58.

Falk, J.L. The behavioral regulation of water-electrolyte balance. In M.R. Jones (Ed.), *Nebraska Symposium on Motivation*. Lincoln: Univ. of Nebraska Press, 1961.

Fitzsimons, J.T. Thirst. Physiol. Rev., 1972, 52, 468-561.

Frank, M. The classification of mammalian afferent taste nerve fibers. Chem. Senses & Flavor, 1974, 1, 53-60.

Gentile, R.L. Depression of intake by saccharin adulteration: The role of taste quality in the control of food intake. In Proceedings of the Third International Symposium on Olfaction and Taste (3rd Ed.). New York: Rockefeller Univ. Press, 1968, 601-607.

Gold, R.M. Aphagia and adipsia following unilateral and bilaterally asymmetrical lesions in rats. Physiol. Behav., 1967, 2, 211-220.

Goodwin, G.M., & Luschei, E.S. Effects of destroying spindle afferents from jaw muscles on mastication in monkeys. J. Neurophysiol., 1974, 37, 967-981.

Grant, G., & Arvidson, J. Transganglionic degeneration in trigeminal primary sensory neurons. Brain Res., 1975, 95, 265-279.

Greene, E.C. Anatomy of the Rat. New York: Hafner, 1935.

Greenwood, L.F., & Sessle, B.J. Pain, brainstem mechanisms, and motor function. In B.J. Sessle & A.G. Hannam (Eds.), Mastication and Swallowing: Biological and Clinical Correlates. Toronto: Univ. Toronto Press, 1976, 108-119.

Gregg, J.M. A surgical approach to the ophthalmic-maxillary nerve trunks in the rat. J. Dent. Res., 1973, 52(2), 392.

Gregg, J.M., & Dixon, A.D. Somatotopic organization of the trigeminal ganglion in the rat. Arch. Oral Biol., 1973, 18, 487-498.

Grill, H.J., & Norgren, R. The taste reactivity test. II. Mimetic responses to gustatory stimuli in chronic thalamic and chronic decerebrate rats. Brain Res., 1978, 143, 281-297.

Grossman, S.P., & Grossman, L. Food and water intake in rats with parasaggital knife cuts medial or lateral to the lateral hypothalamus. J. Comp. Physiol. Psychol., 1971, 74, 148-156.

Guttman, N. Operant conditioning, extinction, and periodic reinforcement in relation to concentration of sucrose used as a reinforcing agent. J. Exp. Psychol., 1953, 46, 213-224.

Hagstrom, E.C., & Pfaffmann, C. The relative taste effectiveness of different sugars for the rat. J. Comp. Physiol. Psychol., 1959, 52, 259-262.

Hall, W.G. Feeding and behavioral activation in infant rats. Science, 1979, 205, 206-209.

Halpern, B.P. Functional anatomy of the tongue and mouth of mammals. In J.A.W.M. Weijnen & J. Mendelson (Eds.), Drinking Behavior: Oral Stimulation, Reinforcement, and Preference. New York: Plenum Press, 1977, 1-92.

Hamilton, C.L. Rat's preference for high fat diets. J. Comp. Physiol. Psychol., 1964, 58, 459-460.

Harlow, H.F. Motivation as a factor in the acquisition of new responses. In Current Theory and Research in Motivation. Lincoln: Univ. of Nebraska Press, 1953.

Harris, L.J., Clay, J., Hargreaves, F.J., & Ward, A. Appetite and choice of diet: The ability of the vitamin B deficient rat to discriminate diets containing and lacking the vitamin. Proc. Roy. Soc., Lond., Ser. B, 1933, 113, 161-190.

Harris, R., Jacquin, M., & Zeigler, H.P. Dissociation of hunger and self-stimulation by trigeminal denervation in the rat. Physiol. Behav., in press.

Henkin, R.I., & Christiansen, R.L. Taste localization on the tongue, palate, and pharynx of normal man. J. Appl. Physiol., 1967a, 22, 316-320.

Henkin, R.I., & Christiansen, R.L. Taste thresholds in patients with dentures. J. Am. Dent. Assoc., 1967b, 75, 118-120.

Herrick, C.J. The central gustatory paths in the brains of bony fishes. J. Comp. Neurol., 1905, 15, 375-456.

Hiiemae, K.M., & Ardran, G.M. A cinefluorographic study of mandibular movement during feeding in the rat. J. Zool. Lond., 1968, 154, 139-154.

Holman, G.L. Intragastric reinforcement effect. J. Comp. Physiol. Psychol., 1969, 69, 432-441.

Huang, Y.H., & Mogenson, G.J. Neural pathways mediating drinking and feeding in rats. Exp. Neurol., 1972, 37, 269-286.

Hull, C.L. Principles of Behavior. New York: Appleton-Century-Crofts, 1943.

Hulse, S.H., & Suter, S. One-drop licking in rats. J. Comp. Physiol. Psychol., 1968, 66, 536-539.

Hulse, S.H., & Suter, S. Emitted and elicited behavior: An analysis of some learning mechanisms associated with fluid intake in rats. Learn. Motiv., 1970, 1, 304-315.

Jacobs, H.L., & Sharma, K.N. Taste versus calories: Sensory and metabolic signals in the control of food intake. In P.J. Morgane (Ed.), Neural Regulation of Food and Water Intake, Ann. N.Y. Acad. Sci., 1969, 157, 1084-1125.

Jacquin, M. Trigeminal orosensory deafferentation in the rat: Effects upon a food-reinforced operant response. Presented at Eastern Psychol. Assoc., Washington, D.C., 1978.

Jacquin, M., & Zeigler, H.P. Peripheral trigeminal mechanisms and drinking in the rat. Presented at Eastern Psychol. Assoc., Washington, D.C., 1978.

Jacquin, M., & Zeigler, H.P. Living from hand to mouth: Effects of orosensory deafferentation upon feeding patterns in rats. Neuroscience Abst., 1979, No. 712, p.219.

Janowitz, H.D., Hanson, M.E., & Grossman, M.I. Effects of intravenously administered glucose on food intake in the dog. Am. J. Physiol., 1949, 156, 87-91.

Janowitz, H.D., & Grossman, M.I. Effect of variations in nutritive density in intake of food of dogs and rats. Am. J. Physiol., 1949a, 158, 184-193.

Janowitz, H.D., & Grossman, M.I. Some factors affecting the food intake of normal dogs and dogs with esophagostomy and gastric fistula. Am. J. Physiol., 1949b, 159, 143-148.

Janowitz, H.D., & Hollander, F. The time factors in the adjustment of food intake to varied caloric requirement in the dog: A study of the precision of appetite regulation. Ann. N.Y. Acad. Sci., 1955, 63, 56-67.

Jerge, C.R. The organization and function of the trigeminal mesencephalic nucleus. J. Neurophysiol., 1963, 26, 379-392.

Johanson, I.B., & Hall, W.G. Appetitive learning in 1-day-old rat pups. Science, 1979, 205, 419-421.

Kaplick, M. Concerning the presence, distribution, and histological aspects of the taste buds on the roof of the mouth of certain mammals, expecially rodents. Z. Zell., 1953, 38, 571-590.

Kawamura, Y. Recent concepts of the physiology of mastication. In P.H. Staples (Ed.), Advances in Oral Biology. London: Academic Press, 1964, 77-109.

Keesey, R.E. Weight regulation and the lateral hypothalamic feeding syndrome. Bull. Neurosci. Res. Progr., 1973, 11, 342-353.

Keesey, R.E., & Powley, T.L. Hypothalamic regulation of body weight. Am. Scient., 1975, 63, 558-565.

Kemble, E.D., Studelska, D.R., & Schmidt, M.K. Effects of central amygdaloid nucleus lesions on ingestion, taste reactivity, exploration, and taste aversion. Physiol. Behav., 1979, 22, 789-793.

Kerr, F.W.L. Neuroplasticity of primary afferents in the neonatal cat and some results of early deafferentation of the trigeminal spinal nucleus. J. Comp. Neurol., 1975, 193, 305-328.

Kidokoro, Y., Kubota, K., Shuto, S., & Sumino, R. Reflex organization of cat masticatory muscles. J. Neurophysiol., 1968, 31, 695-708.

Kiefer, S., & Braun, J. Absence of differential associative responses to novel and familiar taste stimuli in rats lacking gustatory neocortex. J. Comp. Physiol. Psychol., 1977, 91, 498-507.

Kimble, G.A. Hilgard and Marquis' Conditioning and Learning (2nd Ed.). New York: Appleton-Century-Crofts, 1961.

Kissileff, H.R. Oropharyngeal control of prandial drinking. J. Comp. Physiol. Psychol., 1969, 67, 309-319.

Kissileff, H.R. Free feeding in normal and "recovered lateral" rats monitored by a pellet-detecting eatometer. Physiol. Behav., 1970, 5(2), 163-170.

Kissileff, H.R. Nonhomeostatic controls of drinking. In A.N. Epstein, H.R. Kissileff, & E. Stellar (Eds.), The Neuropsychology of Thirst: New Findings and Advances in Concepts. Washington, D.C.: Winston and Sons, 1973.

Kolb, B., & Nonneman, A.J. Prefrontal cortex and the regulation of food intake in the rat. J. Comp. Physiol. Psychol., 1975, 88, 806-815.

Kolb, B., Whishaw, I.Q., & Schallert, T. Aphagia, behavior sequencing, and body weight set point following orbital frontal lesions in rats. *Physiol. Behav.*, 1977, *19*, 93-103.

Konorski, J. *Integrative Activity of the Brain: An Interdisciplinary Approach*. Chicago: Univ. of Chicago Press, 1967.

Kratz, C.M., & Levitsky, D.A. Postingestive effects of quinine on intake of nutritive and non-nutritive substances. *Physiol. Behav.*, 1978, *21*, 851-854.

Kratz, C.M., & Levitsky, D.A. Dietary obesity: Differential effects with self-selection and composite diet feeding techniques. *Physiol. Behav.*, 1979, *22*(2), 245-249.

Kupferman, I. Feeding behavior in *Aplysia*: A simple system for the study of motivation. *Behav. Biol.*, 1974, *10*, 1-26.

Kutscher, C.L. Species differences in the interaction of feeding and drinking. In P.J. Morgane (Ed.), *Neural Regulation of Food and Water Intake*. *Ann. N.Y. Acad. Sci.*, 1969, *157*, 539-551.

LaRue, C., & LeMagnen, J. Responses alimentaires du rat anosmique. *C.R. Soc. Biol.*, 1967, *00*, 161-172.

LaRue, C.G., & LeMagnen, J. The olfactory control of meal pattern in rats. *Physiol. Behav.*, 1972, *9*, 817-821.

Lashley, K.S. Experimental analysis of instinctive behavior. *Psychol. Rev.*, 1938, *45*, 445-471.

LeMagnen, J. Hyperphagie provoquée chez le rat blanc par altération due mécanisme de satiété périphérique. *Comptes Rendus des Séances de la Société de Biologie*, 1956, *150*, 32.

LeMagnen, J. Influence de l'état de faim sur la manifestation d'un appétit discriminatif par le rat blanc. *Comptes Rendus des Séances de la Société de Biologie*, 1960, *154*, 70-73.

LeMagnen, J. Peripheral and systemic actions of food in the caloric regulation of intake. *Ann. N.Y. Acad. Sci.*, 1969, *157*, 1126-1156.

LeMagnen, J. Advances in studies on the physiological control and regulation of food intake. In E. Stellar and J.M. Sprague (Eds.), *Progr. In Physiol. Psychol.*, 1971, *4*. New York: Academic Press.

LeMagnen, J., & Tallon, S. Enregistrement et analyse préliminaire de la "périodicité" alimentaire spontanée chez le rat blanc. *J. Physiol. (Paris)*, 1963, *55*, 286-297.

LeMagnen, J., & Tallon, S. La périodicité spontanée de la prise d'aliments ad libitum du rat blanc. *J. Physiol. (Paris)*, 1966, *58*, 323-349.

LeMagnen, J., & Tallon, S. L'effect du juene prealable sur les caracteristiques temporelles de la prise d'aliments chez le rat. *J. Physiol. (Paris)*, 1968, *58*, 143-154.

LeMagnen, J., & Devos, M. Metabolic correlates of meal onset in the free food intake of rats. *Physiol. Behav.*, 1970, *5*, 805-814.

Levine, M.S., Ferguson, N., Kreinick, C.J., Gustafson, J.W., and Schwartzbaum, J.S. Sensorimotor dysfunctions and aphagia and adipsia following pallidal lesions in rats. *J. Comp. Physiol. Psychol.*, 1971, *77*, 282-293.

Levine, R.R. Extratelencephalic efferent pathways and feeding behavior in the pigeon. Unpublished doctoral dissertation, City University of New York, 1977.

Levitsky, D.A. Feeding patterns of rats in response to fasts and changes in environmental conditions. *Physiol. Behav.*, 1970, *5*, 291-300.

Lewis, D., & Dandy, W. The course of nerve fibers transmitting sensation of taste. *Arch. Surg.*, 1930, *21*, 249-288.

Lidsky, T.I., Buchwald, N.A., Hull, C.D., & Levine, M.S. Pallidal and entopeduncular single unit activity in cats during drinking. Electroencephalog. Clin. Neurophysiol., 1975, 39, 79-84.

Lidsky, T.I., Robinson, J.H., Denaro, F.J., & Weinhold, P.M. Trigeminal influences on entopeduncular units. Brain Res., 1978, 141, 227-234.

Lindquist, C., & Martensson, A. Reflex responses induced by stimulation of hypoglossal afferents. Acta Physiol. Scand., 1969, 77, 234-240.

Lovick, T.A. The behavioral repertoire of precollicular decerebrate rats. J. Physiol., 1972, 226, 4-6.

Lowe, A.A. Neural mechanisms involved in tongue motility. Unpublished doctoral dissertation, Univ. of Toronto, 1976.

Lowe, A.A., & Sessle, B.J. Tongue activity during respiration, jaw opening, and swallowing in cat. Can. J. Physiol. and Pharmacol., 1973, 51, 1009-1011.

Lund, J.P., & Dellow, P.G. Rhythmical masticatory activity of hypoglossal motoneurons responding to an oral stimulus. Exp. Neurol., 1973, 40, 234-246.

Luschei, E.S., & Goodwin, G.M. Patterns of mandibular movement and jaw muscle activity during mastication in monkeys. J. Neurophysiol., 1974, 37, 954-966.

Luschei, E.S., & Goodwin, G.M. Role of monkey precentral cortex in the control of voluntary jaw movements. J. Neurophysiol., 1975, 38, 146-157.

Lyon, M., Halpern, M., & Mintz, E. The significance of the mesencephalon for coordinated feeding behavior. Acta Neurol. Scand., 1968, 44, 323-346.

MacDonnell, M.F., & Flynn, J.P. Sensory control of hypothalamic attack. Anim. Behav., 1966, 14, 399-405.

Marshall, J.F., Turner, B.H., & Teitelbaum, P. Sensory neglect produced by lateral hypothalamic damage. Science, 1971, 174, 523-525.

Marshall, J.F., & Teitelbaum, P. Further analysis of sensory inattention following lateral hypothalamic damage in rats. J. Comp. Physiol. Psychol., 1974, 86, 375-395.

Marshall, J.F., Richardson, J.S., & Teitelbaum, P. Nigrostriatal bundle damage and the lateral hypothalamic syndrome. J. Comp. Physiol. Psychol., 1974, 87, 808-830.

Marwine, A., & Zeigler, H.P. Trigeminal deafferentation and ingestive behavior in the rat. Presented at Eastern Psychol. Assoc., New York, 1975.

Mayer, J. Genetic, traumatic, and environmental factors in the etiology of obesity. Physiol. Rev., 1953, 33, 472-508.

Mayer, J. Regulation of energy intake and the body weight: The glucostatic theory and the lipostatic hypothesis. Ann. N.Y. Acad. Sci., 1955, 63, 15-42.

McIntyre, A.K. Afferent limb of the myotatic reflex arc. Nature, 1951, 168, 168-169.

Mendelson, J., & Chillag, D. Tongue cooling: A new reward for thirsty rodents. Science, 1970, 170, 1418-1421.

Mendelson, J., & Zec, R. Effects of lingual denervation and desalivation on airlicking in the rat. Physiol. Behav., 1972, 8, 711-714.

Miller, I.J. Gustatory receptors of the palate. In Katsuki et al. (Eds.), Food Intake and Chemical Senses. Tokyo: Univ. of Tokyo Press, 1977, 173-185.

Miller, I.J., Gomez, M.M., & Lubarsky, E.H. Distribution of the facial nerve to taste receptors in the rat. Chem. Senses and Flavor, 1978, 3(4), 397-411.

Miller, M.G. The effect of trigeminal deafferentation on food and water intake in the rat. Neuroscience Abst., 1977, No. 506.

Miller, M.G. Behavioral parameters of body weight regulation in the pigeon (*Columba livia*). *J. Comp. Physiol. Psychol.*, 1978a, *92*, 1014-1024.

Miller, M.G. Trigeminal orosensory control of feeding behavior. Presented at Eastern Psychol. Assoc., Washington, D.C., 1978b.

Miller, M.G. The effects of trigeminal deafferentation on caloric regulation of intake in response to dilution. Presented at Eastern Psychol. Assoc., Philadelphia, 1979.

Miller, M.G. Trigeminal deafferentation and ingestive behavior in the rat. Unpublished MS, 1980.

Miller, M.G., Zeigler, H.P., & Miller, A.E. Trigeminal deafferentation and feeding behavior patterns in the pigeon (*Columba livia*). *J. Comp. Physiol. Psychol.*, 1978, *92*, 1025-1040.

Miller, N.E. Behavioral and physiological techniques: Rationale and experimental designs for combining their use. In C.E. Code (Ed.), *Handbook of Physiology*, sect. 6: *Alimentary Canal*, vol. 1: *Control of Food and Water Intake*. Washington, D.C.: Amer. Physiol. Soc., 1967, 51-62.

Miller, N.E., & Kessen, M.L. Reward effects of food via stomach fistula compared with those of food via mouth. *J. Comp. Physiol. Psychol.*, 1952, *45*, 555-564.

Miller, N.E., Sampliner, R.I., & Woodrow, P. Thirst-reducing effects of water by stomach fistula vs. water by mouth measured by both a consummatory and an instrumental response. *J. Comp. Physiol. Psychol.*, 1957, *50*, 1-5.

Milner, P.M. Physiological Psychology. New York: Holt, Rinehart, & Winston, 1970

Mook, D.G. Oral and postingestional determinants of the intake of various solutions in rats with esophageal fistulas. J. Comp. Physiol. Psychol., 1963, 56(4), 645-659.

Mook, D.G. Saccharin preference in the rat: Some unpalatable findings. Psychol. Rev., 1974, 81(6), 475-490.

Moon, R., & Zeigler, H.P. Food preferences in the pigeon. Physiol. Behav., 1979, 22, 1171-1182.

Morgane, P.J. The function of the limbic and rhinic forebrain-limbic midbrain systems and reticular formation in the regulation of food and water intake. Ann. N.Y. Acad. Sci., 1969, 157, 806-848.

Morimoto, T., & Kawamura, Y. Properties of tongue and jaw movements elicited by stimulation of the orbital gyrus in the cat. Arch. Oral Biol., 1973, 18, 361-372.

Morrison, S.D. The constancy of the energy expended by rats on spontaneous activity, and the distribution of activity between feeding and non-feeding. J. Physiol., 1968, 197, 305-323.

Mountcastle, V.B. Neural mechanisms in somesthesia. In V.B. Mountcastle (Ed.), Medical Physiology, vol. 1. St. Louis: Mosby, 1974, 307-347.

Mufson, E.J., & Wampler, R.S. Weight regulation with palatable food and liquids in rats with lateral hypothalamic lesions. J. Comp. Physiol. Psychol., 1972, 80, 382-392.

Mufson, E.J., Balagura, S., & Riss, W. Degeneration in pathways to the pontine taste area in relation to aphagia and adipsia. Neuroscience Abst., 1976, 436.

Mufson, E.J., & Riss, W. Degenerated neuroanatomical pathways associated with aphagia and adipsia following lateral hypothalamic lesions. Neuroscience Abst., 1977, 165.

Nakamura, Y., Nagashima, H., & Mori, S. Bilateral effects of the afferent impulses from the masseteric muscle on the trigeminal motoneuron of the cat. Brain Res., 1973, 57, 15-27.

Nicolaidis, S., & Rowland, N. Long-term self-intravenous "drinking" in the rat. J. Comp. Physiol. Psychol., 1974, 87, 1-15.

Nicolaidis, S., & Rowland, N. Intravenous self-feeding: Long-term regulation of energy balance in rats. Science, 1977, 195, 589-591.

Norgren, R. Gustatory responses in the hypothalamus. Brain Res., 1970, 21, 63-77.

Norgren, R. Gustatory afferents to ventral forebrain. Brain Res., 1974, 81, 285-295.

Norgren, R. Taste pathways to hypothalamus and amygdala. J. Comp. Neurol., 1976, 166, 17-30.

Norgren, R., & Leonard, C. Ascending central gustatory pathways. J. Comp. Neurol., 1973, 150, 217-238.

Norgren, R., & Pfaffmann, C. The pontine taste area in the rat. Brain Res., 1975, 91, 99-117.

Nowlis, G.H. From reflex to representation: Taste-elicited tongue movements in the human newborn. In J.M. Weiffenbach (Ed.), Taste and Development: The Genesis of Sweet Preference. Bethesda: DHEW Publ. No. (NIH) 77-1068, 1977, 190-204.

Nowlis, G.H., Braun, J.J., & Norgren, R. The central gustatory system: Ingestion and rejection functions after lesions. Abst. 6th Int. Conf. Physiol. Food and Fluid Intake, 1977.

Oakley, B. Impaired operant behavior following lesions of the thalamic taste nucleus. J. Comp. Physiol. Psychol., 1965, 59, 202-210.

Oakley, B., & Benjamin, R.M. Neural mechanisms of taste. Physiol. Rev., 1966, 46(2), 173-211.

Oatley, K., & Dickinson, A. Air drinking and the measurement of thirst. Anim. Behav., 1970, 18, 259-265.

Ogawa, H., Sato, M., & Yamashita, S. Multiple sensitivity of chorda tympani fibers of the rat and hamster to gustatory and thermal stimulation. J. Physiol., 1968, 199, 223-240.

O'Laughlin, E., & Feldman, S. Recovery from hypothalamic aphagia after a single intrahypothalamic injection of apomorphine. Neuroscience Abstracts, 1976, 437.

Panksepp, J., & Ritter, M. Mathematical analysis of energy regulatory patterns of normal and diabetic rats. J. Comp. Physiol. Psychol., 1975, 89, 1019-1028.

Parker, S.W., & Feldman, S.M. Effects of mesencephalic lesions on feeding behavior in rats. Exp. Neurol., 1967, 17, 313-326.

Patten, R.L., & Rudy, J.W. Orienting driving classical conditioning: Acquired vs. unconditioned responding. Psychon. Sci., 1967, 7, 27-8.

Peck, J. Rats defend different body weights depending on palatability and accessibility of their food. J. Comp. Physiol. Psychol., 1978, 92, 555-570.

Pfaffmann, C. Taste preference and aversion following lingual denervation. J. Comp. Physiol. Psychol., 1952, 45, 393-400.

Pfaffmann, C. The pleasures of sensation. Psychol. Rev., 1960, 67, 253-268.

Pfaffmann, C. The sensory and motivating properties of the sense of taste. In M.R. Jones (Ed.), Nebraska Symposium on Motivation. Lincoln: Univ. of Nebraska Press, 1961, 71-108.

Pfaffmann, C., Frank, M., & Norgren, R. Neural mechanisms and behavioral aspects of taste. Ann. Rev. Psychol., 1979, 30, 283-325.

Powley, T.L. The ventromedial hypothalamic syndrome, satiety, and a cephalic phase hypothesis. *Psychol. Rev.*, 1977, 84, 89-126.

Richter, C.P. Salt taste thresholds of normal and adrenalectomized rats. *Endocrinol.*, 1939, *24*, 367-371.

Richter, C.P. Salt appetite of mammals: Its dependence on instinct and metabolism. In M. Autuori (Ed.), *L'Instinct dans le Comportement des Animaux et de L'Homme*. Paris: Masson, 1956, 577-629.

Robins, M.W. Biting loads generated by the laboratory rat. *Arch. Oral Biol.*, 1977, *22*, 43-47.

Rodgers, W.L., Epstein, A.N., & Teitelbaum, P. Lateral hypothalamic aphagia: Motor failure or motivational deficit? *Am. J. Physiol.*, 1965, *208*, 334-342.

Rolls, B.J., & Rolls, E.T. Effects of lesions of the basolateral amygdala on fluid intake in the rat. *J. Comp. Physiol. Psychol.*, 1973, *83*, 240-247.

Rowland, N. Regulatory drinking: Do the physiological substrates have an ecological niche? *Biobehav. Rev.*, 1977, *1*, 261-272.

Rowland, N., Grossman, S.P., & Grossman, L. Zona incerta lesions: Regulatory drinking deficits to intravenous NaCl, angiotensin, but not to salt in the food. *Physiol. Behav.*, 1979, *23*, 745-750.

Rozin, P., & Kalat, J.W. Specific hungers and poison avoidance as adaptive specializations of learning. *Psychol. Rev.*, 1971, *78*, 459-484.

Sato, M. The effect of temperature change on the response of taste receptors. In Y. Zotterman (Ed.), *Olfaction and Taste I*. New York: Macmillan, 1963, 151-164.

Scott, J.W., & Chafin, B.R. Origin of olfactory projections to lateral hypothalamus and nuclei gemini of the rat. Brain Res., 1975, 88, 64-68.

Sessle, B.J. Identification of alpha and gamma trigeminal motoneurons and effects of stimulation of amygdala, cerebellum, and cerebral cortex. Exp. Neurol., 1977a, 54, 303-322.

Sessle, B.J. Modulation of alpha and gamma motoneurons by various peripheral stimuli. Exp. Neurol., 1977b, 54, 323-339.

Sessle, B.J., & Greenwood, L.F. Peripheral influences on alpha and gamma motoneurons. In D.J. Anderson & B. Matthews (Eds.), Mastication. Wright: Bristol, 1976, 174-183.

Sessle, B.J., & Hannam, A.G. (Eds.). Mastication and Swallowing: Biological and Clinical Correlates. Toronto: Univ. of Toronto Press, 1976.

Seward, J.P. Secondary reinforcement as tertiary motivation: A revision of Hull's revision. Psychol. Rev., 1950, 57, 362-374.

Seward, J.P. Experimental evidence for the motivating function of reward. Psychol. Bull., 1951, 48, 130-149.

Seward, J.P. Introduction to a theory of motivation in learning. Psychol. Rev., 1952, 59, 405-413.

Seward, J.P. Drive, incentive, and reinforcement. Psychol. Rev., 1956, 63, 195-203.

Share, I., Martyniuk, E., & Grossman, M.I. Effect of prolonged intragastric feeding on oral food intake in dogs. Am. J. Physiol., 1952, 169, 229-235.

Sheffield, F.D., & Roby, T.B. Reward value of a non-nutritive sweet taste. J. Comp. Physiol. Psychol., 1950, 43, 471-481.

Sherrington, C.S. Integrative Activity of the Nervous System. Cambridge: Cambridge Univ. Press, 1906.

Sherrington, C.S. Reflexes elicitable in the cat from pinna, vibrissae, and jaws. J. Physiol. (Lond.), 1917, 51, 404-431.

Smith, D.A. Increased perioral responsiveness: A possible explanation for the switching of behavior observed during lateral hypothalamic stimulation. Physiol. Behav., 1972, 8, 617-621

Smith, R.L. The ascending fiber projections from the principal sensory trigeminal nucleus in the rat. J. Comp. Neurol., 1973, 148, 423-446.

Snowdon, C.T. Motivation, regulation, and the control of meal parameters with oral and intragastric feeding. J. Comp. Physiol. Psychol., 1969, 69, 91-100.

Snowdon, C.T. Gastrointestinal sensory and motor control of food intake. J. Comp. Physiol. Psychol., 1970, 71, 68-76.

Spence, K.W. Behavior Theory and Conditioning. New Haven: Yale Univ. Press, 1956.

Stellar, E. The physiology of motivation. Psychol. Rev., 1954, 61, 5-22.

Stellar, E., & Teitelbaum, P. Recovery from failure to eat produced by hypothalamic lesions. Science, 1954, 120, 894.

Stricker, E.M. Influence of saliva on feeding behavior in the rat. J. Comp. Physiol. Psychol., 1970, 70, 103-112.

Stricker, E.M., & Zigmond, M.J. Recovery of function after damage to central catecholamine-containing neurons: A neurochemical model for the lateral hypothalamic syndrome. In E. Stellar & J.M. Sprague (Eds.), Progress in Psychobiology and Physiological Psychology, vol. 6. New York: Academic Press, 1976, 121-187.

Sumino, R., & Nakamura, Y. Synaptic potentials of hypoglossal motoneurons and a common inhibitory interneuron in the trigemino-hypoglossal reflex. Brain Res., 1974, 73, 439-454.

Szentagothai, J. Anatomical considerations in monosynaptic reflex arcs. J. Neurophysiol., 1948, 11, 445-454.

Takaori, S., Sasa, M., & Fukuda, N. Responses of posterior hypothalamic neurons to electrical stimulation of the inferior alveolar nerve and distension of stomach with cold and warm water. Brain Res., 1968, 11, 225-237.

Taub, E., Heitman, R., & Barro, G. Alertness, level of activity, and purposive movement following somatosensory deafferentation in monkeys. Ann. N.Y. Acad. Sci., 1977, 290, 348-364.

Teitelbaum, P. Sensory control of hypothalamic hyperphagia. J. Comp. Physiol. Psychol., 1955, 48, 156-163.

Teitelbaum, P. Appetite. Proc. Am. Phil. Soc., 1964, 108, 464-472.

Teitelbaum, P. Physiological Psychology. Englewood Cliffs: Prentice-Hall, 1967.

Teitelbaum, P. Levels of integration of the operant. In W.K. Honig & J.E.R. Staddon (Eds.), Handbook of Operant Behavior. Englewood Cliffs: Prentice-Hall, 1977.

Teitelbaum, P., & Epstein, A.N. The lateral hypothalamic syndrome: Recovery of feeding and drinking after lateral hypothalamic lesions. Psychol. Rev., 1962, 69, 74-90.

Teitelbaum, P., & Epstein, A.N. The role of taste and smell in the regulation of food and water intake. In Y. Zotterman (Ed.), Olfaction and Taste. London: Pergamon, 1963, 347-360.

Thexton, A.J. Oral reflexes elicited by mechanical stimulation of palatal mucosa in the cat. *Arch. Oral Biol.*, 1973, *18*, 971-980.

Thomas, D.W., & Mayer, J. Meal taking and regulation of food intake by normal and hypothalamic hyperphagic rats. *J. Comp. Physiol. Psychol.*, 1968, *66*, 642-653.

Towbin, E.J. Gastric distension as a factor in the satiation of thirst in esophagostomized dogs. *Am. J. Physiol.*, 1949, *159*, 533-541.

Turner, B.H. Sensorimotor syndrome produced by lesions of the amygdala and lateral hypothalamus. *J. Comp. Physiol. Psychol.*, 1973, *82*, 37-47.

Twitchell, T.E. Sensory factors in purposive movement. *J. Neurophys.* 1954, *14*, 239-254.

Ungerstedt, U. Is interruption of the nigrostriatal dopamine system producing the "lateral hypothalamic syndrome"? *Acta Physiol. Scand.*, 1970, *80*, 354-364.

Waldbillig, R.J., & Lynch, W.C. Oroesophageal factors in the patterning of drinking. *Physiol. Behav.*, 1979, *22*, 205-209.

Wayner, M. Specificity of behavioral regulation. *Physiol. Behav.*, 1974, *12*, 851-869.

Weijs, W.A., & Dantuma, R. Electromyography and mechanics of mastication in the albino rat. *J. Morph.*, 1975, *146*, 1-34.

Welker, W.I. Principles of organization of the ventrobasal complex in mammals. *Brain Behav. Evol.*, 1973, *7*, 253-336.

Wolf, G., & DiCara, L. Impairments in sodium appetite after lesions of gustatory thalamus: Replication and extension. *Behav. Biol.*, 1974, *10*, 105-112.

Wolgin, D.L., & Teitelbaum, P. Role of activation and sensory stimuli in recovery from lateral hypothalamic damage in the cat. *J. Comp.* Physiol. Psychol., 1978, 92, 474-500.

Woods, J.W. Behavior of chronic decerebrate rats. *J. Neurophysiol.*, 1964, *27*, 635-644.

Wyrwicka, W. Conditioned behavioral analysis of feeding mechanisms. In C.E. Code (Ed.), *Handbook of Physiology*, sect. 6: *Alimentary Canal*, vol. 1: *Control of Food and Water Intake*. Washington, D.C.: Am. Physiol. Soc., 1967, 63-78.

Wyrwicka, W. Sensory regulation of food intake. *Physiol. Behav.*, 1969, *4*, 853-858.

Wyrwicka, W., & Chase, M.H. Projections from the buccal cavity to brainstem sites involved in feeding behavior. *Exp. Neurol.*, 1970, *27*, 512-519.

Wyrwicka, W., Chase, M.H., & Clemente, C.D. The effects of lateral hypothalamic lesions on the masseteric reflex. *Anatom. Rec.*, 1975, *181*, 514.

Yokota, T., Suzuki, K., & Nakano, K. Reflex control of extrinsic tongue muscle activities by lingual mechanoreceptors. *Jap. J. Physiol.*, 1974, *24*, 73-91.

Young, P.T. Reversal of food preference of the white rat through controlled prefeeding. *J. Gener. Psychol.*, 1940, *22*, 33-66.

Young, P.T. The role of hedonic processes in motivation. In M.R. Jones (Ed.), *Nebraska Symposium on Motivation*. Lincoln: Univ. of Nebraska Press, 1955, 193-238.

Young, P.T. Palatability: The hedonic response to foodstuffs. In C.E. Code (Ed.), *Handbook of Physiology*, sect. 6: *Alimentary Canal*, vol.

1: Control of Food and Water Intake. Washington, D.C.: Am. Physiol. Soc., 1967, 353-366.

Young, R.C., Gibbs, J., Antin, J., Holt, J., & Smith, G.P. Absence of satiety during sham feeding in the rat. J. Comp. Physiol. Psychol., 1974, 87, 795-800.

Zeaman, D. Response latency as a function of the amount of reinforcement. J. Exp. Psychol., 1949a, 39, 466-483.

Zeaman, D. An application of ${}_{S}E_{R}$ quantification procedure. Psychol. Rev., 1949b, 56, 341-350.

Zeigler, H.P. Trigeminal deafferentation and hunger in the pigeon (Columba livia). J. Comp. Physiol. Psychol., 1975a, 89, 827-844.

Zeigler, H.P. Dissociation of operant and consummatory responses by trigeminal deafferentation in the pigeon. Physiol. Behav., 1975b, 14, 871-874.

Zeigler, H.P. Feeding behavior in the pigeon. In J. Rosenblatt, R.A. Hinde, C. Beer, & E. Shaw (Eds.), Advances in the Study of Behavior, vol. 7. New York: Academic Press, 1976, 285-389.

Zeigler, H.P. Trigeminal deafferentation and feeding behavior in the pigeon: Dissociation of tonic and phasic effects. Ann. N.Y. Acad. Sci., 1977, 290, 331-345.

Zeigler, H.P., & Feldstein, S. A feedometer for the pigeon. J. Exp. Anal. Behav., 1971, 16, 181-187.

Zeigler, H.P., & Karten, H.J. Brain mechanisms and feeding behavior in the pigeon (Columba livia): I. Quinto-frontal structures. J. Comp. Neurol., 1973a, 152, 59-82.

Zeigler, H.P. The trigeminal system and ingestive behavior. In E. Satinoff and P. Teitelbaum (Eds.), Handbook of Behavioral Neurobiology: Motivation. Plenum Press: New York, 1981.

Zeigler, H.P., & Karten, H.J. Brain mechanisms and feeding behavior in the pigeon (*Columba livia*): II. Analysis of feeding behavior deficits following lesions of quinto-frontal structures. *J. Comp. Neurol.*, 1973b, *152*, 83-102.

Zeigler, H.P., & Karten, H.J. Central trigeminal structures and the lateral hypothalamic syndrome in the rat. *Science*, 1974, *186*, 636-638.

Zeigler, H.P., Miller, M.G., & Levine, R.R. Trigeminal nerve and eating in the pigeon (*Columba livia*): Neurosensory control of the consummatory response. *J. Comp. Physiol. Psychol.*, 1975, *89*, 845-858.

Zlatin, M.A. Development of speech, language, auditory, and oral function in the presence of congenital sensory neuropathy. In J.F. Bosma (Ed.), *Third Symposium on Oral Sensation and Perception. The Mouth of the Infant*. Springfield: Thomas, 1972, 381-390.

Zweers, G.A. Structure, movement, and myography of the feeding apparatus of the Mallard. A functional study of anatomy. *Neth. J. Zool.*, 1974, *24*, 323-467.