CASE WESTERN RESERVE UNIVERSITY

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Date June 17, 1991

# GROWTH AND DEVELOPMENT FOLLOWING EXPERIMENTAL RESTRICTION OF TRANSVERSE MAXILLARY GROWTH OF THE RAT

by

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Submitted in partial fulfillment of the requirements
for the Degree of Master of Science

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August 1991

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Abstract

by

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This study examined growth of the maxillary complex during and after passive, transverse restraint. Thirty-nine rapidly growing Sprague Dawley rats were randomly assigned control (n=18) and experimental (n=21) groups.

The experimental group was subjected to twenty-one days of passive restraint of the maxillary complex, utilizing custom-fabricated bonded appliances. After removal of the restraining appliance, the groups were subdivided. One-half of the control and one-half of the experimental animals had their maxillary molars reduced to the gingival margin. Unrestricted maxillary growth was monitored for the next forty-one days. Data analysis consisted of measurement taken from dental impressions measurements and cephalometric radiographs.

The results indicated the following:

1) Passive transverse restraint of the maxillary complex alters the vertical, anteroposterior and transpalatal dimensions.
2) An intact maxillary dentition is necessary for maximum transverse development of the maxilla.
3) On average, the restrained maxilla rebounds during the post-restraint phase.
4) Even with an experimental animal population, there was considerable variation in individual response during the rebound phase.
5) Modification of the maxillary dentition caused noticeable asymmetry in the snout of the rat.
6) In addition to transverse deficiency, an increase in A-P length of the snout and vertical height of the palate was observed in the experimental group.

These results imply that clinical correction of transverse arch deficiencies in human subjects should address vertical and A-P changes as well as dental arch asymmetries that often accompany transverse problems. Human subjects would not be expected to rebound to the same degree as the experimental rats because of: a more diverse genetic pool, dental interferences and the multifactorial etiology of transverse arch deficiency.

**ACKNOWLEDGEMENTS**

The author wishes to extend his sincere appreciation to the following individuals:

Dr. Mark Hans, Executive Officer and Graduate Program Director for his expert guidance in designing this study and for accepting the responsibility of being my thesis advisor. His warm friendship made the many hours spent on this manuscript enjoyable. His uncommon understanding of the difficulties in writing in a second language gave me confidence and I am grateful for his patience.

Dr. Donald Enlow, Ph.D., Professor Emeritus, for his editorial comments in the preparation of the manuscript and his commitment to the field of facial growth.

Dr. Lawrence Scaletta, Professor of Oral Biology, for the hours spent discussing the perils of research and the subject of craniofacial biology.

Dr. David Cain for the many hours he spent with me in the laboratory. His hard work and friendly support in all stages of the experiment had a great deal to do with the present manuscript.

Dr. Anastasios Tsolakis, my brother, for his enthusiastic support and especially for his labor on the statistics relating to our experiments.

Drs. Chen-Wen Tseng and Mark Price, who helped me tremendously with the photographic illustrations in this manuscript.

Dr. Kathleen Corcoran and the staff at the Animal Resource Center for their advice and cooperation in the supervision of the care of the experimental animals.

Dr. Stanley Hirsch, Assistant Dean for Graduate Studies, for his patience and attention to detail and demands for a quality manuscript.

Mrs. LaVerne Vogel, Department Assistant, for typing this thesis with all our many changes and revisions.

Mary, George, Phil and Philitsa Vasilakis, the family who befriended us and made us welcome in Cleveland in every way possible.

Drs. Daniel Kruse, Wulfran Moron, Michael Taylor, Chen-Wen Tseng and Martin Writer, my classmates, with whom I have spent the past two years in an atmosphere of camaraderie and friendship.

DEDICATED

TO

My parents, whose love and
financial support made
my education possible.

My wife, Effie
for her love and support
and understanding.

TABLE OF CONTENTS

Page

ABSTRACT. . . . . ii

ACKNOWLEDGEMENTS. . . . . iv

DEDICATION. . . . . vi

TABLE OF CONTENTS . . . . . vii

LIST OF TABLES. . . . . viii

LIST OF FIGURES . . . . . x

LIST OF PLATES. . . . . xii

INTRODUCTION. . . . . 1

REVIEW OF THE LITERATURE. . . . . 5

STATEMENT OF THESIS . . . . . 51

MATERIALS AND METHODS . . . . . 52

RESULTS . . . . . 84

DISCUSSION. . . . . 129

SUMMARY AND CONCLUSION. . . . . 154

Appendices

A. ANIMAL WEIGHT OVER TIME . . . . . 158

B. MEANS AND STANDARD DEVIATIONS OVER TIME . . . . . 160

LITERATURE CITED. . . . . 174

LIST OF TABLES


| Table | | Page |
|---|---|---|
| I. | AP and mandibular variables measured in dorsoventral view. . . . . | 77 |
| II. | Transverse and cranial base variables measured in dorsoventral view . . . . . | 78 |
| III. | Summary table for weight and weight gain during experimental phases, for all groups . . . . . | 89 |
| IV. | Reliability of measured variables. . . . . | 109 |
| V. | Animal weight over time. . . . . | 159 |
| VI. | Mean values (in mm) and standard deviations for variables reflecting anteroposterior changes in midfacial bony size or displacement of the midfacial complex for each rat group at time 1. . . . . | 161 |
| VII. | Mean values (in mm) and standard deviations for variables reflecting anteroposterior changes in midfacial bony size or displacement of the midfacial complex for each rat group at time 2. . . . . | 162 |
| VIII. | Mean values (in mm) and standard deviations for variables reflecting anteroposterior changes in midfacial bony size or displacement of the midfacial complex for each rat group at time 3. . . . . | 163 |
| IX. | Mean values (in mm) and standard deviations for variables reflecting transverse changes in midfacial dimension for each rat group at time 1 . . . . . | 164 |

LIST OF TABLES Continued


| Table | | Page |
|---|---|---|
| X. | Mean values (in mm) and standard deviations for variables reflecting transverse changes in midfacial dimension for each rat group at time 2 . . . . . | 165 |
| XI. | Mean values (in mm) and standard deviations for variables reflecting transverse changes in midfacial dimension for each rat group at time 3 . . . . . | 166 |
| XII. | Mean values (in mm) and standard deviations for variables reflecting changes in the cranial base or cranium for each rat group at time 1 . . . . . | 167 |
| XIII. | Mean values (in mm) and standard deviations for variables reflecting changes in the cranial base or cranium for each rat group at time 2. . . . . | 168 |
| XIV. | Mean values (in mm) and standard deviations for variables reflecting changes in the cranial base or cranium for each rat group at time 3. . . . . | 169 |
| XV. | Mean values (in mm) and standard deviations for variables reflecting changes in mandibular dimension for each rat group at time 1 . . . . . | 170 |
| XVI. | Mean values (in mm) and standard deviations for variables reflecting changes in mandibular dimension for each rat group at time 2 . . . . . | 171 |
| XVII. | Mean values (in mm) and standard deviations for variables reflecting changes in mandibular dimension for each rat group at time 3 . . . . . | 172 |
| XVIII. | Results of analysis of covariance for significant ($p \leq 0.05$) variables . . . . | 173 |

LIST OF FIGURES


| Figure | | Page |
|---|---|---|
| 1. | The main categories of factors controlling morphogenesis. . . . . | 25 |
| 2. | Thirty-three day-old rat cranium -- vertical apsect . . . . . | 39 |
| 3. | Thirty-three day-old rat cranium -- lateral apsect. . . . . | 41 |
| 4. | Schematic representation of the experimental design. . . . . | 55 |
| 5. | Cephalometric landmarks -- dorsoventral projection . . . . . | 74 |
| 6. | Cephalometric analysis -- variables to measure anteroposterior changes in midfacial bony size or displacement of the midfacial complex. . . . . | 80 |
| 7a. | Construction of variables to measure changes in the mandible. . . . . | 82 |
| 7b. | Construction of variables to measure transverse changes in midfacial dimension. . . . . | 82 |
| 8. | Construction of variables to measure changes in the cranial base or cranium . . . . . | 83 |
| 9. | Linear model describing fixed treatments covarying for weight . . . . . | 92 |
| 10a. | Plot of means of transverse dimension directly measured in dental impression as a function of time for each rat group . . . . . | 94 |
| 10b. | Plot of standard deviations of transverse dimension directly measured in dental impression as a function of time for each rat group . . . . . | 94 |
| 11a. | Plot of means of SO-UM1 as a function of time for each rat group. . . . . | 113 |

LIST OF FIGURES Continued


| Figure | | Page |
|---|---|---|
| 11b. | Plot of standard deviations of SO-UMl as a function of time for each rat group. | 113 |
| 12a. | Plot of means of IS-UMl as a function of time for each rat group | 115 |
| 12b. | Plot of standard deviations of IS-UMl as a function of time for each rat group | 115 |
| 13a. | Plot of means of AB-UMl as a function of time for each rat group | 117 |
| 13b. | Plot of standard deviations of AB-UMl as a function of time for each rat group | 117 |
| 14a. | Plot of means of I-N as a function of time for each rat group. | 119 |
| 14b. | Plot of standard deviations of I-N as a function of time for each rat group | 119 |
| 15a. | Plot of means of ZGr-ZGl as a function of time for each rat group | 121 |
| 15b. | Plot of standard deviations of ZGr-ZGl as a function of time for each rat group | 121 |
| 16a. | Plot of means UMr-UMl as a function of time for each rat group. | 123 |
| 16b. | Plot of standard deviations of UMr-UMl as a function of time for each rat group | 123 |
| 17a. | Plot of means of MXr-MXl as a function of time for each rat group | 125 |
| 17b. | Plot of standard deviations of MXr-MXl as a function of time for each rat group | 125 |
| 18. | Significant variables -- anteroposterior measures | 127 |
| 19. | Significant variables -- transverse measures. | 128 |

LIST OF PLATES


| Plate | | Page |
|---|---|---|
| 1. | General anesthesia by intramuscular injection of the anethetic solution . . . . | 59 |
| 2a. | Surgical retractor (left) and customized wire mouth prop (right). . . . . | 61 |
| 2b. | Surgical retractor and customized wire mouth prop as used for the Sprague Dawley rat. . . . . | 61 |
| 3. | Materials used for impression technique -- from left to right; laboratory torch, crown button, and spatulla . . . . . | 63 |
| 4. | Bolton-Brush cephalostat model 1K 500 modified for the Sprague Dawley rat. . . . | 64 |
| 5a. | Sprague Dawley rat cephalometric technique -- dorsoventral view . . . . . | 66 |
| 5b. | Sprague Dawley rat cephalometric technique -- lateral view. . . . . | 66 |
| 6a. | Acid etching of molar crowns . . . . . | 69 |
| 6b. | Restraint appliance in place -- ventral view of the palate . . . . . | 69 |
| 7. | Dorsoventral cephalogram of a Sprague Dawley rat skull . . . . . | 72 |
| 8a. | Experimental animal #2 with unilateral tooth reduction -- asymmetry with right side being longer; dorsoventral view . . . | 88 |
| 8b. | Experimental animal #2 with unilateral tooth reduction -- asymmetry with right side being longer; ventral view of the palate . . . . . | 88 |

LIST OF PLATES Continued


| Plate | | Page |
|---|---|---|
| 9. | Control animal #5 with teeth demonstrating transverse deficiency -- frontal view. . . . . | 95 |
| 10a. | Control animal #5 with teech demonstrating transverse deficiency -- oblique view; right side. . . . . | 97 |
| 10b. | Control animal #5 with teech demonstrating transverse deficiency -- oblique view; left side . . . . . | 97 |
| 11. | Control animal #1 without teeth demonstrating normal transverse relationships -- frontal view. . . . . | 99 |
| 12a. | Control animal #1 without teeth demonstrating normal transverse relationships -- oblique view; right side . . . . . | 101 |
| 12b. | Control animal #1 without teeth demonstrating normal transverse relationships -- oblique view; left side. . . . . | 101 |
| 13. | Experimental animal #9 with teeth which demonstrates transverse deficiency remaining at the end of the rebound phase -- frontal view. . . . . | 102 |
| 14a. | Experimental animal #9 with teeth which demonstrates transverse deficiency remaining at the end of the rebound phase -- oblique view; right side . . . . . | 104 |
| 14b. | Experimental animal #9 with teeth which demonstrates transverse deficiency remaining at the end of the rebound phase -- oblique view; left side. . . . . | 104 |
| 15. | Pilot study animal sacrificed three weeks after placement of the contriction appliance demonstrating posterior cross bite -- frontal view . . . . . | 105 |

LIST OF PLATES Continued


| Plate | | Page |
|---|---|---|
| 16a. | Pilot study animal sacrificed three weeks after placement of the contriction appliance demonstrating posterior cross bite -- oblique view; right side . . . . . | 107 |
| 16b. | Pilot study animal sacrificed three weeks after placement of the contriction appliance demonstrating posterior cross bite -- oblique view; left side. . . . . | 107 |

## INTRODUCTION

Historically, clinical orthodontics has been unduly influenced by isolated clinical case reports and other forms of empirical evidence of treatment efficacy. Recently, the profession has been challenged by its leaders to provide a scientific basis for making orthodontic treatment decisions. For example, is it better to treat a posterior cross bite in the primary dentition, the mixed dentition, or the permanent dentition? If untreated, to what extent will a cross bite spontaneously improve? What factors influence the spontaneous correction of transverse maxillary deficiency? Is there a genetically determined limit to maxillary transverse growth? These are but a few of the questions that must be answered if practicing orthodontists are to have a scientific basis for clinical practice.

Since 1960 a good deal of research has been conducted on facial growth and development and the effects of orthodontic treatment on the growth pattern of an individual's face. Both experimental animal studies and retrospective human clinical trials indicate that environmental influences have an effect on growth. As a

result, the orthodontist of today is more receptive to early treatment of skeletal disharmony. Because contemporary orthodontics now attempts to influence and guide growth to a more orthognathic pattern, studies on basic growth processes are clinical relevant.

Stimulation, limitation or redirection of growth has become an orthodontic treatment goal and has received a considerable amount of attention in the orthodontic literature. The clinical finding that orthodontic and orthopedic forces can affect growth of facial structures is not new. Growth restraining appliances have been used since the early part of the nineteenth century. In addition, oral habits (thumb sucking) or pathological situations leading to abnormal function (impaired breathing) have also been demonstrated to affect the growing face. According to the functional paradigm, all restraining factors are environmental and epigenetic. These factors limit the individual's (intrinsic genetic) growth potential.

Craniofacial growth theories can provide a basis for clinical practice if the theories undergo scientific validation. For example, if the width of the maxilla is influenced by extrinsic factors, will it achieve normal dimensions when those factors are eliminated?

Unfortunately, there has been little experimental evidence relevant to the phenomenon of compensatory growth after the removal of the environmental restraining factors. This research project explores such compensatory growth phenomena by comparing the amount of growth of the maxilla following experimental restraint to an unrestricted control group. The functional paradigm was tested and the results could have a clinical application to early treatment cases.

The maxillary complex of young, growing rats was restrained in the transverse dimension by the use of a passive intraoral appliance. These restraining appliances were removed after twenty-one days (this is equivalent to three years for human subjects) and the initial rat population was subdivided into two groups. In one group the crowns of all maxillary molars were reduced to the gingival margin while in the other group maxillary molar crowns were left intact. Following removal of the local growth restricting appliance, maxillary growth was allowed to proceed for the remainder of the experimental period.

By subdividing the control and experimental rat population into two subgroups, the influence of the soft tissue functional matrices (tongue against teeth and mastication forces) were studied. Compensatory growth changes were analyzed, using measurements taken from dental impressions and serial dorsoventral roentgenographic

cephalograms.

The results of this investigation constitute an important first step in understanding the morphologic and genetic limits of maxillary transverse growth. Once these limits have been established, it will be possible for the clinician to determine analytically when and if a maxilla should be expanded. The clinical question of expansion or extraction will no longer be made based on "clinical experience." Rather, it will be made based on a clear understanding of the patient's morphologic limits of arch dimension. This shift in orthodontic decision making from anecdotal to analytic findings must occur if orthodontics is to proceed as a clinical science.

## LITERATURE REVIEW

### Growth and Development

Historically, there have been cyclical swings of the major theories regarding the concepts of craniofacial growth and development and the cause of dental malocclusion. Current concepts of growth and development originated early in the 17th century. Since that time, the two main theories of facial growth, the genetic and functional paradigm, have competed, with the latter prevailing today.

Looking at the past, one might be surprised to find that "modern" functional theory is about 900 years old. Fauchard (1728) and Hunter (1778), according to their clinical experience, stated that maintenance of both the permanent and deciduous dentition was important for the proper formation of jaws. Wolff (1870), an early proponent of the functional paradigm, stated that when bones which are pathologically changed are restored to normal function, they assume the internal architecture of normally shaped bones. In addition the external bony form becomes normal. Kingsley (1880) described an appliance that could influence the maxillary dentition and supporting bone with the aid of

extraoral forces. John Koch (1917) extended Wolff's theory to the jaw bones. Wolff, Kingsley, Hunter and others believed in the late 1800's that treatment or intervention to alter function could alter the form of any bone (including the facial bones).

Helman (1933), using anthropometric measurements on more than 1,100 orthodontically treated cases, questioned the validity of the functional paradigm. He stated, "Growth of the face is apparently not dependent upon the effects of orthodontic treatment". Helman's findings signaled the beginning of the genetic paradigm. Followers of the genetic basis believed craniofacial growth pattern was genetically predetermined and could not be influenced by environmental factors. Exception was made for obvious environmental influences such as accidental trauma. The introduction of roentgenographic cephalometry in 1931 presented the profession with a method by which a more precise analysis of longitudinal changes in the craniofacial skeleton could be made. In 1938 Brodie used this new method to conclude that the skeletal bone pattern was predetermined and that actual bone changes accompanying the correction of malocclusion were restricted to the alveolar processes. Brodie's influential work established the primary of genetics as the basis for malocclusion. This thinking prevailed until the 1960's.

As always, there were investigators proposing different points of view regarding the subject of facial growth. Washburn (1947) opposed the genetic paradigm. He carried out experiments involving unilateral removal of the temporal muscle on rats. His findings suggested that musculature does affect the size and shape of both the cranial bones and the mandible.

In contrast, Weinman and Sicher (1947, 1955) added one more brick to the "genetic building" by proposing that cranial vault and jaw growth is due to the innate genetic growth at the sutures. According to their theory, the sutures of the craniofacial complex are most important in the growth of the maxilla. Connective tissue proliferation in the suture system, composed of the frontomaxillary, zygomaticomaxillary and the suture between the pyramidal process of the palatine bones and the pterygoid process of the sphenoid bone would be responsible for downward and forward growth changes in the maxillary complex. Growth changes in the lateral dimension were suggested to be due to bone proliferation by the sagittal suture system (medial palatine, intermaxillary, metopic sutures).

Extensive investigations of Massler and Schour (1951) and Baer (1954) on the growth of the rat vault supported Weinman and Sicher's theory. Their results suggested that sutures are autonomous growth centers which have intrinsic

growth potential like epiphyseal plates. Experimental work of Mednick (1956) on infant pigs also supported the "sutural" concept by concluding that sutures are active sites of skull growth, accounting for the primary extensions of the bones of the vault.

The "sutural" concept was disputed by Selman and Sarnat. They studied the growth of a rabbit's snout following extirpation of the frontonasal suture. Relying on their experimental results, they came to the conclusion that maximal injury to facial sutures fails to produce growth arrest. Their results did not support the concept of sutures being autonomous growth centers.

Young (1959) also gave a different explanation for the factors controlling sutural growth. He stated that intracranial forces are converted by the sutural fibers in tension stimuli which stimulates osteogenesis. So according to Young, sutural growth is regulated by intracranial forces and not by innate genetic factors.

Scott (1953, 1954, 1956) suggested that the hyaline cartilage of the chondrocranial and chondrofacial skeleton has certain physical properties which allow it to determine growth in the cranial base and nasal area. Therefore, the growth of the maxillary complex was presumed to be genetically regulated by endochondral proliferation in the associated nasal septum, together with the growth of the

adjacent organs (brain, orbital contents) which was subsequently regulated by the cranial base cartilage.

Ford (1958), after studying a collection of dried skulls, came to the conclusion that cranial growth is largely dependent on the growth of the brain, while growth of the anterior part of the cranial base is due to pneumatization of the frontal and ethmoid bones. These statements were the first steps to a new theory.

Moss (1960, 1962, 1968b, 1969b, 1971a, 1972a) in the early 1960's developed the mathematical formula:

$$FC = (FM + I + SKU)$$

where

FC = Functional Cranial component which consists of functional matrix and skeletal units.

FM = Functional Matrix (what people understand as "soft tissue", i.e., muscles, nerves, glands, etc.)

SKU = Skeletal units (bone, cartilage or tendinous tissues)

I = Boundary between FM, SK U

This formula opposed the genetic theory and gave birth to the Functional Matrix Theory. The new theory considered the presence, form (size and shape), growth and position in space, of skeletal units are secondary, compensatory and mechanical responses to the temporal (and morphologic) prior demands of related soft tissues.

The skeletal units are divided into macroskeletal (e.g., mandible, maxilla) and microskeletal units (e.g., posterior tuberosity unit, alveolar unit, premaxillary units) while the Functional Matrix is divided into two categories:

1. Periosteal functional matrix, which refers to muscles being responsible for the development and morphology of microskeletal units.

2. Capsular matrices, whose growth and functional demands allow bones to be passively and secondarily translated in space.

The Capsular matrices are:

a. Neurocranial (covered with skin dura matter).

b. Orofacial (skin and mucosa for limiting layers).

Each capsule surrounds and protects a functional matrix, the neural mass (brain, leptomeninges, cerebrospinal fluid) and the oronasopharyngeal functioning spaces. It is the volumetric growth of these spaces that is the primary morphogenetic event in the splanchnocranial growth.

Bjork (1964, 1970) studied the pattern of maxillary growth by the use of metallic implants. According to Bjork, maxillary growth in length is sutural towards the palatine bone and is accompanied by periosteal deposition at the maxillary tuberosity. Growth in height takes place at the sutural articulations of the frontal and zygomatic processes and by periosteal deposition on the lower border

of the alveolar process. The nasal floor is lowered through resorption, combined with periosteal deposition on the hard palate, and the anterior nasal spine is likewise lowered through resorptive remodeling. On the floor of the orbits this process occurs in the opposite direction, with deposition on the upper surface and resorption on the lower. Bjork's studies suggested that both sutural and condylar growth can be influenced by external forces.

At the same time that Moss was formulating his ideas, Enlow (1963, 1965, 1966, 1968, 1975, 1982, 1990) developed another theory of craniofacial growth and development. Enlow established his theories based on his unique method, of mapping the localized distribution of endosteal-periosteal fields of bone deposition. According to Enlow, growth in each region of the face involves two basic factors; first, the **amount** of growth by any given part, and second, the **direction** of growth. Because the floor of the cranium is the template upon which the face is constructed, the brain and cranial base establish the boundaries that determine the amount of facial growth. The directions of regional growth among the different parts of the face are inseparably associated with the special sense organs. These two factors establish a prescribed growth perimeter that defines the borders of the growth compartment occupied by the nasomaxillary complex. Growth boundaries, though,

can be violated. For example, thumb sucking and various developmental defects can move teeth and bones outside the limits of the normal growth process. This, in turn, creates structural and functional imbalances. According to Enlow, if the overriding ectopic factors are removed, the normal balance of the functional, intrinsic forces work to a greater or lesser degree to return to normal positions.

Bones during growth and development move in space in two ways. First, by **primary displacement**, which is a movement of a bone due to its own growth and remodeling by resorption and deposition. For example, the maxilla is anteriorly displaced due to posterior elongation by bone deposition on the maxillary tuberosity. The second type of bone translation is by **secondary displacement.** For example, the expansion of the middle cranial fossa regulated both by brain expansion and by cartilaginous growth at the sphenooccipital synchondrosis has a major second anterior displacement effect on the anterior cranial floor and the nasomaxillary complex.

The expanding V principle described by Enlow (1963) is also operative in providing increases in the width of the maxillary complex. The principle describes the growth of a V shaped bony structure which increases in size by deposition on the inner surface and resorption on the outer surface of the V. Viewed from the frontal aspect, the

maxilla can be thought of as an inverted V. Growth takes place by resorption on the outer surface of V (nasal surface, labial cortex) and deposition at the inner surface (oral surface).

Moss and Enlow's theories rejected many old concepts and added a new dimension to our understanding and thinking about growth and development of the human face. Their new theories stimulated a great amount of investigation from 1960 to 1980. Although conflicting with previously held principles, these investigations shed new light on the mechanisms of facial growth and development.

Dubruland and Laskin (1961), in a very interesting investigation on Albino rats, pointed out the adaptability of the mammalian skull. When the spheno-occipital synchondrosis was removed in young animals, there were changes in shape and size of the entire skull of the adult animals. The adult skull form simulated the classical changes always associated with the upright posture.

Koski and Ronning (1969, 1970) examined the behavior of transplanted cranial base synchondrosis in the rat. They concluded that cranial base synchondroses appear to possess an inherent bone growth promoting potential which is greater than that of the condylar cartilage, but not as great as that of epiphyseal cartilages of long bones.

Organ culture studies by Lewis (1969) and Lewis and Irving (1970) of the rat calvarium revealed a remodelling pattern similar to that found in the intact animal. These findings contrasted with Moss's functional theory and supported the investigators' hypothesis that the osseous skeletal system has some inherent control over its pattern of growth. However, it is more sensitive to functional demands than embryonic cartilaginous precursors. According to Lewis and Irving, there is little evidence to support the contention that environmental forces (orthodontic and orthopedic forces) can increase or decrease the morphogenetic growth rate or pattern of individual bones. Such forces may act to redirect growth or change the relationship between the various bones of the craniofacial complex.

The human cyclops, (Latham 1971) exhibits a normal maxillary growth pattern (characterized by a downward and forward displacement) despite the absence of nasal structures. This finding supports the genetic basis for nasomaxillary growth. Histologic examination of these specimens showed normal patterns of bone deposition on posterior and superior surfaces. This suggested that bone growth, by acting against the adjacent masses of fatty tissue, may be a basic causitive factor in the normal downward and forward displacement of the maxilla.

Kvinnsland (1973a, 1973b) supported the "nasal septum" theory proposed by Scott in the early 1950's. He studied the growth of autotransplanted nasal septum in the rat. The findings of his experiments supported the theory that the cartilaginous nasal septum has its own growth potential and is a structure of great importance in normal upper facial growth. Kvinnsland's findings are not in agreement with the concepts proposed by Enlow and Moss and tend to support the genetic paradigm of facial growth.

Servos (1975) studied the inherent growth of synchondrosal cartilage in rats. He reported that synchondroses grown in organ culture retained their capacity for growth without benefit of neighboring tissues. These findings led Servos to suggest that the spheno-occipital synchondrosis possesses an inherent potential for growth and is not merely reactive or adaptive in nature.

A corollary to Moss' Functional Matrix Hypothesis was that neurotrophic processes were responsible for regulation of the growth of the functional matrices. The functional matrices were, in turn, responsible for growth of the craniofacial skeleton. Behrents (1975) tested this theory by producing unilateral, intracranial, electrolytic lesions of the trigeminal nerve sterotaxically in 113 rats (10-20 days of age). In addition to determining the effect of simple sectioning of the trigeminal, a concurrent

dissertation of the study was to determine the relative role of the trigeminal nerve in accordance with trophic theory. To accomplish these ends, lesions were placed in one of three locations:

1) gasserian ganglion (location of cell bodies),

2) anterior to the ganglion (axon processes), and

3) posterior to the ganglion (central connections).

At 50 days of age the animals were examined for sensory loss and/or motor impairment. The animals were killed and the trigeminal nerves were examined histologically for verification of the location of the lesion. The "neurotrophic effect" on growth of the face was evaluated by means of dorso-ventral cephalograms. Cephalometric measurements of the experimental animals showed cranial asymmetries resulting from a change in both the magnitude and direction of growth. The greatest effect was noted, as expected according to Trophic Theory, in those animals which had suffered ganglionic lesions followed in order of severity, by posterior and anterior lesions. Deviation of the facial skeleton and reduction in size was noted on the ipsilateral side, except in the case of efferent (motor) destruction, which resulted in ipsilateral deviation of the mandible and contralateral deviation of the rostral portion of the skull. It was concluded that interruption of the trigeminal nerve in young rats produced a significant

asymmetry of the facial complex; however, the magnitude of the asymmetry was small. Furthermore, cranial asymmetries were produced by both sensory and motor nerve deficits. While some of the bony changes may be due to a change in the afferent-efferent functional pathways, the nerve does exert a trophic infulence on the craniofacial complex. However, the magnitude of the changes did not support Moss' view that trophic effects constitute a **major** factor in the regulation of craniofacial growth.

Stutzmann and Petrovic (1970, 1975a, 1975b, 1976) methodically studied the mechanisms controlling upper jaw growth. Rats were used as experimental animals, and local extrinsic factors affecting forward and lateral growth of the upper jaw were introduced, using a variety of different experimental designs. These designs involved total excision of the nasal septal cartilage, partial glossectomy, total glossectomy and isolated experimental macroglossia. Total excision of the nasal septal cartilage resulted in a decrease in the rate of both forward and lateral growth of the upper jaw. Partial and total glossectomy resulted in a significant "slow down" in forward upper jaw growth (specifically, in the area of premaxilla-maxillary suture). Both partial and total glossectomy had no significant effect on the lateral growth of the premaxilla, but did produce a decrease in the growth

rate of the maxillary bones. Isolated macroglossia (produced with plastic inserts in the tip of the tongue) revealed an adaptation of the oral cavity to the volume of the tongue. This adaptation was expressed as increased forward growth of the lower jaw and increased transverse growth of the premaxilla. These results suggest a functional paradigm of maxillary growth and support the premise that facial growth can be modified by local extrinsic factors and is not totally controlled by the genome.

Solow and Greve (1979) studied the influence of the head posture upon craniofacial morphology. They suggested that changes in head posture, caused by respiratory obstruction of the nasopharyngeal airway, could be an environmental factor capable of influencing cranial base flexion.

Dr. Rolf Frankel (1980, 1983) brought the Functional Matrix Theory into everyday clinical practice. According to Frankel, facial bone elements place or displace themselves in the direction of functional forces and increase their mass to reflect the amount of these forces. Therefore, neuromuscular functions, as they operate within a physiologic range, are assumed to provide epigenetic information. Frankel proposed that neuromuscular functions were capable of providing the fullest expression of the

growth and development of the associated skeletal facial structures.

The functional regulator (FR) invented by Frankel, utilizes vestibular shields as an exercise device in combination with lip-seal training. According to Frankel, vestibular shields and lip-seal devices enable the clinician to directly interfere with the functional environment. These environmental interferences can lead, according to patients' needs, to more favorable tooth eruption (FR-type I), to stimulation of mandibular growth (FR-type II) or to stimulation of maxillary growth (FR-type III). When these appliances are inserted, the orofacial capsule is increased where it failed to expand during growth. At the same time, the external muscular environment is forced to adapt to the device in the vestibule in structure and function.

Oyen and Russel (1989) support the theory of functional paradigm and suggested a new model of facial bone remodeling according to functional demands. Materials examined in their studies include samples from cross-sectional collections of cercopithecoid monkeys, ceboid monkeys and the anthropoid apes. Bone research from these materials revealed the significance of the woven bone in facial skeleton growth. Woven bone is characterized by rapid growth rate and relative independence from endocrine

control. According to Oyen and Russel, when the biomechanical demands on a facial structure change, woven bone tissue can provide a rapidly constructed scaffold for a new version of the structure whose cross-sectional area and distribution of mass are better able to withstand the strains resulting from the newly changed stress vectors. If the recently changed stress vectors stabilize, the woven bone scaffold may be slowly remodeled by secondary (Haversian) bone. Alternatively, lamellar tissue may fill in the cancellous spaces between trabeculae of woven bone, thus adding mass to the structure without altering shape. In this model, normal postnatal facial growth is a process in which lamellar bone and woven bone tissues are alternately deposited and remodeled in various parts of the facial skeleton, in accordance with varying biomechanical demands.

Melsen and Melsen (1989) studied the postnatal development of the palatomaxillary region on human autopsy material. The findings of this study gave a new value to the role that the palatal bone plays in facial growth. It was suggested that the palatal bone acts as a "buffer" between two areas of differing intrinsic growth patterns and that the remodeling processes in the area reflect different functional demands placed on the bone by the pharynx and the maxillary complex. The rigidity of the

area results from the sutural complexity and indicates that the center of rotation for the observed spatial changes in the maxillary complex caused by orthopedic forces could be localized in the palatomaxillary area.

Bacon and Mathis (1983) studied the craniofacial characteristics of cyclopia in man and swine. Despite the thought that cartilaginous bone formation is less sensitive to exogenous or matrix influences than membranous bone formation, they found that the cranial base was strongly affected in cyclopia. The basicranium was shorter and seemed to have adapted partially to the morphogenic influence of the growing brain. This adaptation was similar in man and swine. The proposed cause of the adaptation was the absence of the septo-ethmoidal process. Thus, according to Bacon and Mathis, the ethmoidal strut is a major component in developmental equilibrium of the basicranium.

Wijdevel et al., (1988) investigated maxillary growth after palatal surgery at different ages in beagle dogs. A soft tissue cleft was created in the median region of the palate to allow placement of metalic implants. Subsequent growth was studied using lateral and dorsoventral cephalograms. Results of this study suggested that palatal surgery has no influence on vertical and antero-posterior maxillary growth. Transverse palatal growth was influenced

to a minor degree, especially when surgery was performed before or during the eruption of the permanent teeth. Alteration of the soft tissue matrix did not significantly influence transverse development of the palate.

On the other hand, results from a similar experiment conducted by Beck (1988) led to a different conclusion. This study examined the postnatal transverse growth of the lamb palate after a palatal soft tissue cleft was surgically created in utero. Gross observations and width measurements revealed that the total posterior palatal width in operated animals was significantly narrower than that of control animals. These results support the idea that bones grow in response to normal function of soft tissue matrixes.

Nordenram and Thilander (1989) studied growth in persons with maxillonasal dysplasia. Orthodontically treated persons were compared with untreated persons, and persons with orthognathic profiles and normal occlusion. Even if orthodontic treatment led to acceptable dental conditions, no influence on craniofacial growth could be demonstrated. The growth pattern seemed to follow about the same rate in both treated and untreated groups. It seemed that the growth potential was the same for both groups and could not be influenced by induced local environmental factors such as orthodontic treatment.

Thimaporn, Goldberg and Enlow (1990) studied the maxillofacial complex growth following unilateral premature fusion of the zygomaxillary suture. The effects of sutural fusion were both cephalometrically and histologically examined. Even if the immobilization successfully constrained the anteroinferior displacement of the maxilla and zygomatic bone on the fused side, no gross anatomic asymmetry of the facial complex, as a whole, was detected. Adaptive compensation involving periosteal bone deposition occured at the junction of the lower maxillary process and the maxilla proper on the fused side. This, together with periosteal bone resorption in corresponding areas on the non-fused side, served to offset any developmental asymmetry that might have occured. They concluded that compensatory adaptations preclude the development of gross anatomic asymmetries. The above experiment points out the adaptability of facial growth to external, local stimuli and the dynamic relationship between environmental factors and biological compensations.

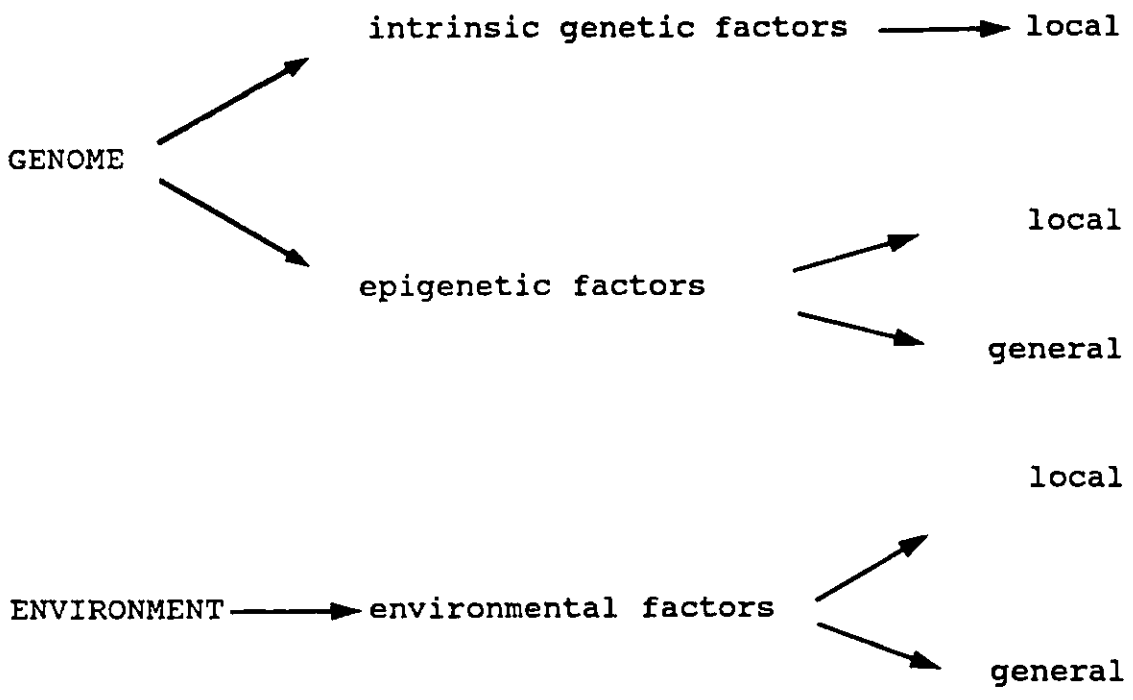
Richtsmeier et al., (1991) studied the growth of the cranial base in craniosynostosis in human infants. Three dimensional landmarks were used and data collected from pre- and postoperative computed tomographic (CT) scans of eleven patients. This study documented the deformities of the cranial base in preoperative patients. In the post-

operative interval (one year) every basicranial landmark showed a large amount of regression towards normal limits. These results support the idea of a structural and functional relationship between the neurocranium and basicranium and suggest direct communication between the two systems.

There are still many questions to be answered concerning the processes involved in normal growth and development of the face. Although, we know at this point in time what actually happens anatomically during facial growth and development, there is much disagreement over how it happens.

Therefore, one question remains. What are the controlling factors of postnatal craniofacial morphogenesis? It is clear that these controlling factors cannot be solely genetic (genetic paradigm) or environmental (functional paradigm). Rather, a combination of these two factors is probably involved, as illustrated in Figure (1).

Figure 1. The main categories of factors controlling morphogenesis



The growth of cartilage (mainly in the spheno-occipital synchondrosis) seems to be controlled by intrinsic genetic factors. On the other hand, the growth of the periosteal and sutural connective tissues and the processes of bone formation are much less independent. Both the observations in cases of malformations, like hydrocephalus and microcephalus, (Limborgh 1972) and the results obtained in many other experiments (Moss 1969, 1972) have clearly shown that these growth processes are influenced by adjacent structures that are under local epigenetic control. In addition, clinical experience (Frankel 1980, 1983) as well as the result of experimental studies (Stutzmann and Petrovic 1976, 1977) allow the conclusion that the growth processes are highly dependent on external stimuli. Local environmental factors, such as masticatory muscle forces and local external pressure, are able to produce considerable modifications. The intrinsic genetic factors apparently play a non-specific morphogenetic role. Genome determines general characteristics, such as the growth capacity, growth period and possibly the outermost limits of growth.

Growth Restraint

Restraint of growth can be either clinically induced or due to the following factors: a) airway obstruction; b) habitual growth pattern, and c) developmental defects.

1. Clinically induced growth restraint - The idea that external pressure can modify the direction of bone growth has been established for centuries. Primitive tribes of Colombian Indians bound the skulls of their infants to create a characteristic cranial morphology which in those early societies was thought desirable. Similarly, the Chinese, who considered small feet esthetically pleasing, bound women's feet during the early period of growth in order to restrict their size. These early examples suggest that the shape and spatial position of bones can be altered. External force has also been applied to the craniofacial region. Cellier (1809) and Fox (1803) utilized extraoral occipital anchorage and a modified hairnet with leather bands attached to a chin cap. Kingsley (1855) described an extraoral appliance which was used against the maxillary arch in 1855 (Weinberger, 1926). Extraoral traction was popular in the latter half of the 19th century; in 1895 Case applied the term "orthopedic" to the use of extraoral force, stating that a "movement of other parts quite as important in the reduction of certain facial deformities as the movement of the teeth" has long been recognized as within the possibilities of dental force application.

At the turn of the century, the use of extraoral force fell into disfavor. Hellman (1933) reported that the development of the face occurred regardless of orthodontic treatment. Brodie et al., (1938) advanced the concept of the immutability of the growth pattern of the craniofacial complex.

Oppenheim (1934, 1936) revived the use of extraoral traction which was later popularized by Kloehn (1947). The cervical headgear was used with very light force for the mass distal movement of the teeth. The treatment concept held by many orthodontists during this period was that extraoral traction either held the maxillary molars stationary or else moved them distally while the maxilla and mandible grew forward. Kloen (1953) discussed the possibility of influencing the growth pattern, guiding the direction of growth towards normal development in order to establish proper alignment and balance of teeth and jaws.

During the 1950's several investigators reported skeletal changes in "basal" bone that accompanied the dentoalveolar correction that resulted from the use of extraoral force. Watson (1955), Klein (1957) and Newcomb (1958) reported treatment changes which appeared to influence the position of the palatal plane relative to cranial base. Moore (1959)

emphasized the favorable influence upon facial growth following treatment with cervical anchorage. In clinical studies, Wieslander (1963) and Sandusky (1965) reported that extraoral traction not only affected the spatial relationships of the maxilla, but also that a "clockwise rotation" of the sphenoid bone had occurred. Before long, articles began to appear suggesting that the direction of force application was an important factor to consider (Paulton, 1959; Nelsen and Enemark, 1969). Treatment mechanics began to emphasize the importance of vertical growth and vertical dimension (Isaacson et al., 1971). More recently (Armstrong 1971; Watson 1972; Badell 1976) have suggested that magnitude and duration of extraoral force application are important considerations in the use of extraoral traction. Further, they proposed that the use of heavy extraoral force will elicit even more dramatic orthopedic changes in skeletal relationships.

Henry (1976) investigated the effects of heavy posteriorly directed extraoral force on the craniofacial complex of the growing monkey (Macaca mulatta). Heavy forces in this experiment affected both spatial position of the maxilla and the facial bones, and resulted in a "clockwise" rotation of the

frontal bone complex, enclosing the orbits and the anterior cranial fossa. The bones comprising the cranial vault were also altered. This experiment demonstrated that heavy forces applied to the maxillary effect growth of the total craniofacial complex. Baumrind (1981) documented changes in facial height and in mandibular dimensions associated with forces used to retract the maxilla.

Teuscher (1986) studied the mechanics of extraoral anchorage and showed the importance of the direction of force application to induced growth changes.

From this very brief review, we can see that many studies have been performed to prove that restraint of maxillary growth is possible and to test the various types of appliances, and their most effective force levels. In contrast, there are only a few studies reported which follow post restraint compensatory changes.

2. Habitual growth pattern

   a. Thumb or finger sucking (Age consideration and characteristics) - The thumb sucking instinct may develop soon after birth. There is controversy in the dental profession about the age at which thumbsucking becomes detrimental. Most investigators agree that infantile

thumbsucking is natural and normal and that no attempt should be made to correct the habit at this early stage. Usually sucking habits are dropped before the appearance of permanent teeth. Fletcher (1975) in his review of literature, found some practitioners who felt that intervention to prevent anomalies should begin as early as two years of age. Others felt intervention should not begin until five years of age. Many authors (Larson 1987, Brickbauer 1988, Hannuksela 1987, Linder 1989) have reported that a finger or thumb sucking habit continuing beyond the age of four years has restraining effects on the transverse maxillary growth. Like many habits, thumbsucking is subject to various quantitative and qualitative influences which determine, in varying degrees, the harmful effects of the habit. Quantitative characteristics include the frequency, forcefulness and duration of the habit. Qualitative characteristics include the number of fingers involved, position and depth of insertion of the fingers.

b. Skeletal effects of thumbsucking - Moore et al., (1972) studied the effects of digit sucking

on the growth pattern and facial morphology of four monkeys. The habit produced a progressive anterior open bite with a histologic pattern of bone deposition consistent with forward advancement of the premaxilla, relative to the maxilla. With cessation of sucking, there was a downward and backward rotation of the maxilla and the open bite had a tendency to close. It was also observed that there was a restraining effect on transverse maxillary growth which did not improve when the sucking stopped.

Larson (1978), using lateral cepholometric radiographs, and clinical observation of the occlusion, conducted longitudinal studies of children at nine, twelve and sixteen years of age. His study supported previous findings that finger sucking is a major etiological factor in the development of posterior crossbite in the deciduous dentition, and restrains future transverse maxillary growth. According to Larson, the main reason the habit causes posterior crossbites is a combination of the finger position in the mouth and tongue function. Fingers occupy the anterior part of the oral cavity, thus forcing the tongue to a lower

position. This will leave the upper canine region and posterior maxillary region without lingual support during sucking. This, in combination with expansive forces to the lower arch resulting from the lower tongue position, creates a posterior crossbite The crossbite acts as an extrinsic factor interfering with subsequent transverse maxillary growth.

Haryette et al., (1967) reported that facial asymmetries may develop as a result of tooth interferences in the molar area. The tooth interferences were caused by the maxillary contraction that resulted from extreme duration and intensity of the sucking habit and from activity of the buccinator muscle.

An epidemiological study by Infante (1976) showed a significant relationship of the habit to posterior lingual crossbite and protrusive position of maxillary molars relative to mandibular molars. Brickbauer (1988) gives the following explanation for the habit's restraining effect on maxillary transverse growth.

> "Usually the thumb habit is assisted by - or followed by - a reverse swallowing habit. This combination, if persisting, will create a deep palatal vault and lack of lateral development in the buccal segments of the maxillary arch due to heavy buccal muscular action. The upper anterior teeth may remain

> intruded or become protrusive; the lower anterior teeth will also either be intruded or develop a lingual inclination. These conditions usually lead to bilateral crossbite and disto-occlusion."

According to Brickbauer, a crossbite will always need appliance therapy. It is not self correcting after discontinuing the thumb or tongue habit.

3. Impared breathing problems - Respiratory infections can have a significant effect on transverse maxillary growth. Hannuksela (1987) encountered posterior crossbites in children with recurrent respiratory infections more often ($p<0.05$) than in other children. The number of mouth breathers among the children with recurrent respiratory infections was significantly higher ($p<0.01$) than among control children.

Passive airway obstructions resulting from airway pathologies such as adenoid hyperplasia, tonsil hypersplasia, turbinate hyperplasia, divided nasal septum can also restrain transverse growth of maxilla. The breathing impaired population demonstrated characteristic combinations of craniofacial deformities and malocclusions. In particular, this group had significantly smaller nasopharyngeal heights, larger midcranial base angles and vertically longer and transversely more narrow craniofacial

features. (Enlow and Cheng 1988). Maxillary intermolar and intercuspid widths were also narrow. The patients presented with deep palate and posterior lingual crossbites. There was a higher incidence of anterior crowding in breathing impaired subjects. The increased crowding might be due to the narrowed maxillary arch and/or aberrant muscle function. The younger the breathing impaired subject, the less marked is the expression of these craniofacial morphologic and occlusal characteristics. These observations underscore the importance of early diagnosis and treatment of breathing impaired individuals. However, the degree to which post-treatment growth tends towards a more orthognatic profile is still unknown (Bresolin et al., 1983, 1984).

Post Restraint Compensatory Changes

Although many well-documented experiments have evaluated the restraining effect of extraoral traction on the craniofacial complex, few were designed to evaluate the changes that occurred following removal of the force.

Watson (1972), in a study of high-pull traction therapy, found that rebound from periodontal space condensation, tipping, bone bending and suture or fiber adaptation occurred within one to three months after force

application. Wieslander and Buck (1974), in a study of patients treated with Kloehn headgear, used lighter forces than those suggested by Watson and found "an overall picture of relatively good stability with a minor tendency for post-treatment changes." Tuenge et al., (1974) applied heavy extraoral forces (700 grams.) to the maxillae of Rhesus monkeys. Post-treatment changes were studied at two weeks, six months and ten months. The results from this study suggest that the widened craniofacial complex grew towards a normal direction when the restraining fractor was removed. Dental changes were the first to appear, while changes in direction of bone growth appeared later. However, none of the animals managed to overcome the Class III skeletal and dental relationship created during the headgear period.

Henry (1976) restrained and redirected the growth of the maxillary complex of growing monkeys with heavy, posteriorly directed forces (800 grams) per side) delivered by a high-pull headgear. The positions of facial and cranial bones were altered relative to each other. During a twenty-one day post-headgear observation period, a partial "recovery" of experimentally induced skeletal and dental changes occurred. Although no long term cephalometric documentation was available, Henry postulated that the recovery observed was bone deformation and/or soft

Figure 2. Thirty-three-day-old rat cranium-vertical aspect (Adapted from "The postnatal development of the rat skull" Baer et al., 1984)

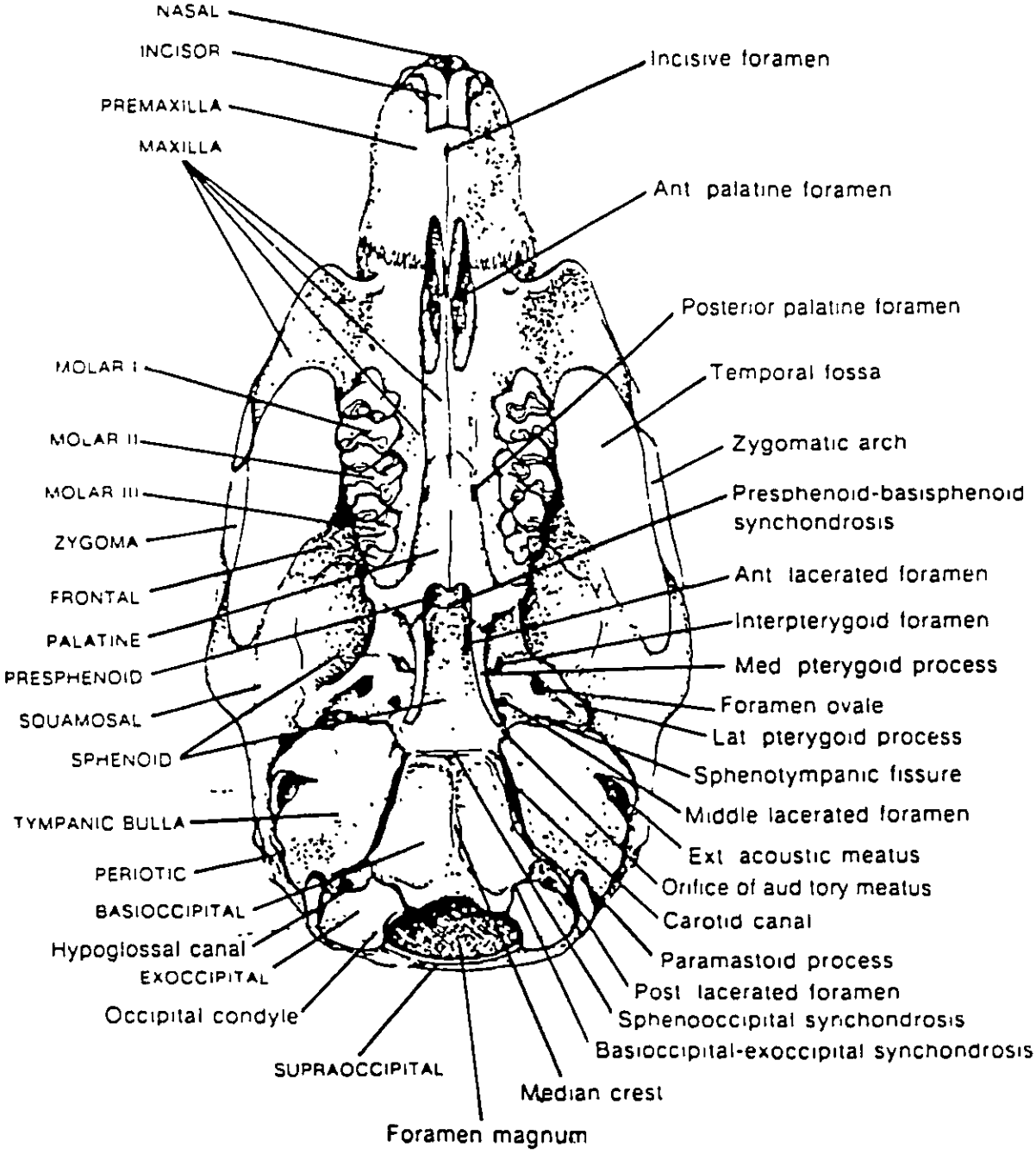

NASAL
INCISOR
PREMAXILLA
MAXILLA
MOLAR I
MOLAR II
MOLAR III
ZYGOMA
FRONTAL
PALATINE
PRESPHENOID
SQUAMOSAL
SPHENOID
TYMPANIC BULLA
PERIOTIC
BASIOCCIPITAL
Hypoglossal canal
EXOCCIPITAL
Occipital condyle
SUPRAOCCIPITAL
Foramen magnum
Median crest
Basioccipital-exoccipital synchondrosis
Sphenooccipital synchondrosis
Post lacerated foramen
Paramastoid process
Carotid canal
Orifice of aud tory meatus
Ext acoustic meatus
Middle lacerated foramen
Sphenotympanic fissure
Lat pterygoid process
Foramen ovale
Med pterygoid process
Interpterygoid foramen
Ant lacerated foramen
Presphenoid-basisphenoid synchondrosis
Zygomatic arch
Temporal fossa
Posterior palatine foramen
Ant palatine foramen
Incisive foramen

Figure 3. Thirty-three-day-old rat cranium-lateral aspect (Adapted from "The postnatal development of the rat skull: Baer et al., 1984)

Anatomy and Postnatal Development of the Rat Cranium

The cranium of the rat is illustrated in Figures 2 and 3 to demonstrate the vertical and lateral aspect of the skull. The anatomy and postnatal development of the rat snout will be discussed in greater detail since the majority of the induced experimental changes are going to occur in this area.

Anatomy of the Snout The snout of the rat includes the nose and nasopharyngeal duct, the mouth, the eyes and their associated structures. The skeleton of the snout encloses the nasal chamber and nasopharyngeal duct and supports the nasal conchae. The snout forms the bony, or oral palate, and the upper and lower jaws. The skeleton of the upper part of the snout is in continuity with the calvaria and basicranium. The cribriform plate of the ethmoid bone is common to the snout and the brain case. The septal cartilage contacts the body of the presphenoid, dorsal to the nasopharyngeal duct. Portions of the vomer and palatine bones meet the presphenoid and the pterygoid process of the basisphenoid at sutures. The maxilla shares a suture with the frontal bone in the nasal shell. The mandible articulates with the squamous portion of the temporal bone. The mandible is also functionally related to the calvaria by the extensive elevating musculature.

The temporal muscle attaches to the lateral aspect of the calvaria, inferior to the temporal ridge and rostral to the nuchal crest. Major portions of the superficial and deep masseter muscles are attached to the zygomatic arch. Portions of the lateral and medial pterygoid muscles attach to the palatine bone and the pterygoid process of the basisphenoid.

In addition to the septal cartilage, the snout of the rat is composed of the following bones: nasal, premaxilla, maxilla, lacrimal, palatine, vomer, ethmoid and mandible.

1. Nasal bone is of membranous origin and is composed of a plate of bone, which is a portion of the shell of the snout, and a turbinal, which projects into the respiratory portion of the nasal chamber. The plate is flanged on its ventral aspect of the internasal and nasopremaxillary sutures. Its postnatal enlogation is rostralcaudal. During postnatal development the nasoturbinate is progressively fused with the plate of the nasal bone. The nasal bone is displaced dorsal maintaining its relation with the dorsal margin of the enlarging premaxilla which it abuts without interdigitation.

2. The premaxilla is formed intramembranously. It is related to the nose, to the lacrimal apparatus and to the mouth. The premaxilla encloses the curved shaft of the incisor; the formative end of the incisor is in the

maxilla. The ventral portions of the paired premaxillae are the rostral part of the hard palate. They partly enclose the anterior palatine foramina. The inferior margin of the septal cartilage is enclosed by the paramedian flanges of the premaxillae. These flanges are in continuity of contour with those of the vomer. At its caudal margin, the premaxilla interdigitates with the maxilla and with the frontal bone. These interdigitations deepen progressively during postnatal growth. At its dorsomedial margin the premaxilla approximates the nasal bone to form the roof of the respitatory part of the nasal chamber and of the nares. The premaxillae and nasal bones support the mobile structures of the nostril and the upper lip, including the vibrissae. The midpalatine suture at the median approximation of the premaxillae is digitated in its dorsal portion, adjacent to the nasal chamber.

The postnatal development of the premaxilla reflects the growth of the snout and also the growth and eruption of upper incisor. Elongation in its rostrocaudal axis is principally by growth of the premaxillo-maxillary suture.

The development of the respiratory portion of the nasal chambers is a major determinant of the enlargement of the premaxilla. The principal direction of this enlargment is dorsal. The adjacent nasal bone is correspondingly displaced dorsally. The premaxilla is also displaced

laterally by growth adjacent to the premaxillomaxillary suture and, to a lesser extent by reciprocal deposition and resorption in combination with the lateral arching of the incisor. The transverse diameter of the nasal chamber is thus increased. The bony palate undergoes ventral displacement by deposition on its oral aspect and resorption on the nasal aspect. The palate is enlarged transversely by growth at the median suture.

Forward growth of the septal cartilage - The forward growth of the septal cartilage in the rat produces a forward shift of the premaxillary bone that gives rise to an increase in the growth of the premaxillomaxillary suture and, to a lesser extent, the maxillomaxilla suture. It also results in a forward traction by means of the septopremaxillary ligament and the labionarinary muscles on the anterior end of the premaxilla, which results in local stimulation of bone growth.

Thrust effect - The anterior extremity of the nasal septal cartilage spreads laterally on both sides of the median line in an anteroinferior direction to penetrate directly into the premaxillary bone. Such a configuration supports the hypothesis that forward growth of the nasal septal cartilage produces a significant force to stimulate growth at the premaxillomaxillary suture and, to a lesser extent, at the maxillopalatal suture. The thrust effect on

the premaxillary bone is presumed to be caused by the attachment of a ligament between the nasal septum and premaxilla. This ligament is composed of collagen fibers which connect the nasal septum cartilage and the bone trabeculae located immediately posterior. According to studies on the septopremaxillary ligament in the young rat (Stutzmann and Petrovic 1976, 1978a), the number of dividing preosteoblasts as well as the osteoblastic activity is significantly greater where this ligament contacts the premaxillary bone. However, the histologic characteristics of the septopremaxillary ligament suggest that this structure is not capable of providing the necessary traction on the premaxillary bone necessary to increase growth at the premaxillomaxillary suture. In other words, histologically it is misnamed aa a ligament.

Findings after resection of the septopremaxillary ligament in the young rat (Stutzmann and Petrovic 1976, 1978a) clearly show that a stimulating action on the growth at the premaxillomaxillary suture have been overestimated. However, the ligament does have a local, induction-like, stimulating effect on subperiosteal growth.

Labionarinary muscle traction effect - The forward growth of the septal cartilage brings about a forward traction on the premaxillary bone via the labionarinary muscles, resulting in biomechanical stimulation of forward

growth of the upper jaw.

Unilateral resection of the labionarinary muscles in the young rat produces a unilateral decrease in forward growth of the premaxilla on the operated side. On the opposite side outward growth of the premaxilla is slightly increased.

Experimental investigations in young rats on the mechanisms of action of the Frankel (1973) appliance have shown that the superior labial frenum and the labionarinary muscles act as mediators to transmit the force of the superior retrolabial "lip pads" to stimulate sagittal growth of the maxilla.

3. The maxilla, like the premaxilla, is also of membranous origin. It is related to the nose, to the lacrimal apparatus and to the mouth. The maxilla encloses the rostral portion of the maxillary sinus. The orbital process of the maxilla, along with the lacrimal, forms the shell of the snout lateral to the sinus. Zygomatic arch growth correlates with growth of the masseter and temporal muscles. The masseter originates at the zygomatic arch and the temporal muscle lies beneath the arch.

The maxilla contains the maxillary dentition and serves as the origin of the majority of muscles which elevate the mandible. The formative end of the incisor and the roots of the molars are contained in the alveolar

portion of the maxilla which is a linear mass lateral to the palatal process. The buccal wall and the buccinator muscles attach at the alveolar process of the maxilla. The superficial and deep masseter muscles originate from the zygomatic arch and the adjacent maxillary bone.

Participation of the maxilla in the postnatal enlargement and change in form of the snout reflects its relation to maturation of the nose and the mouth. The maxilla is involved in the rostralcaudal enlongation of the snout by growth at its rostral suture with the premaxilla and caudally with the ala of the sphenoid. Within the palate, rostrocaudal enlogation occurs at the transverse premaxillomaxillary and the maxillopalatal sutures. The portion of the maxilla in the nasal shell enlarges in dorsoventral axis by growth at the premaxillomaxillary suture, at the frontomaxillary suture adjacent to its orbital process and at the ventral aspect of the palatine process. Interdigitation increases at the sutures with the premaxilla, presphenoid and frontal.

The greatest growth in <u>mass</u> of the maxilla is in its alveolar portion. This correlates with the growth, eruption and utilization of the dentition. Growth in width of the maxillary portion of the bony palate is effected principally at the intermaxillary suture.

The intermaxillary suture of the rat is characterized by pleomorphic development. As early as nineteen days in utero, cartilage forms in the suture (Mohamed, 1957). However, the appearance of cartilage is transient, and by fifteen days postnatally, there is a resurgence of the cartilage formation, and again the suture has a synchondrotic appearance, presenting as a bilateral epiphyseal plate. During the following four weeks, the intermaxillary suture remains cartilaginous. However, at seven weeks, the suture reverts to a syndesmosis. Thereafter, the intermaxillary suture is a fibrous type of articulation. Several features of the cartilage formation in the intermaxillary suture are significant. First, the type of cartilage that forms is designated as secondary. It develops after the appearance of bone. The concept that secondary cartilage is induced by mechancial forces has been advocated by several investigators (Hall 1968, 1972, 1978; Stutzmann and Petrovic 1970; Muray 1963). Specifically Hall has shown that intermittent rather than constant forces elicit preferential differentiation of the chondroblasts over osteoblasts. Another feature of the cartilage of the intermaxillary suture is that it manifests postnatally at the time of the eruption of the first molars and when weaning occurs.

Weijs and Dantuma (1975) reported that during mastication the resultant vector of forces is medial in the rat. Vinkka (1989) has suggested that the molars of the rat, by their intermittent masticatory forces, could be responsible for secondary cartilage formation. In the present study possible differences between rats with teeth and without teeth in the post-restriction period of growth will have an input to this theory.

4. The palatine bone is formed in membrane and is located at the junction of the nose, mouth and pharynx. Its horizontal or transverse portion is the caudal part of the bony palate and of the floor of the nasopharyngeal canal. The rostral portion of the vertical process meets the maxilla in the lateral wall of the nasopharyngeal canal. The caudal portion of the vertical process of the palatine meets the prephenoid. The bony palate is displaced ventrally by deposition on its oral aspect and resorption of its surface. The median suture becomes denticulated. The vertical process enlarges dorsal at its intersection with the presphenoid.

## STATEMENT OF THESIS

Studies involving clinically induced restraining factors have shown that the growth of the maxillary complex can be slowed, both in anterior-posterior direction as well as in the transverse. It is unclear how much the growth inhibited by restraining factors is compensated for when these factors are removed. (Haas 1948; Blount and Clarke 1949; Logan 1962; Shudy 1974; Henry 1976; Melsen 1978; Fotis 1985)

Therefore, it is the objective of this investigation to evaluate the nature of compensatory changes that occur in the maxillary complex of growing rats after removal of a maxillary transverse growth restraining appliance.

Compensatory growth changes, between control and experimental groups, were quantitated to determine to what extent the potential for full maxillary growth is expressed when the restraining effect is eliminated.

## METHODS AND MATERIALS

### Sample

Thirty nine growing white female Sprague-Dawley rats (Rattus Nozvegicus Albinus) were utilized in this study. All rats were 20 days old at the beginning of the experimental period. Sex of the experimental animals was not considered to be a significant factor. Moss and Baer (1956) stated that "postpubertal growth is slightly slower in females than in males reflecting their small growth potential, but there is no discernible difference in skull form". Hughes, Tanner and Williams (1978) confirmed the absence of sexual dimorphism in the rat skull as observed in longitudinal radiographs. Initial weights ranged from 43.5 to 61 grams (see Appendix A).

The rat was chosen as an experimental model primarily because of its rapid growth and ease of handling. The 20th day after birth was chosen as the start of the experimental period because the prepubertal period begins at this time. Between 20 and 50 days the pubertal growth spurt takes place and at the age of 90-100 days more than 85% of growth has been achieved. Growth is completed at 180 days. The growth rate from 90-180 days is extremely slow. (Baer, Bossa, Ackerman 1984). Very early postnatal growth is not

constant and varies with maternal nutrition and litter size (Park and Nowosielski-Slepowron 1976), while growth between 21 and 55 days is rapid and the rate relatively constant.

In addition, some specific characteristics regarding the chronology of the rat dentition and maxillary growth were taken into account in determining the experimental period. These specific characteristics were:

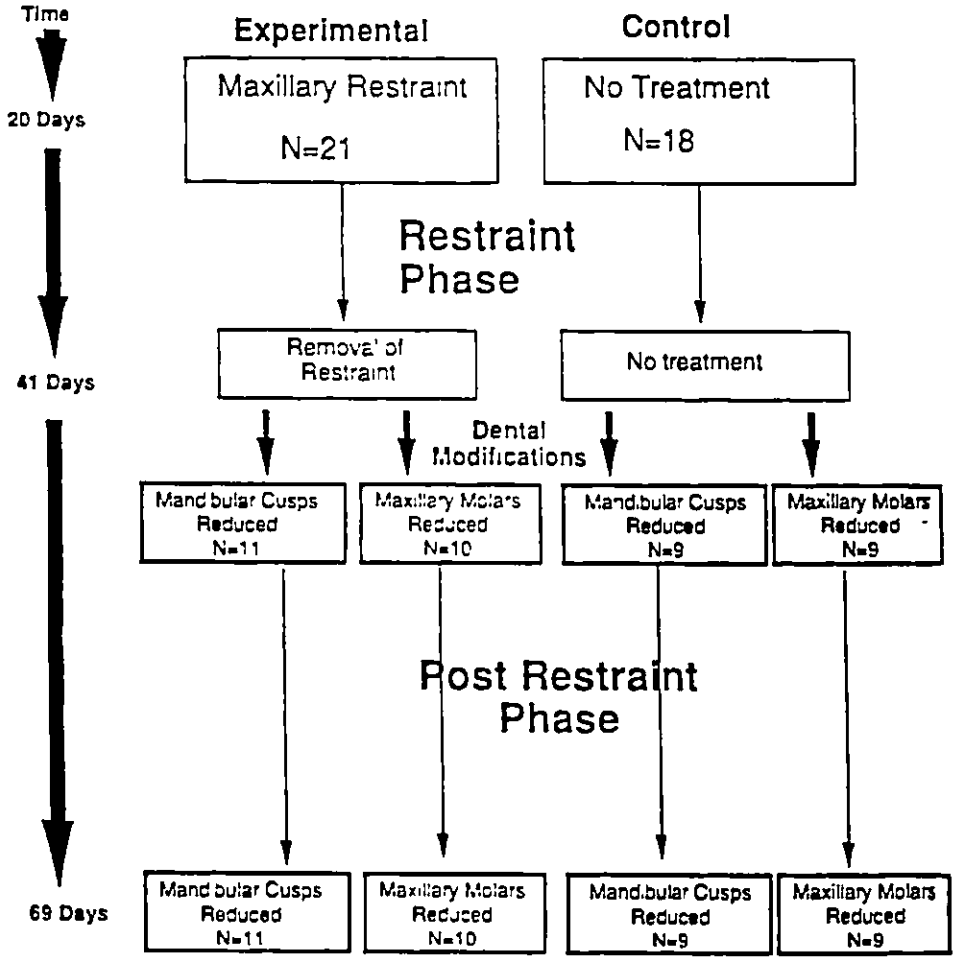
1. The greatest maxillary growth correlates with the growth and eruption of maxillary molars. (Baer, Bosma, Ackerman 1984.)

2. Eruption of the first molar in rats does not occur until day seventeen. The second molar erupts on day nineteen; the third molar on day thirty or later (Mohammed 1957.)

Experimental Design

Thirty-nine 20-day old rats were divided into two groups at the beginning of the experiment (Figure 4). To minimize "litter effect", each litter was divided into control and experimental groups. The experimental group (Group E) was composed of 21 littermates which received maxillary restraining appliances. The control group (Group C) was composed of 18 littermates that served as unrestrained controls. Three weeks following the restraint phase of the experiment, the appliances were removed and Group E was divided into two sub-groups ($E_1$ and $E_2$). In the $E_1$ group, the clinical crowns of the maxillary first and second molars were reduced to the gingival margin. A

Figure 4. Schematic Representation of Experimental design


Time
20 Days
41 Days
69 Days
Experimental
Control
Maxillary Restraint
N=21
No Treatment
N=18
Restraint
Phase
Removal of
Restraint
No treatment
Dental
Modifications
Mandibular Cusps
Reduced
N=11
Maxillary Molars
Reduced
N=10
Mandibular Cusps
Reduced
N=9
Maxillary Molars
Reduced
N=9
Post Restraint
Phase
Mandibular Cusps
Reduced
N=11
Maxillary Molars
Reduced
N=10
Mandibular Cusps
Reduced
N=9
Maxillary Molars
Reduced
N=9

formocresol pulpotomy was performed following crown reduction. The rationale behind the first and second molar reduction was to eliminate lateral tongue pressure which may stimulate transverse maxillary growth. The third molars were left intact to serve as landmarks for accurate measurement of future unrestrained transverse growth in the maxillary arch. In the $E_2$ group, minimal reduction of mandibular molar cusps was performed. The rationale for reducing the mandibular molar cusps was to eliminate buccal cross bite interferences which might inhibit subsequent transverse growth of the maxilla. The maxillary molars were left undisturbed in Group $E_2$.

As was stated earlier, the control group had no maxillary restraining appliances. However, the teeth of the animals were adjusted in the same manner as the experimental animals to produce two sub-groups ($C_1$, $C_2$). Group $C_1$ received total reduction of the clinical crown of the first and second maxillary molars with the third molar left intact. Group $C_2$ received minimal cusp reduction of the mandibular molars while maxillary molars remained intact.

All the rats were allowed to grow for another four weeks. On day 59 all animals were sacrificed and final records were taken.

In summary, the restraint phase consisted of restriction of maxillary growth for a three week period. This was followed by a four week period of unrestricted maxillary growth (Physiologic Rebound Phase). If the potential for compensatory growth exists upon removal of the restraining influence, these compensations should more intensely express themselves during the Physiologic Rebound Phase (Stutzmann and Petrovic 1977).

Experimental Procedures

A. Pilot Study - A pilot study was conducted using one litter of 12 animals to determine:

1. A technique for the taking serial dorsoventral roentgenograns of the rats on the Broadbent-Bolton cephalometer;

2. An impression technique which would produce detailed casts of maxillary dentitions;

3. An appliance which would produce maxillary restriction without the use of any surgical procedures, and thereby avoid any post-surgical growth inhibition.

B. Main Experiment - Four different litters of rats were utilized for this project. Identical numbers of experimental and control animals were selected from each litter. The animals were identified by the ear-notching method described by Stark (1989). Throughout the entire experimental period rats were kept in the Animal Resource Center of the Case Western Reserve University Medical School and were under the daily care of veterinarian

physician. The animals were kept under the following physical conditions: temperature 72°F, humidity 45%, 12 hours of light and 12 hours of darkness.

Anesthesia Regimen (see Plate 1) - All data collection, and experimental procedures were performed under general anesthesia. The animals were anesthetized by intramuscular injection of mixture of 0.9 cc of ketamine hydrocloride (Ketalar 100 mg/ml [Parke-Davis, Div. of Warner Lambert Co., Morris Plains, N.J. 07950 U.S.A.]) and 0.1 cc of Xylarime (Rompun 20 mg/ml [Haver, Moby Corporation. Animal Health Division, Shawnee, Kansas 66261, U.S.A.]) The dose was 0.12 cc - 0.15 cc/100 grs. of body weight.

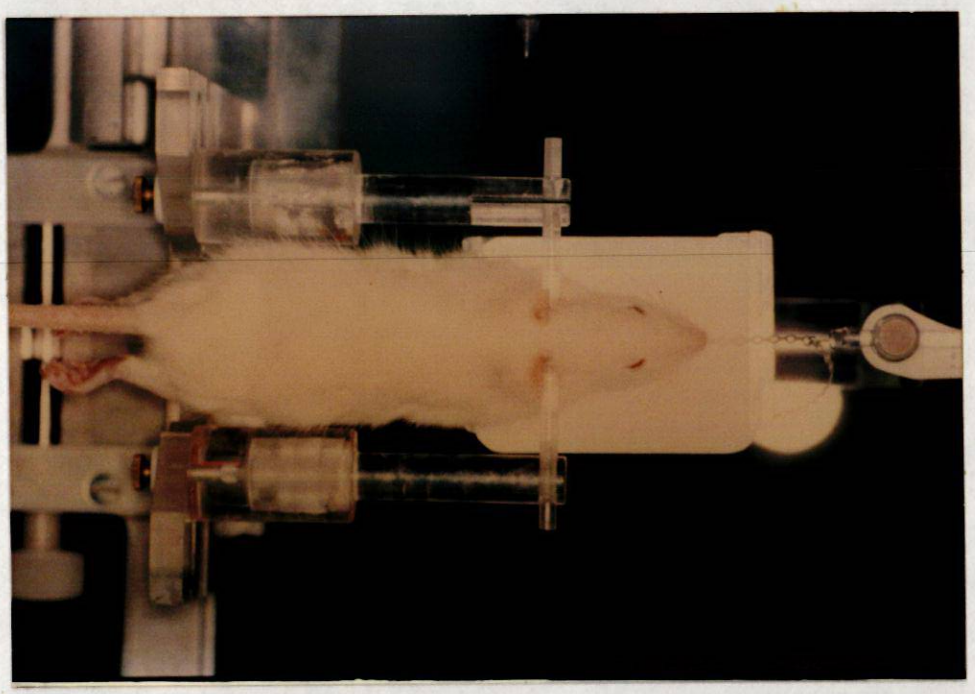
Impression Technique - Under general anethesia, the animals were positioned in supine posture with all four extremities extended and fixed. The mouth was maintained in the open position and the tongue was kept out of the oral cavity using a customized adjustable wire. The wire was positioned immediately behind the upper and lower incisors pressing the tongue outside, downward and laterally (see Plate 2a). An adjustable surgical retractor was used to keep the cheeks away and to increase transverse optical depth (see Plate 2b). Temporary Crown Matrix Buttons(R) (Advance Dental Products, Inc., P.O. Box 214767, Aubury Hills, Michigan 48391) were used as an impression

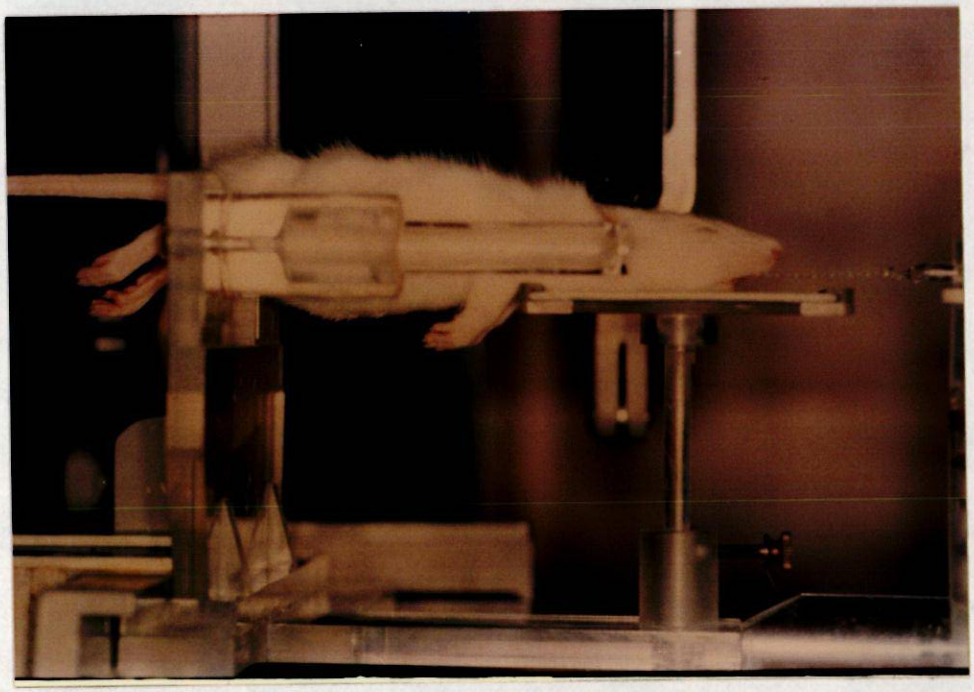
Plate 1. General anestesia by intramuscular injection of the anesthetic solution



Plate 3. Materials used for impression technique from left to right; laboratory torch, crown buttons and spatulla







bonding agent was cured for 15 seconds. Light cured composite was then applied and cured for 30 seconds (see Plate 6b). (Light Bond-Light Cured Orthodontic Adhesive, Reliance Orthodontic Products, Inc., P.O. Box Itasca, IL 60143). The composite was applied to create a restraining appliance, having the following specifications:

1) Extending from the depth of one buccal vestibule of the maxillary complex, over and across the teeth (molars) of the maxilla proper to the buccal vestibule on the opposite side.

2) Transversing and contacting the soft tissue of the palatal vault.

3) Having adequate thickness (0.5-1 mm) to act as a biteplate and resist fracture by the forces of mastication.

4) Extending posteriorly no further than the maxillary tuberosity area and the soft palate.

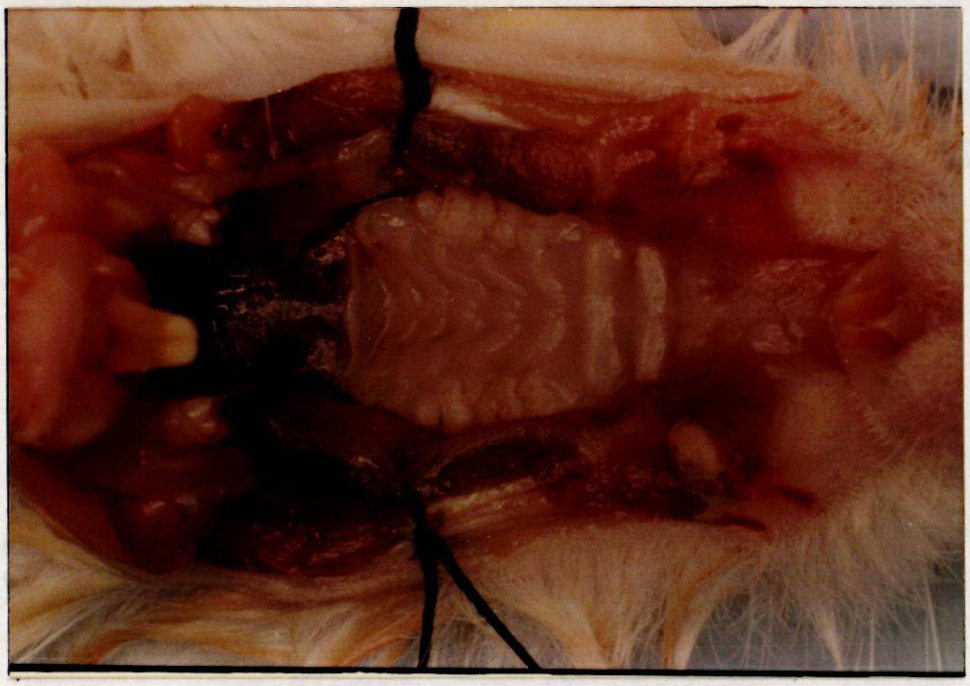
5) Extending anteriorly only as far as the maxillary aveolus that supports the first molar.

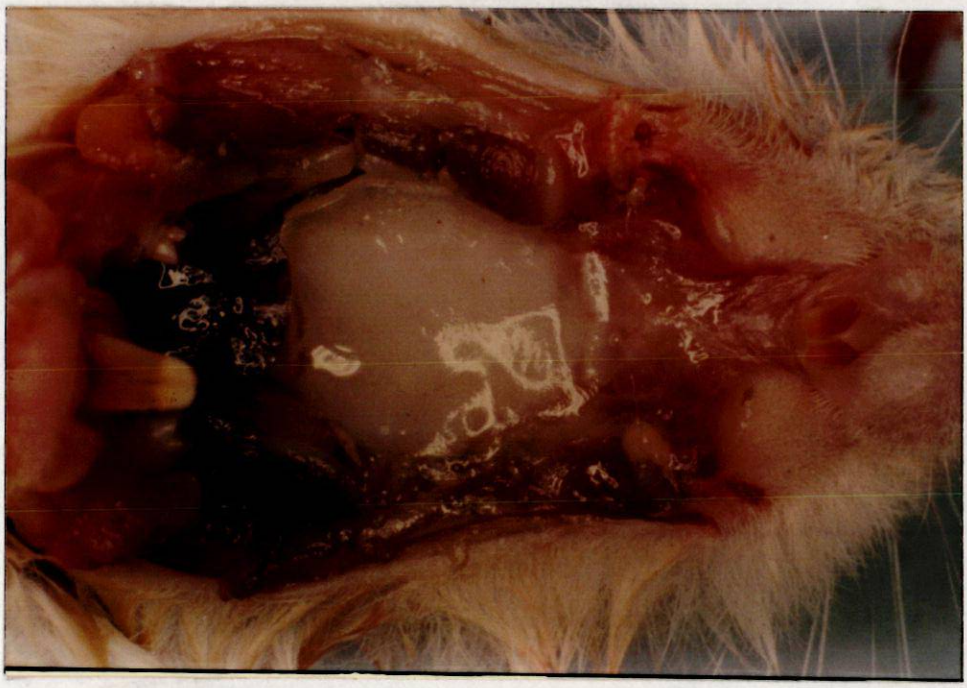
The diastema between the first premolar and the incisors of the premaxilla, was not to be encompassed by the appliance.

Following the construction of the restraining appliance, both the experimental and control animals were placed on a soft diet. (Purina Powered Chow, Purina Mills, Inc., 505 North 4th St., Box 548, Richmond, IN 47375.) This design minimized nutritional variables between the control (unoperated) group and the experimental (restrained) group. The rats were observed twice daily for overall health and stability of restraining appliance. Any

Plate 6a. Acid etching of molar crowns

Plate 6b. Restraint appliance in place. Ventral view of the palate





necessary repairs to the appliance were performed immediately. The restraining appliance did not affect weight gain or overall somatic growth of experimental animals. All animals were weighed twice a week and no significant differences were identified. (see Appendix A)

Physiologic Rebound Phase - Removal of Maxillary Restraint and Dental Modification On the 21st day of the experiment, the rats were anesthetized, and the appliances were atraumatically removed using a dental scaler. Maxillary impressions and dorsoventral radiographs were taken on all the animals by the previously described method. The rats were then divided into four groups: $E_1$, $E_2$, $C_1$, $C_2$, (see Figure 4) and under general anethesia, the following dental modifications were performed:

1) **For groups $E_1$, $C_1$:** Total reduction of the maxillary first and second molars followed by formocresol pulpotomy.

2) **For groups $E_2$, $C_2$** - minimal reduction of mandibular molar cusps.

The dental modifications were accomplished using a fibroptic handpiece with a 5/11 tapered diamond. Water and air spray was used to minimize thermal insult to the tissues. Following dental modification, all animals were allowed to grow for another four weeks prior to sacrifice.

Final Data Collection - The animals were sacrificed at 69 days (49 days after the start of the experiment). Weights ranged from 213 to 288 grams. (see Appendix A)

Sacrifice of the animals met the following criteria:

1) Rapid death following the definition of euthanasia.

2) Performer proficiency.

3) Safe and aesthetically acceptable.

4) Compatible with scientific objectives.

5) Out of sight, sound and smell of other conscious animals.

6) Confirm death.

The specific euthanasia agent was a saturated solution of sodium pentobarbitol used at 3-6 ml/kgr at minimum concentration of 65 mg/ml injected intraperitoneally. Pentobarbitol is a common anesthetic agent whose mode of action is central nervous system depression.

After sacrifice, final records (dorsoventral radiographs and impressions) were taken on all animals.

Gross Observations - The initial effects of appliance insertion were noted during the experimental period. A gross comparison between control and experimental animal facial form and outline was made and evaluated. Similarly, the initial, intermediate and final dental casts were examined to determine alterations in arch form, palatal vault depth and symmetry. Gross observation of each animal head was made and recorded at the time of animal sacrifice.

Cephalometric Analysis - The radiographs obtained for each animal (see Plate 7) were enlarged three times to

Plate 7. Dorsoventral cephalogram of a Sprague Dawley rat skull



reduce tracing error. A photographic enlarger was used and landmarks for each radiograph were indicated by pinholes placed on a single sheet of bond paper (Hans 1981). Data reduction was facilitated by using a process known as "digitization". A commercially available software program, Dentofacial Planner™ (Dentofacial Software, Ind., P.O. Box 950, Station A, Toronto, Ontario; M5W 1G9, Canada 1990) was customized for data collection.

Before data collection began each radiograph was registered using point BA and I (see Figure 5) to serve as the abscissa (Hans 1981). A perpendicular constructed to this line formed the ordinate to complete the Cartesian coordinate system. Point BA was arbitrarily assigned the coordinates (1, 1) to place all cephalograms in the positive quadrant of the coordinate system. Points were entered in the same sequence for each animal. The accuracy of landmark determination was within the limits of resolution of the digitizing board (0.025 mm).

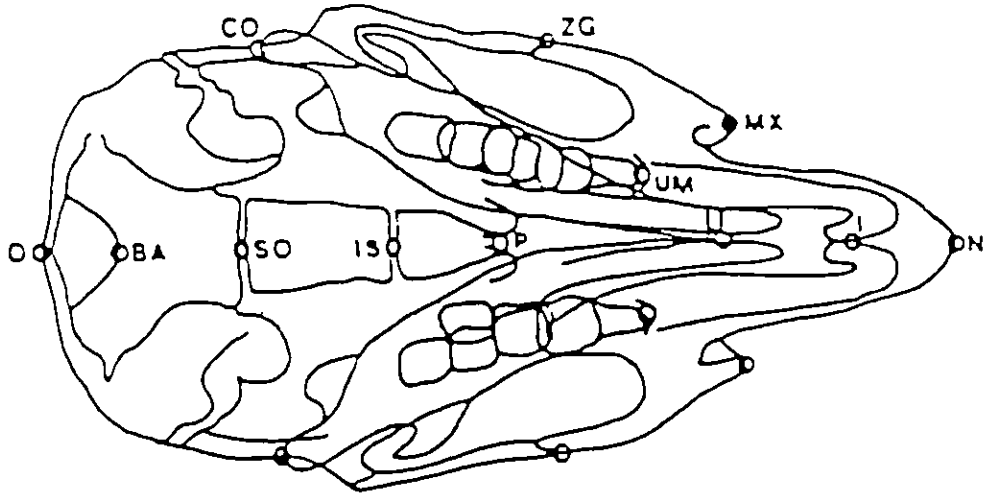
Cephalometric Landmarks - The following landmarks were identified to aid in the dorsoventral analysis. These points are illustrated on the diagram in Figure 5.

BA. The most anterior point on the outline of the foramen magnum;

CO. The most posterior point on the mandibular condyle;

I. A point in the median plane that lies on a line tangent to the inner curvature of the maxillary incisor.

Figure 5. Cephalometric Landmarks Dorsoventral Projection



IS. The middle of the intersphenoidal synchondrosis at the midline;

LI. A point in the median plane denoting the border between the mandible lingual surface of the mandibular incisors;

MX. The most anterior point on the maxillary bone at the infra-orbital foramen;

N. The most anterior point on the nasal bone;

O. The most posterior point on the external occipital protuberance;

P. The most posterior point on the palatal bone at the midline:

S. The middle of the sphenoccipital synchondrosis (at the midline);

UM. The interface betwen the maxilla and the mesial surface of the maxillary first molar root;

ZG. The most lateral point on the zygomatico-maxillary suture;

Cephalometric Measurements - Thirty-eight linear measurements were used to characterize the craniofacial dimensions of each animal. A description of each measure can be found in Tables I and II, along with its construction shown in Figures 6 through Figure 8. This analysis was adapted from earlier works (Behrents 1975; Palmer 1978; Hans 1981).

Impression Analysis

Direct measurements were taken from the dental impressions to quantify transverse changes in the dentition. Due to the size of the impressions and the technical difficulty in

creating plaster casts from the impression material measurements were taken directly from the impressions. This allowed a positive seat for the point of the dial calipers and increased the accuracy of the measurements. Measurements were taken between maxillary first molars and recorded as the greatest distance between mesial lingual cusps. Using a dial vernier calipers (Helios Calipers, D.C.A. Corporation, Washington, D.C.) measurements were taken to the nearest 0.05 millimeter. These values were averaged to determine the mean change in transpalatal width among groups at the three different experimental time periods.

TABLE I

AP AND MANDIBULAR VARIABLES MEASURED IN DORSOVENTRAL VIEW

A) VARIABLES TO MEASURE ANTEROPOSTERIOR CHANGES IN MID-FACIAL BODY SIZE OR DISPLACEMENT OF THE MID-FACIAL COMPLEX

| Variable | Landmark Employed | Measures |
|---|---|---|
| A1 | *MX-N | Rostral development |
| A2 | *SO-UM | Sphenoid-maxillary dental development |
| A3 | *IS-UM | Maxillary dental advancement |
| A4 | P-I | Palatal length |
| A5 | *AB-ZG | Anterior zygomatic development |
| A6 | *AB-MX | Anterior maxillary development |
| A7 | *AB-UM | Anterior maxillary dental development |
| A8 | *BA-MX | Maxillary-cranial base development |
| A9 | *SO-MX | Sphenoid-maxillary development |
| A10 | *IS-MX | Maxillary advancement |
| A11 | I-N | Anterior nasal position |
| A12 | *O-MX | Maxillary advancement |

B) VARIABLES TO MEASURE CHANGES IN MANDIBLE

| | | |
|---|---|---|
| M1 | *AB-CO | Anterior condylar position |
| M2 | CO-CO | Bicondylar width |
| M3 | *O-CO | Condylar advancement |
| M4 | *CO-LI | Mandibular length |

* Bilateral Measurements

TABLE II

TRANSVERSE AND CRANIAL BASE VARIABLES MEASURED IN DORSOVENTRAL VIEW

A) VARIABLES TO MEASURE TRANSVERSE CHANGES IN MIDFACIAL DIMENSION

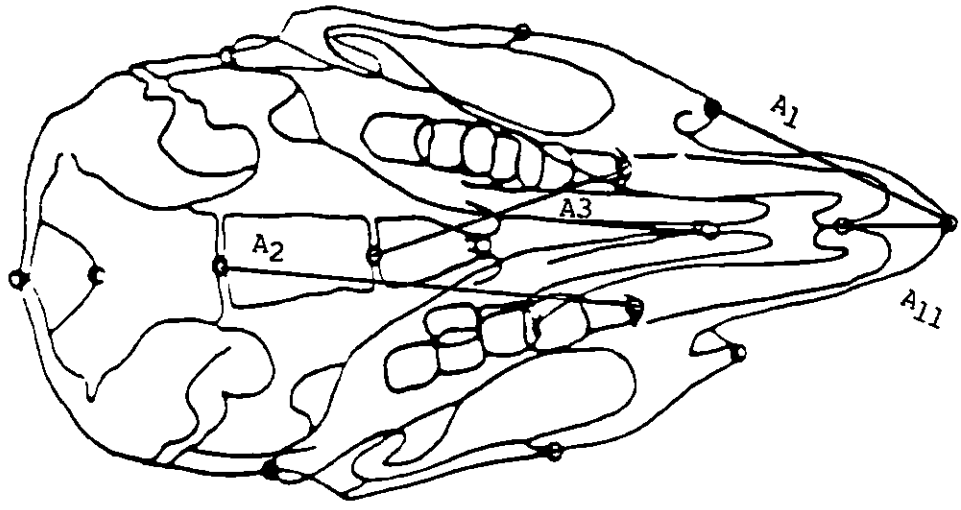
| Variable | Landmarks Employed | Measures |
|---|---|---|
| T1 | ZG-ZG | Bizygomatic width |
| T2 | UM-UM | Maxillary dental width |
| T3 | MX-MX | Maxillary width |
| T4 | *ZG-MX | Maxillary zygomatic bone length |

* Bilateral measure

B) VARIABLES TO MEASURE CHANGES IN THE CRANIAL BASE OF CRANIUM

| | | |
|---|---|---|
| C1 | O-BA | Sphenoid advancement |
| C2 | BA-SO | Sphenoid length |
| C3 | IS-P | Palatal advancement |
| C4 | BA-IS | Pre-sphenoid advancement |

Figure 6. Cephalometric analysis. Variables to measure Anteroposteror changes in midfacial bony size or displacement of the midfaical complex (dorsoventral cephalometric orientation)




AB

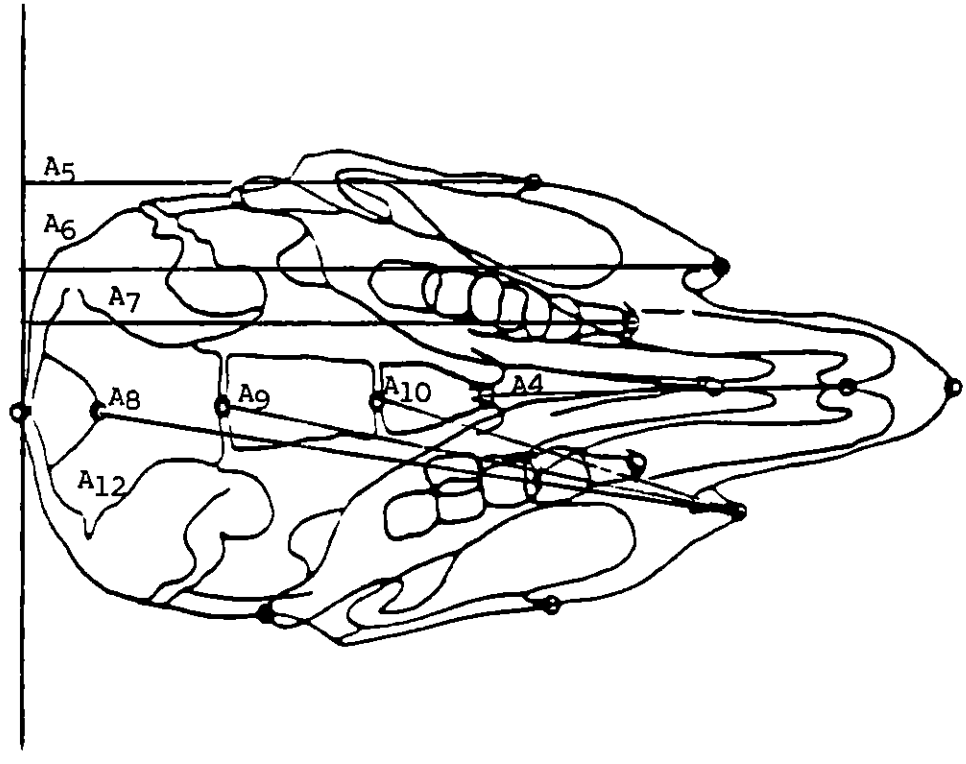
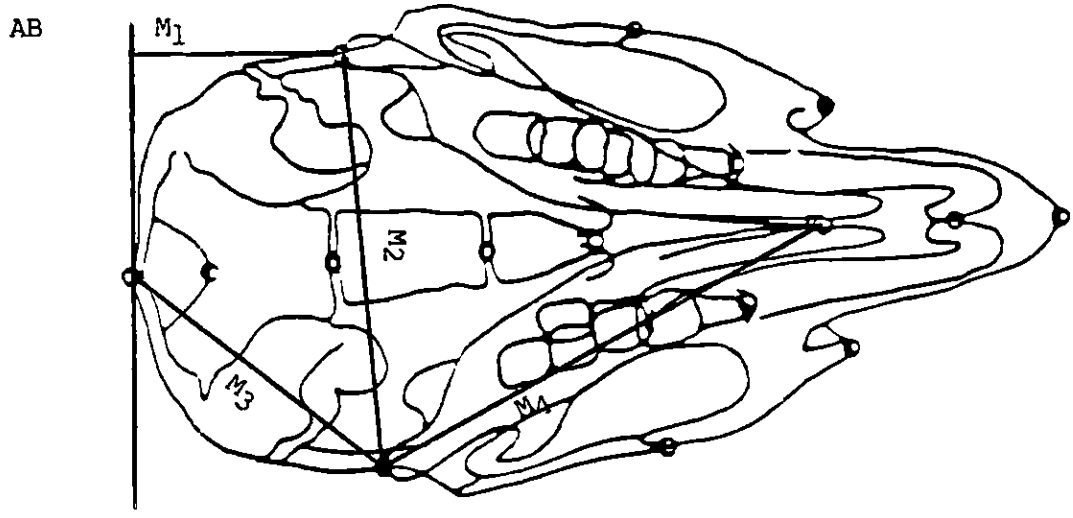


Figure 7a. Construction of variables to measure changes in the mandible

Figure 7b. Construction of variables to measure transverse changes in midfacial dimensions


AB
M1
M2
M3
M4

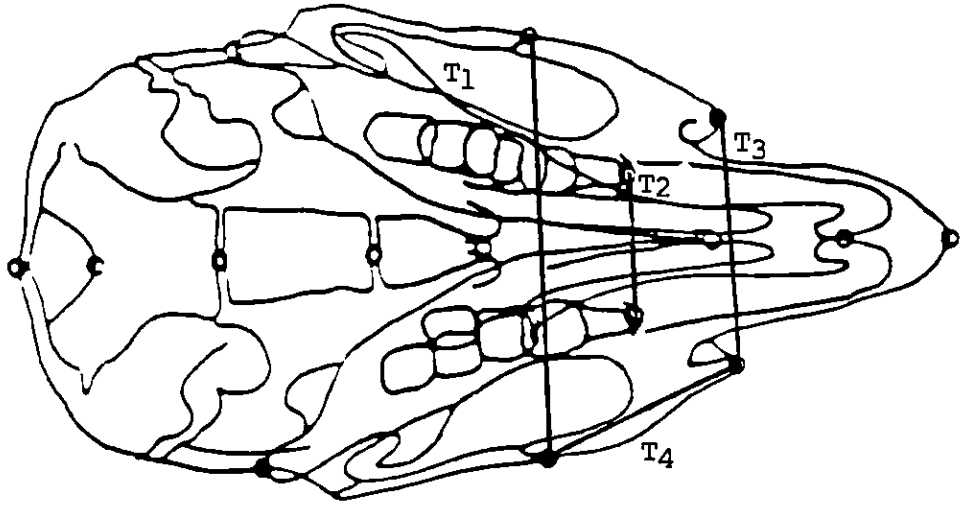
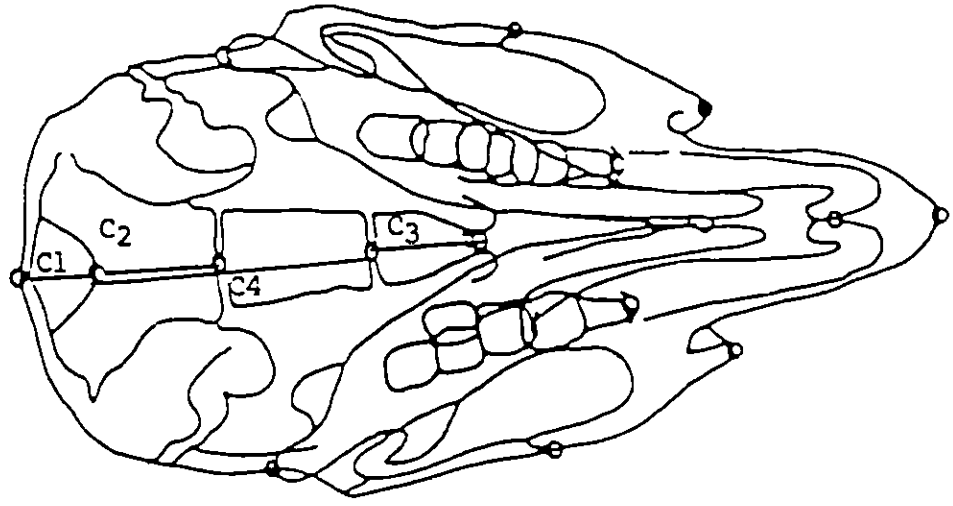

T1
T2
T3
T4

Figure 8. Construction of variables to measure changes in the cranial base or cranium



## RESULTS

The results of the present study are presented under the following headings: (1) Gross Observations, (2) Weight Gain, (3) Dental Cast Analysis, and (4) Cephalometric Analysis.

Description of the sample results:

The timetable in which the experiment took place and data collected is indicated as follows:

a) Time 1 (T1) = First experimental day (20 day old animals)

b) Time 2 (T2) = Twenty first experimental day (41 day old animals)

c) Time 3 (T3) = Forty ninth experimental day (69 day old animals)

Between T1 and T2 the restraint phase of the experiment was conducted. Between T2 and T3, the physiologic rebound phase of the experiment was conducted. (See figure 4)

The original experimental design included thirty-nine animals randomly selected and assigned to experimental and control groups. The data from the experimental and control groups were divided into four groups: $E_1$, $E_2$, $C_1$, and $C_2$ (See figure 4):

$E_1$: represents the experimental group of rats with restraining appliances at time 1 and maxillary dental

modifications at time 2.

$E_2$: represents the experimental group of rats with restraining appliances at time 1 and mandibular dental modifications at time 2.

$C_1$ represents the control group of rats with no restraining appliances at time 1 and with maxillary dental modifications at time 2.

$C_2$ represents the control group of rats with no restraining appliances at time 1 and with mandibular dental modifications at time 2.

1. Gross Observations Visual examination of the animals with the restraining appliance revealed an induced open bite due to the bite-plane effect caused by the bonding material on the occlusal surfaces of the molars. This effect prevented the usual attrition of the incisors and allowed for over-eruption of the incisor teeth. No attempt was made to correct this experimentally-induced over-eruption once the restraining appliance was removed because no effect on eating habits were noted.

Daily observation during the restraint phase of the experiment revealed no intraoral infections due to the appliance in the experimental group. During the physiologic rebound phase, mandibular molars over-erupted in animals that had had maxillary dental modifications. There was no evidence of pathology related to the dental modifications. Dry skull examination of rat #2 belonging to group $E_1$ revealed noticable deviation of the entire snout to the right side. Intraoral examination of the same rat

indicated the maxillary molars were not equally reduced. The right side was reduced to the gumline and the left side had only one-half of the crown removed. This discrepancy was due to technical problems associated with the dental modification (i.e., small intraoral dimensions and minimum optical depth) (see Plates 8a, 8b).

2. Weight Gain The mean and the standard deviation of the weight for each group for T1, T2 and T3 is shown in Table VI.

In analyzing the weight data, an attempt was made to determine if significant weight differences existed between groups $E_1$, $E_2$, $C_1$, and $C_2$. Analysis of variance (ANOVA) was used to examine weight differences at time T1, T2 and T3. (see Appendix A)

The results of the ANOVA indicated that the weight was not significantly different among the four groups of rats for time 1 (T1). The results of ANOVA for time 2 (T2) and time 3 (T3) indicated that the weight was statistically significantly different among groups $E_1$, $E_2$, $C_1$ and $C_2$.

The computed weight gain during the restraint phase for the control animals was slightly greater than that of the experimental animals (see Table III). During the physiologic rebound phase, both experimental groups seemed to be physically smaller. However, the weight gain for the experimental groups during the rebound phase was greater

Plate 8a. Experimental animal #2 with unilateral tooth reduction. Asymmetry with right side being longer. Dorsoventral view

Plate 8b. Experimental animal #2 with unilateral tooth reduction. Asymmetry of the maxilla with the right side being in a more anterior position. Ventral view of the palate. Arrows indicate unilateral tooth reduction.





TABLE III

Summary Data of Weight and Weight Gain
During Experimental Phases, for All Groups

| GROUP | TIME 1 | | | | TIME 2 | | | | TIME 3 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | Mean | S.D. | wt. gain | N | Mean | S.D. | wt. gain | N | Mean | S.D. |
| $C_1$ | 9 | 54.7 | 4.2 | M=129.5 | 9 | 184.2 | 12.1 | M=79.4 | 9 | 263.7 | 15.7 |
| $C_2$ | 9 | 51.1 | 4.8 | M=113.9 | 9 | 165.1 | 11.5 | M=80.6 | 9 | 245.6 | 11.4 |
| $E_1$ | 10 | 55.3 | 3.4 | M=118.3 | 10 | 173.6 | 13.2 | M=85.3 | 10 | 258.0 | 16.9 |
| $E_2$ | 11 | 53.7 | 3.9 | M=100.1 | 11 | 153.8 | 13.1 | M=92.3 | 11 | 246.1 | 20.1 |

than the control groups. Therefore, all groups were physically similar at the end of the experiment.

3. Dental Cast Examination and Analysis Visual observations of initial, intermediate and final dental impressions revealed varying degrees of change for all groups. The average palatal depth of the control group gradually increased throughout the course of the experiment. Dental modifications in the control group did not seem to have any effect on palatal depth. However, the average palatal depth for the experimental animals increased sharply during the restraint phase and then gradually decreased during the physiologic rebound phase. Palatal depth in animals of $E_1$ group (maxillary molar modifications) seemed to decrease at a slower rate throughout the physiologic rebound phase.

Transverse dental measurements recorded on initial intermediate and final impressions demonstrated arch dimension differences among groups. Transverse dental measurement data was analyzed for groups $E_1$, $E_2$, $C_1$ and $C_2$ during and between times T1, T2 and T3. The above experimental design represents a split-plot or nested design (Snedecor et. al., 1980; Winner 1971) for statistical analysis. Previous analysis of weight data indicated that the weight was significantly different among groups $E_1$, $E_2$, $C_1$, and $C_2$. The systematic variability

associated with weight suggested the use of a split-plot design analysis of covariance (ANCOVA) with animal weight as the covariate. Weight was chosen as the covariate because it exhibited no treatment effect while maintaining a high correlation with craniofacial dimensions in a controlled population of experimental animals. (Paulus, 1976, Winner, 1971, Hans, 1981)

The statistical model for data analysis is described in Figure 9. Bar line plots (see Figure 10) for the mean and the standard deviation demonstrated the following:

a) The rate of increase in maxillary dental arch width for the $C_2$ group was gradual during the restraint phase of the experiment and greater (a more "sharp" increase) during the physiologic rebound phase of the experiment.

b) For group $C_1$ (maxillary molars reduced) increase in maxillary dental arch width was similar to that of $C_2$ during the restraint phase, while during the physiological rebound phase, growth in width was slower and did not achieve the same growth potential, compared to group $C_2$.

The standard deviation for group $C_2$ was greater than that observed for group $C_1$. Exceptions to the above findings were noticed in the following cases:

(1) Rat #5, belonging to group $C_2$, exhibited an edge to edge bite and the maxillary transverse growth did not achieve the same potential compared with his groupmates. (see Plates 9, 10a, 10b)

(2) Rat #1, belonging to group $C_1$, exhibited a normal buccal overjet similar to that observed in the animals

Figure 9. Linear Model Describing Fixed Treatments Covarying for Weight

$$Yijk = m + ai + Pk(i) + b\ (\bar{X}ijk-X) + P'k(ij) + Eijk,$$

where,

Yijk = a measurement of the ith treatment for the jth rat in group k

for

i = 1,2 or 3, j = 1,2....n., k = 1,2,3 or 4

and

m = the population mean

ai = the effect of the ith treatment

Pk(i) = the effect of group k within level ai

b = the slope of the common regression line for the weight covariate in the population

$(\bar{X}ijk-X)$ = the deviation of the weight covariate associated with the ith treatment, jth rat in group k, from the total mean

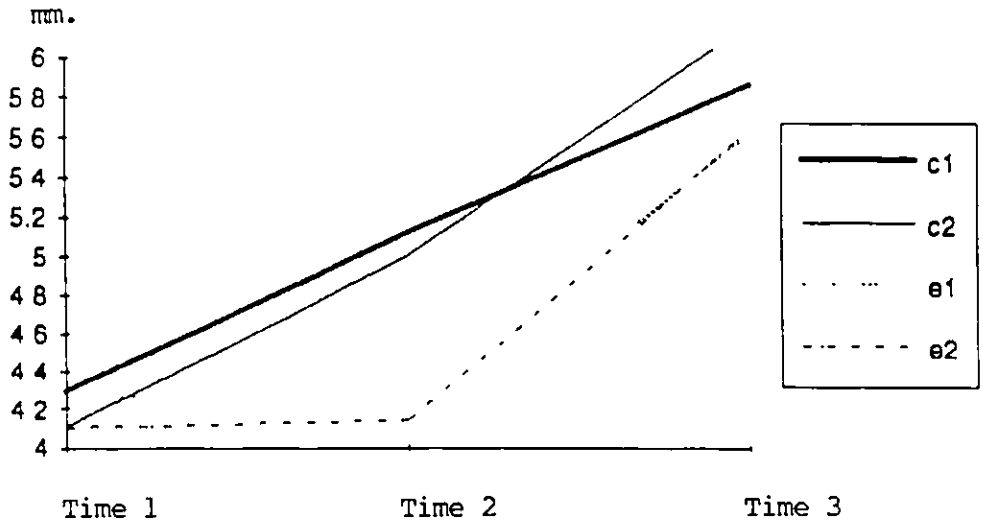
P'k(ij) = the residual group effects and;

Eijk = the experimental error associated with the ith treatment, jth rat and group k.

Figure 10a Plot of means of transverse dimension directly measured in dental impression as a function of time for each rat group.

Figure 10b Plot of standard deviations of transverse dimension directly measured in dental impression as a function of time for each rat group.

Mean


mm.
6
5 8
5 6
5 4
5.2
5
4 8
4 6
4 4
4 2
4
c1
c2
e1
e2
Time 1
Time 2
Time 3

Sigma

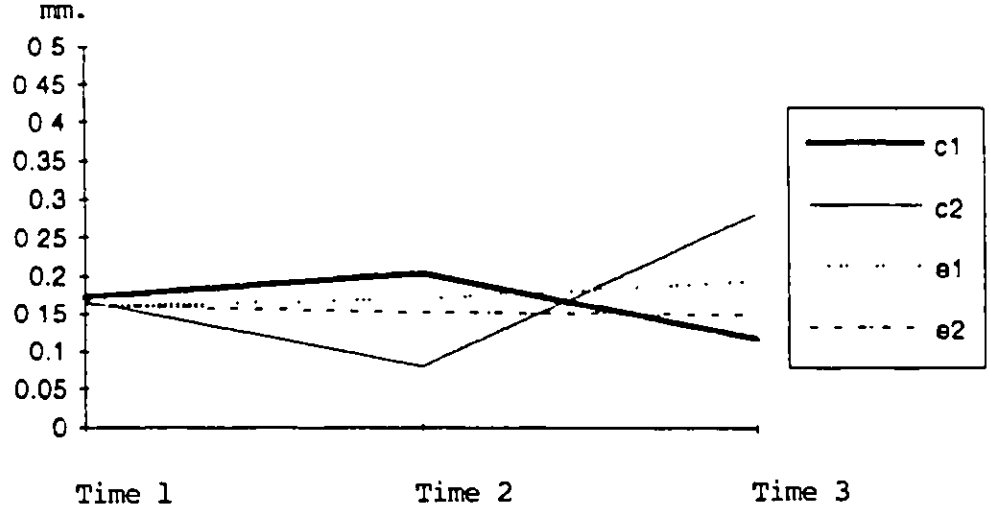

mm.
0 5
0 45
0 4
0.35
0.3
0 25
0.2
0 15
0.1
0.05
0
c1
c2
e1
e2
Time 1
Time 2
Time 3

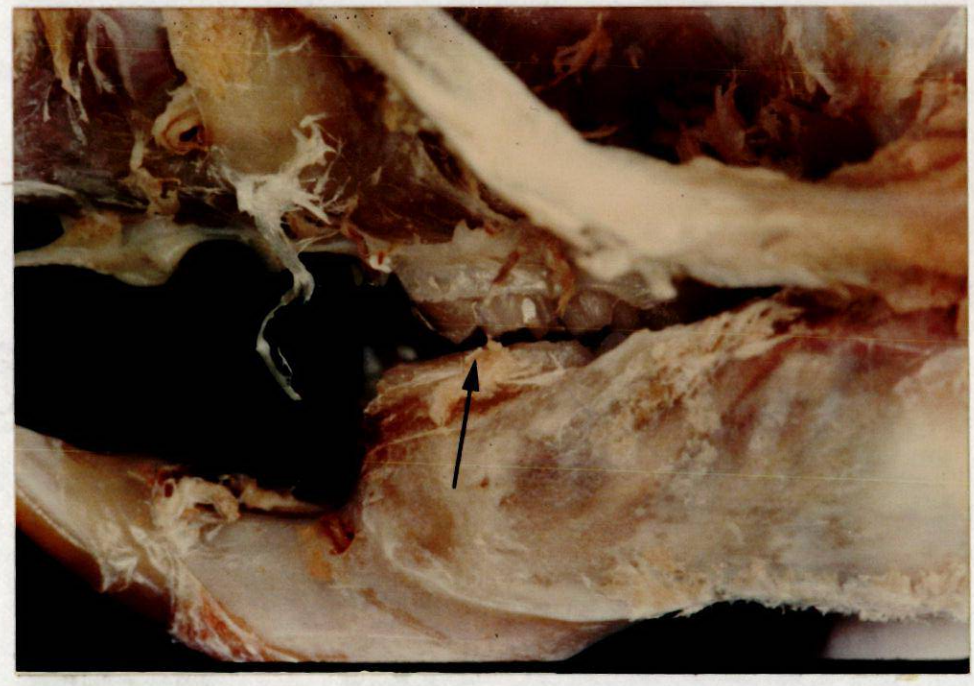
Plate 9. Control animal #5 with teeth demonstrating transverse deficiency. Frontal view. Arrows indicate molar region.



Plate 10a. Control animal #5 with teeth demonstraing transverse deficiency. Oblique view, right side. Arrows indicate molar region.

Plate 10b. Control animal #5 with teeth demonstrating transverse deficiency. Oblique view, left side. Arrows indicate molar region.





belonging to $C_2$. (see Plates 11, 12a, 12b)

c) In both experimental groups ($E_1$, $E_2$) the rate of maxillary dental arch width increase was from very slight to none during the restraint plase of the experiment. Group $E_2$ showed a substantial increase in maxillary dental arch width during the physiologic rebound phase of the experiment. This increase was much greater than the one observed in the control groups during the same period of time.

d) In group $E_1$ (maxillary molars reduced) the rate of maxillary dental arch width was substantially greater, compared to the control groups during the physiologic rebound phase. This increase, though, was slightly smaller (less "sharp") compared to the one observed in group $E_2$ during the same period of time.

An exception to these conclusions was noticed in rat #9, belonging to group $E_2$, which did not manage to recover from the initial restriction during the physiologic rebound phase. This rat exhibited maxillary lingual crossbite at the end of the experiment (See Plates 13, 14a, 14b). Similar variability was also observed during the pilot study (see Plates 15, 16a, 16b).

4. Cephalometric Analysis

a) Reliability Analysis Two types of reliability of data were analyzed; the reliability of the cephalometric and the reliability of the digitizing system. The reliability of the tracing data was estimated by selecting ten animals and repeating the following sequence. Each cephalogram was enlarged three times. Each enlarged cephalogram was traced twice and measurements were taken for each tracing. The reliability of the trace data was

Plate 11. Control animal #1 without teeth demonstrating normal transverse relationships. Frontal view. Arrows indicate molar region.



Plate 12a. Control animal #1 without teeth demonstrating normal transverse relationships. Olbique view, right side. Arrows indicate molar region.

Plate 12b. Control animal #1 without teeth demonstrating normal transverse relationships. Olbique view, left side. Arrows indicate molar region.



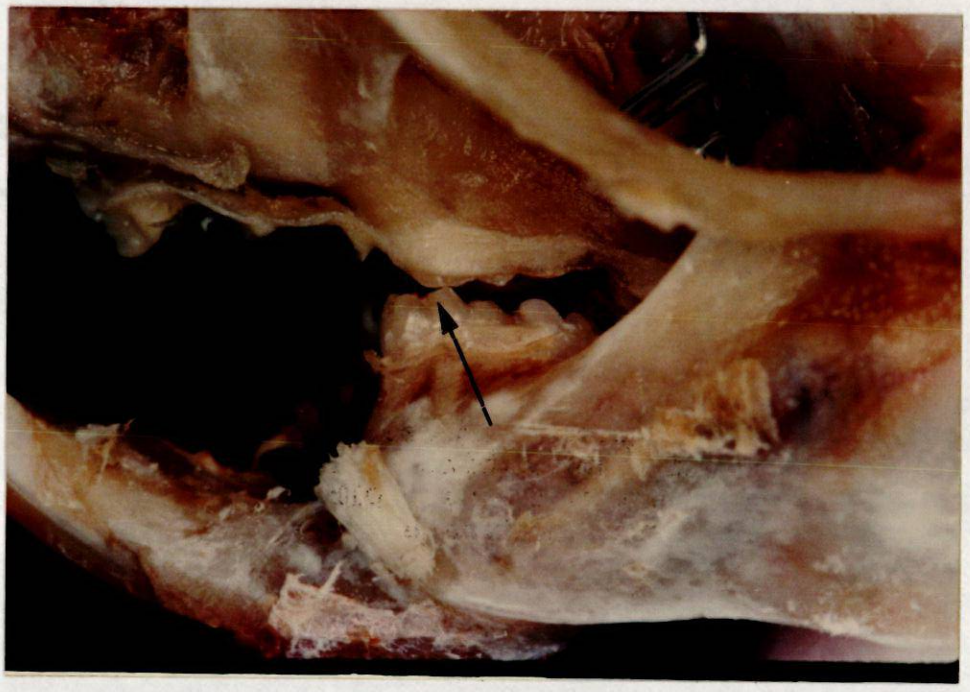


Plate 13. Experimental animal #9 with teeth which demonstrates transverse deficiency remaining at the end of the rebound phase. Frontal view. Arrows indicate molar region.



Plate 14a. Experimental animal #9 with teeth which demonstrates transverse deficiency remaining at the end of the rebound phase. Oblique view, right side. Arrows indicate molar region.

Plate 14b. Experimental animal #9 with teeth which demonstrates transverse deficiency remaining at the end of the rebound phase. Oblique view, left side. Arrows indicate molar region.



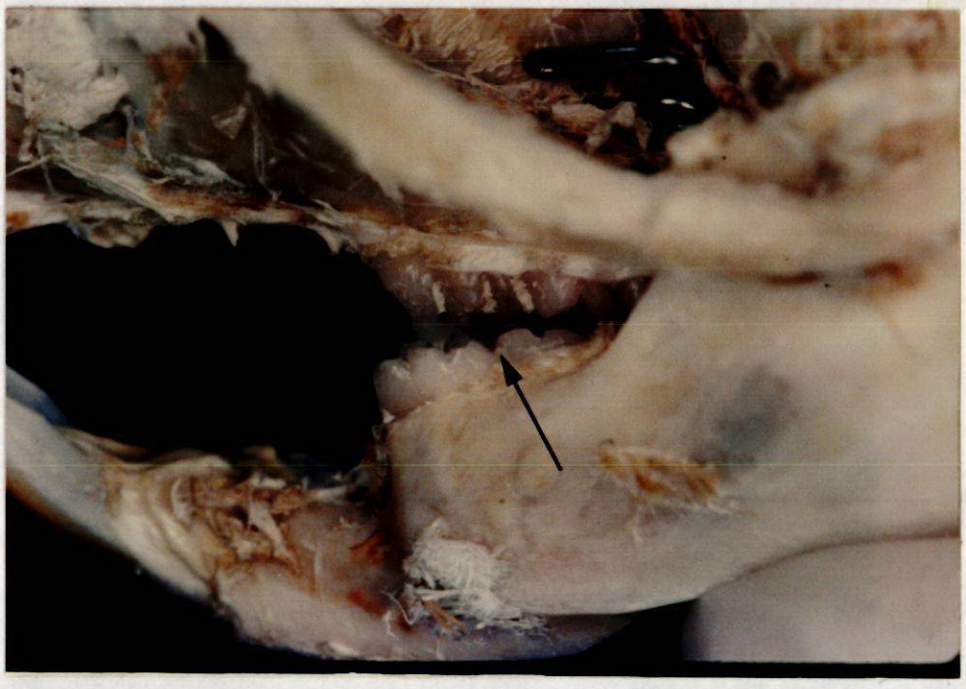


Plate 15. Pilot study animal sacrificed three weeks after placement of the constriction appliance, demonstrating posterior cross bite. Frontal view. Arrows indicate molar region.

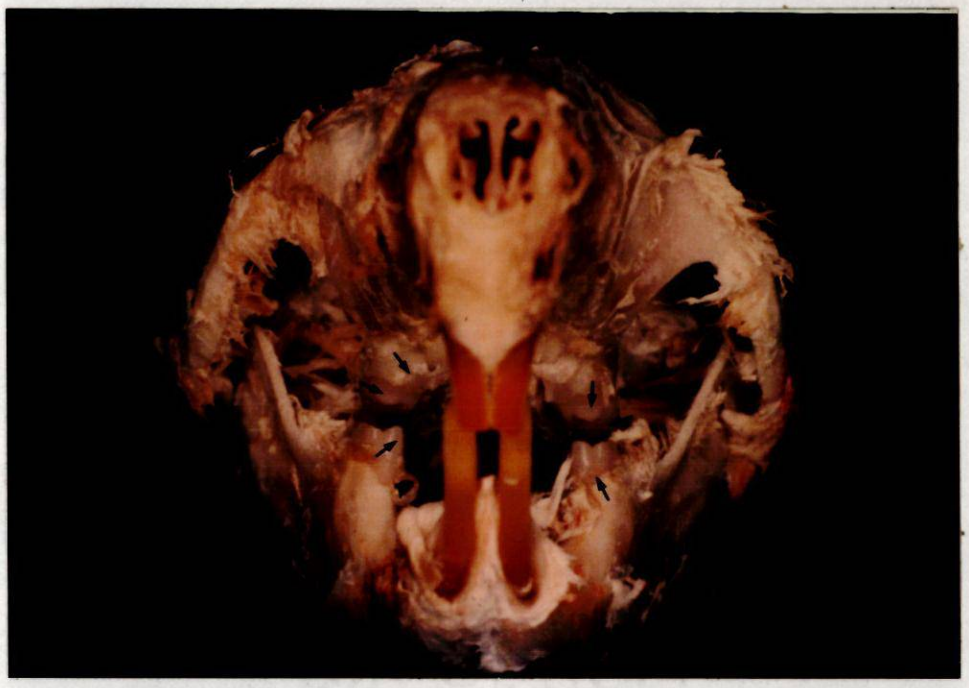


Plate 16a. Pilot study animal sacrificed three weeks after placement of the constriction appliance, demonstrating posterior cross bite. Oblique view, right side. Arrows indicate molar region.

Plate 16b. Pilot study animal sacrificed three weeks after placement of the constriction appliance, demonstrating posterior cross bite. Oblique view, left side. Arrows indicate molar region.





computed by the following (Snedecor, et. al., 1986, Winner 1971):

$$Rk = \frac{s^2Yk}{s^2Yk + s^2ek} \times 100,$$

where

$s^2Yk$ = variance of the Yk parameter

$s^2ek$ = error variance due to tracing the Yk parameter

The digitizer system reliability was calculated by selecting the cephalogram trace of ten animals and measuring the cephalometric landmarks twice with the digitizer. The reliability then was calculated, using the above reliability equation. The cephalometric landmarks' reliability due to trace and the digitizer measurement system are listed in Table IV.

b) Descriptive Statistics In order to categorize significant treatment changes, the 38 variables were divided into four functional groups on an anatomic basis. These groups, along with the rationale for including measures within each group are listed below:

1. Anteroposterior midfacial dimension Twenty-two variables were included in this group. Some of these variables reflect changes in the anteroposterior length of bones within the midface. Others measure the anteroposterior displacement of the midfacial

TABLE IV

Reliability of Measured Variables

| Variable | Tracing Reliability Percent of Total | Digitizer Reliability Percent of Total |
|---|---|---|
| MXr-N | 81.4 | 99.7 |
| MXl-N | 84.1 | 99.97 |
| SO-UMr | 74.7 | 99.87 |
| SO-UMl | 85.5 | 99.95 |
| IS-UMr | 68.0 | 99.99 |
| IS-UMl | 85.7 | 99.86 |
| P-I | 91.1 | 99.83 |
| BA-MXr | 98.2 | 99.29 |
| BA-MXl | 98.0 | 99.93 |
| AB-COr | 75.5 | 99.70 |
| AB-COl | 87.0 | 99.89 |
| AB-ZGr | 71.5 | 99.93 |
| AB-ZGl | 84.6 | 99.96 |
| AB-UMr | 67.4 | 99.96 |
| AB-UMl | 80.0 | 99.86 |
| AB-MXr | 98.32 | 99.28 |
| AB-MXl | 98.2 | 99.98 |
| SO-MXr | 94.4 | 99.51 |
| SO-MXl | 93.3 | 99.66 |
| IS-MXr | 72.7 | 99.74 |
| IS-MXl | 63.2 | 99.92 |
| I-N | 71.0 | 99.51 |
| O-MXr | 99.1 | 99.32 |
| 0-MXl | 96.4 | 99.88 |
| COr-COl | 85.7 | 99.72 |
| O-COr | 74.1 | 99.46 |
| O-COl | 68.7 | 99.76 |
| COr-LI | 84.3 | 99.91 |
| COl-LI | 87.2 | 99.84 |
| ZGr-ZGl | 81.2 | 99.84 |
| UMr-UMl | 96.8 | 98.76 |
| MXr-MXl | 92.0 | 98.85 |
| ZGr-MXr | 64.0 | 99.97 |
| ZGl-MXl | 84.3 | 99.96 |
| O-BA | 95.3 | 99.94 |
| BA-SO | 20.2 | 99.81 |
| IS-P | 73.7 | 99.85 |
| BA-IS | 71.2 | 99.68 |

complex relative to the neurocranium (see Appendix B, Table VI).

2. Transverse midfacial dimension Five variables were placed in this group on the basis that they measure changes in width of the midfacial complex as determined from the dorsoventral cephalograms (see Appendix B, Table IX).
3. Cranial base and cranium dimensions Three cranial base measurements and one transcranial measurement were included in this group. These four measurements reflect the changes in the synchondroses (see Appendix B, Table XII).
4. Mandibular dimension The seven variables in this group reflect changes in mandibular dimension and cranial mandibular relative positioning (see Appendix B., Table XV).

The means and the standard deviations for all variables adjusted for the weight covariate with the formula described in Figure 9 are listed by functional group in Appendix B, Tables VI through XVII.

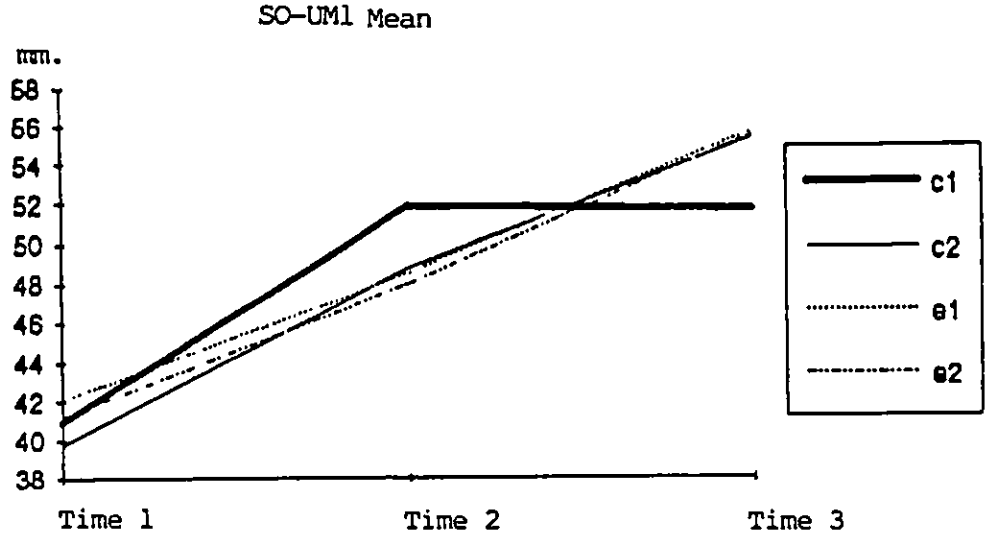
Inferential Statistics Differences among treatment groups were examined by using the analysis of covariance method (ANCOVA) with animal weight as the covariate (see Figure 9). The covariance analysis results for the eight variables which demonstrated significant differences

between treatments are listed in Appendix B, Table XVIII.

Figures 11 through 17 depict plots of means and standard deviations of variables which showed significant differences among graphs. Figures 18 and 19 depict the aforementioned midfacial variables.

Figure 11a Plot of means of SO-UML as a function of time for each rat group.

Figure 11b Plot of standard deviations of SO-UML as a function of time for each rat group.


SO-UM1 Mean
mm.
58
56
54
52
50
48
46
44
42
40
38
Time 1
Time 2
Time 3
c1
c2
e1
e2

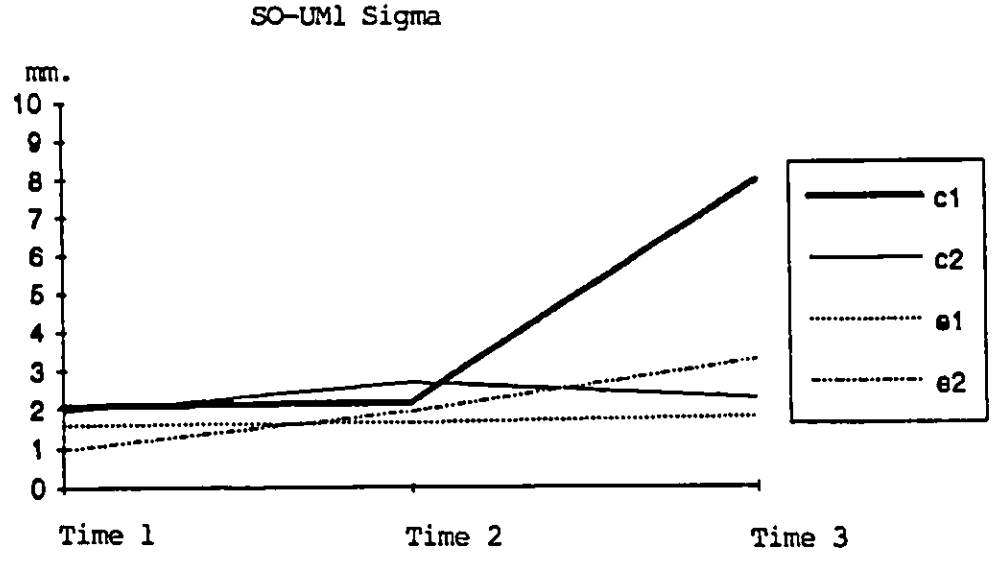
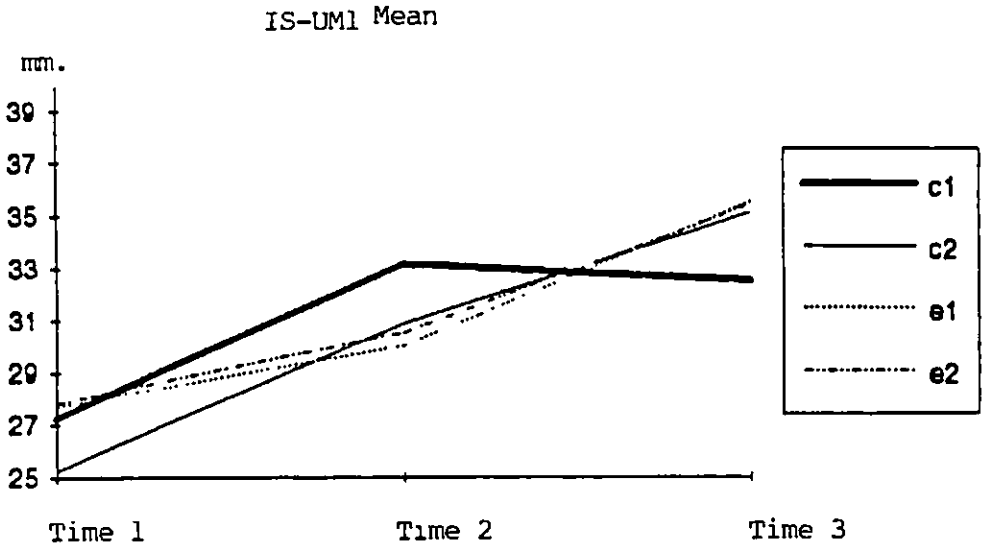

SO-UM1 Sigma
mm.
10
9
8
7
6
5
4
3
2
1
0
Time 1
Time 2
Time 3
c1
c2
e1
e2

Figure 12a Plot of means of IS-UML as a function of time for each rat group.

Figure 12b Plot of standard deviations of IS-UML as a function of time for each rat group.


IS-UM1 Mean
mm.
39
37
35
33
31
29
27
25
Time 1
Time 2
Time 3
c1
c2
e1
e2

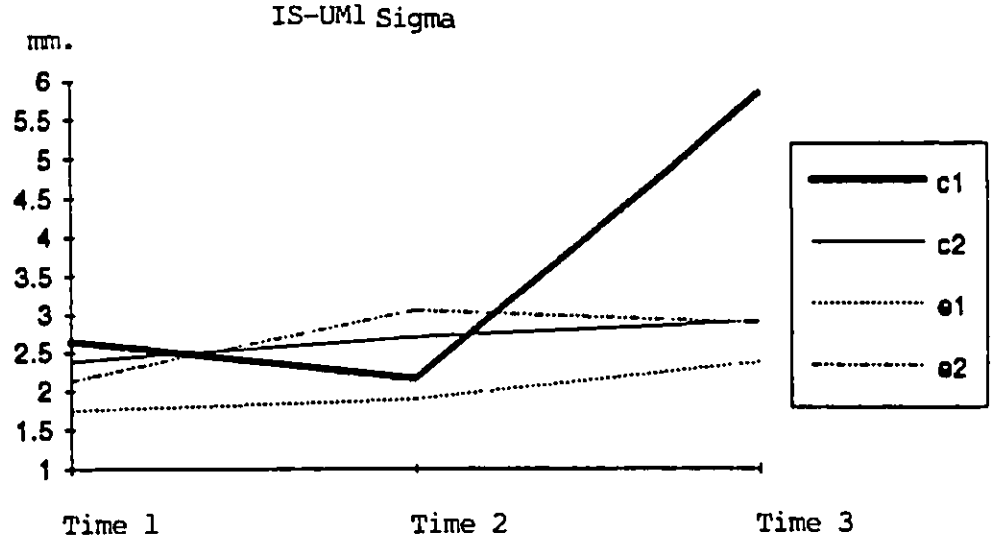
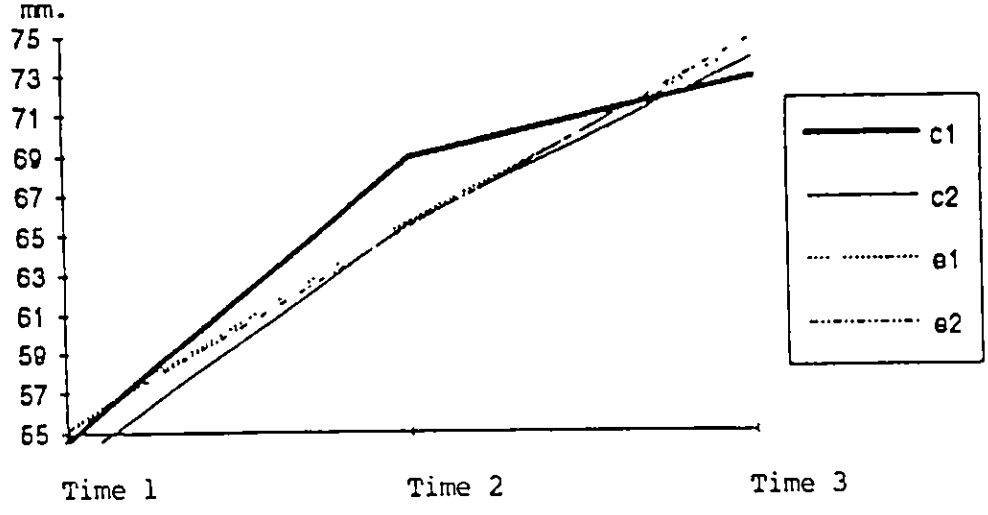

IS-UM1 Sigma
mm.
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
Time 1
Time 2
Time 3
c1
c2
e1
e2

Figure 13a Plot of means of AB-UM1 as a function of time for each rat group.

Figure 13b Plot of standard deviations of AB-UM1 as a function of time for each rat group.

AB-UM1 Mean




AB-UM1 Sigma

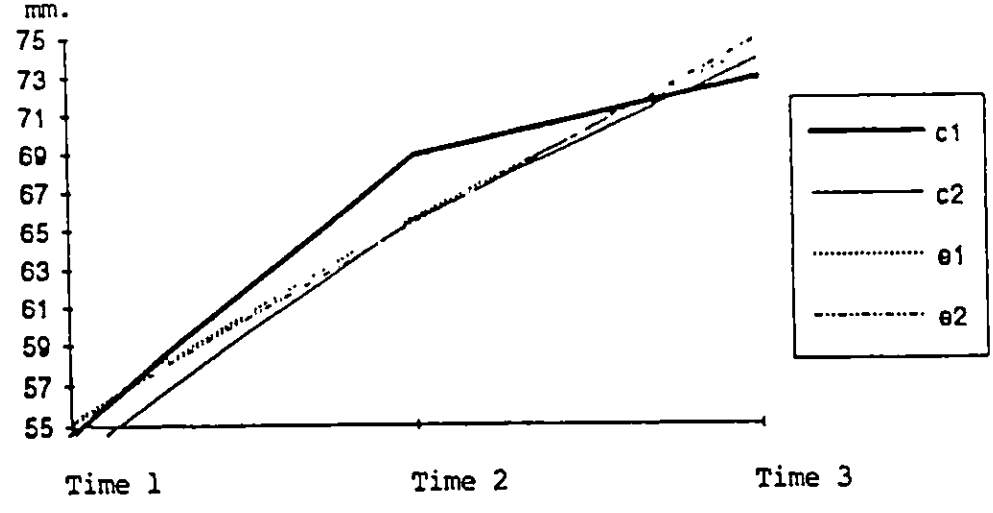
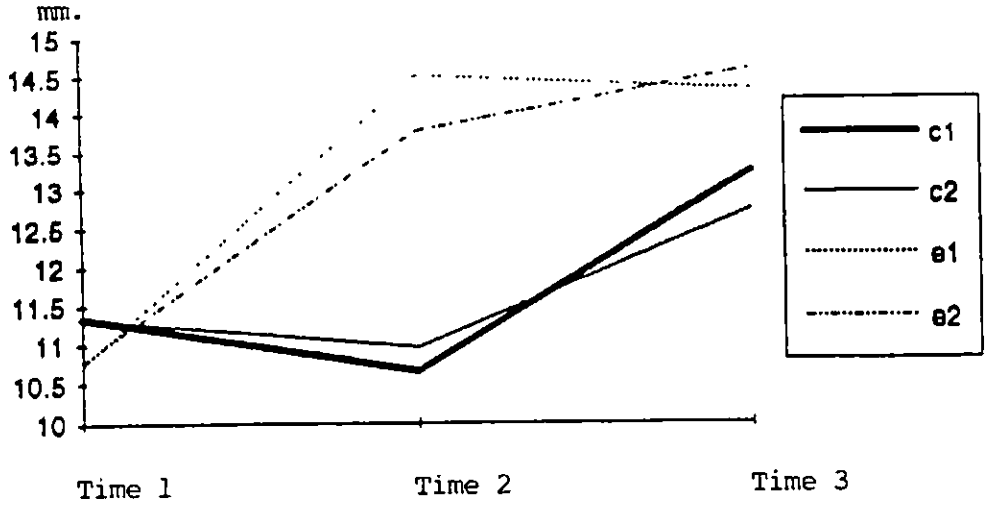


Figure 14a Plot of means of I-N as a function of time for each rat group.

Figure 14b Plot of standard deviations of I-N as a function of time for each rat group.

I-N Mean




I-N Sigma

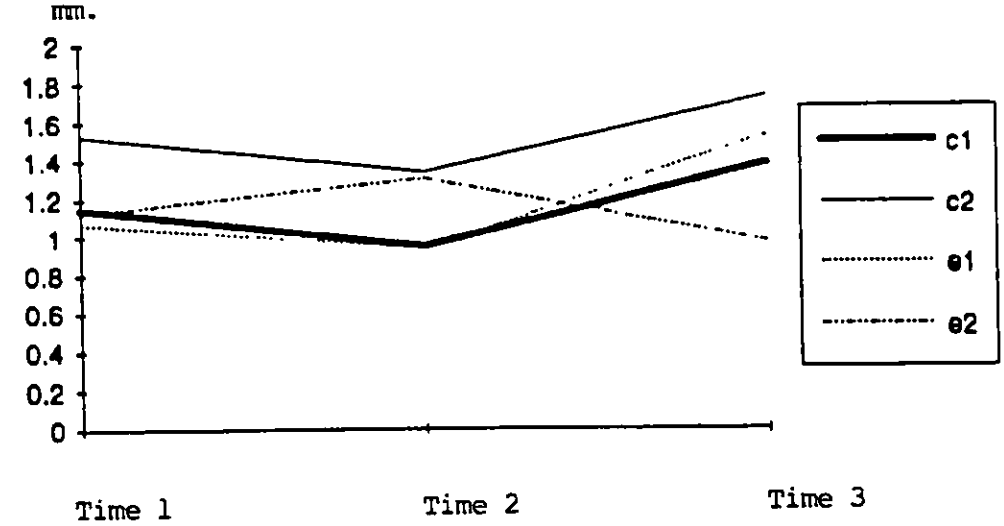
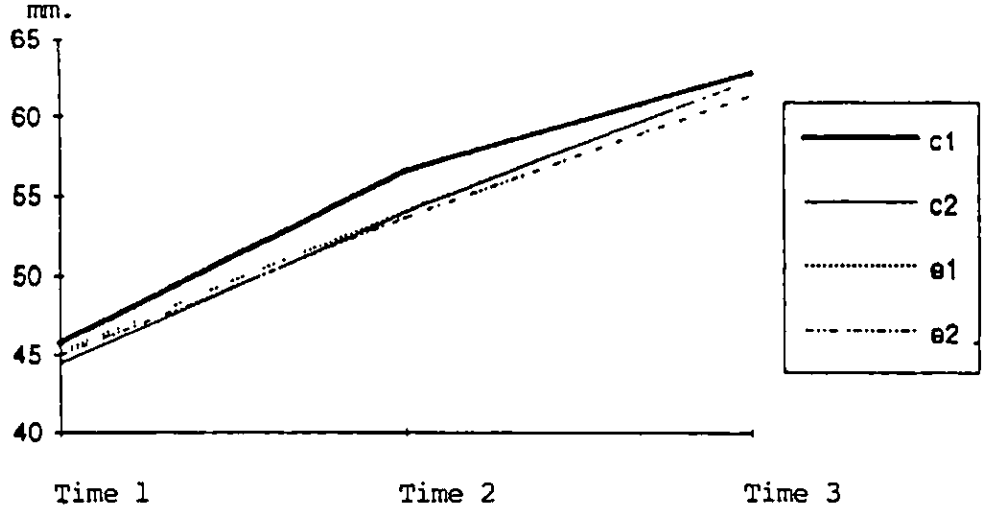


Figure 15a Plot of means of ZGR-ZGL as a function of time for each rat group.

Figure 15b Plot of standard deviations of ZGR-ZGL as a function of time for each rat group.

ZGr-ZGl Mean




ZGr-ZGl Sigma

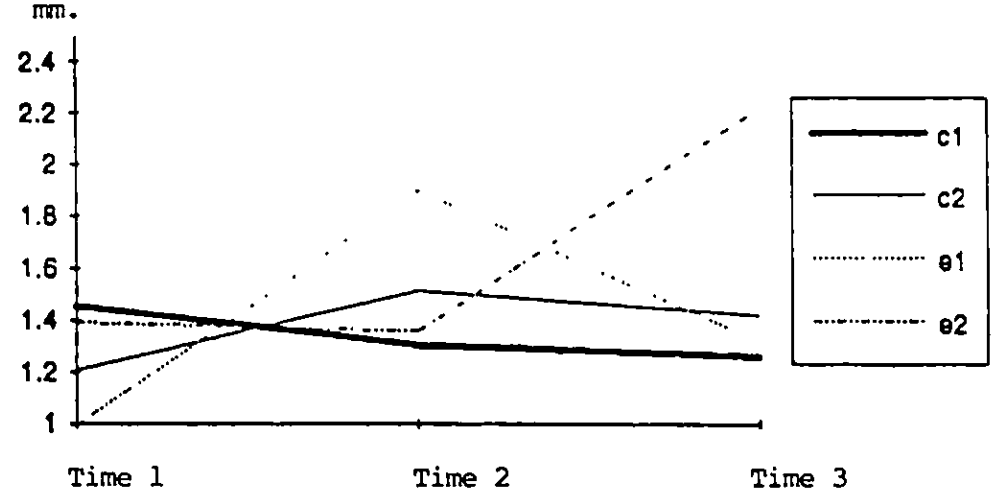
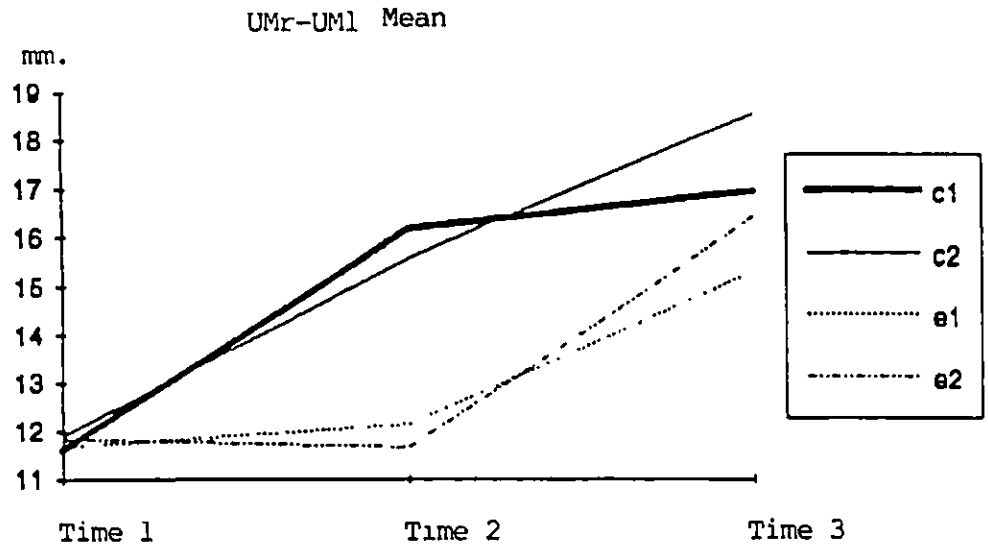


Figure 16a Plot of means of UMR-UML as a function of time for each rat group.

Figure 16b Plot of standard deviations of UMr-UMl as a function of time for each rat group.


UMr-UMl Mean
mm.
19
18
17
16
15
14
13
12
11
Time 1
Time 2
Time 3
c1
c2
e1
e2

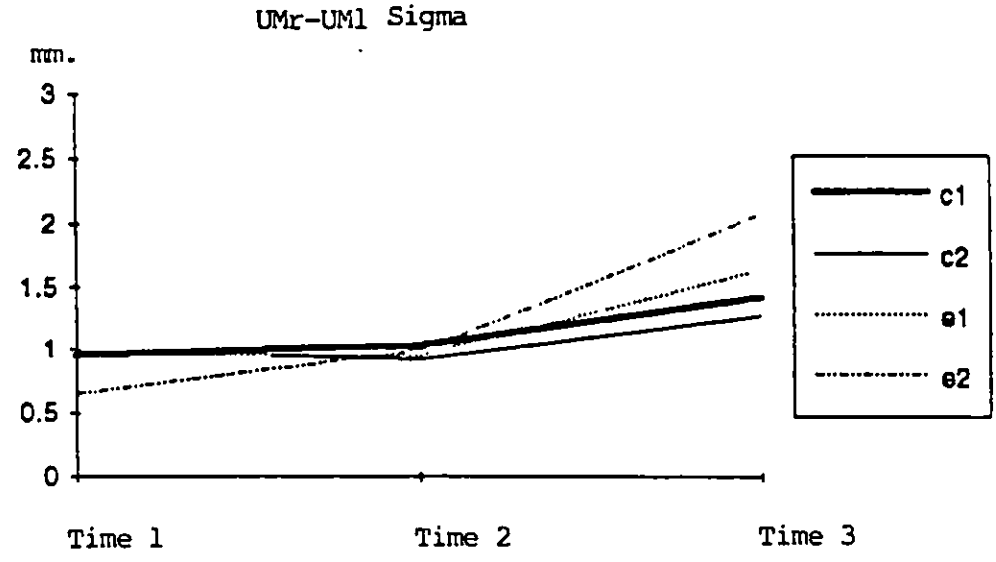
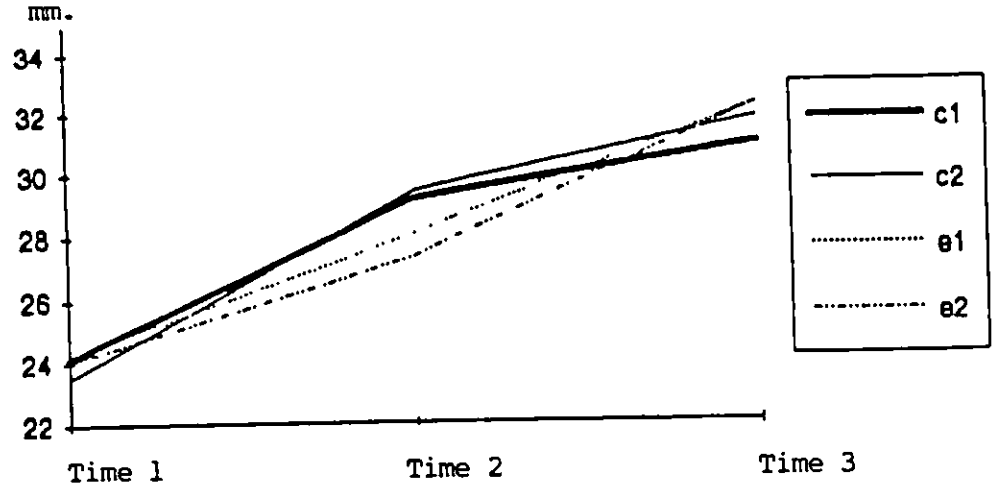

UMr-UMl Sigma
mm.
3
2.5
2
1.5
1
0.5
0
Time 1
Time 2
Time 3
c1
c2
e1
e2

Figure 17a Plot of means of MXr-MXl as a function of time for each rat group.

Figure 17b Plot of standard deviations of MXr-MXl as a function of time for each rat group.

MXr-MXl Mean




MXr-MXl Sigma

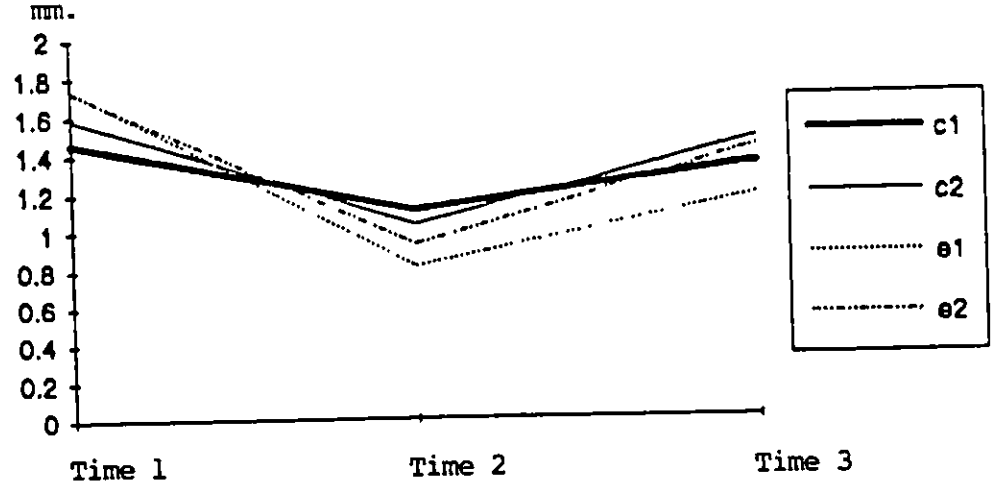
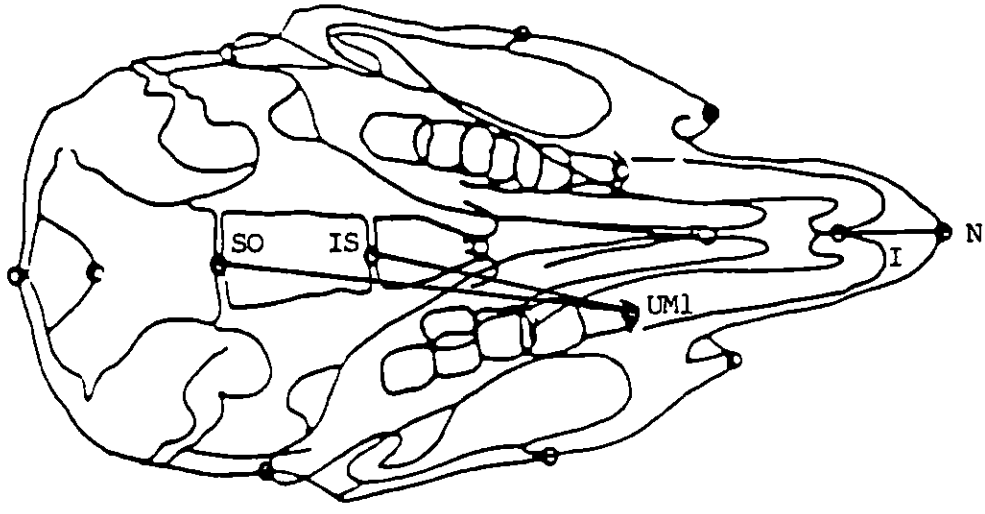


Figure 18 Significant Variables (anteroposterior measures)


SO
IS
N
I
UM1

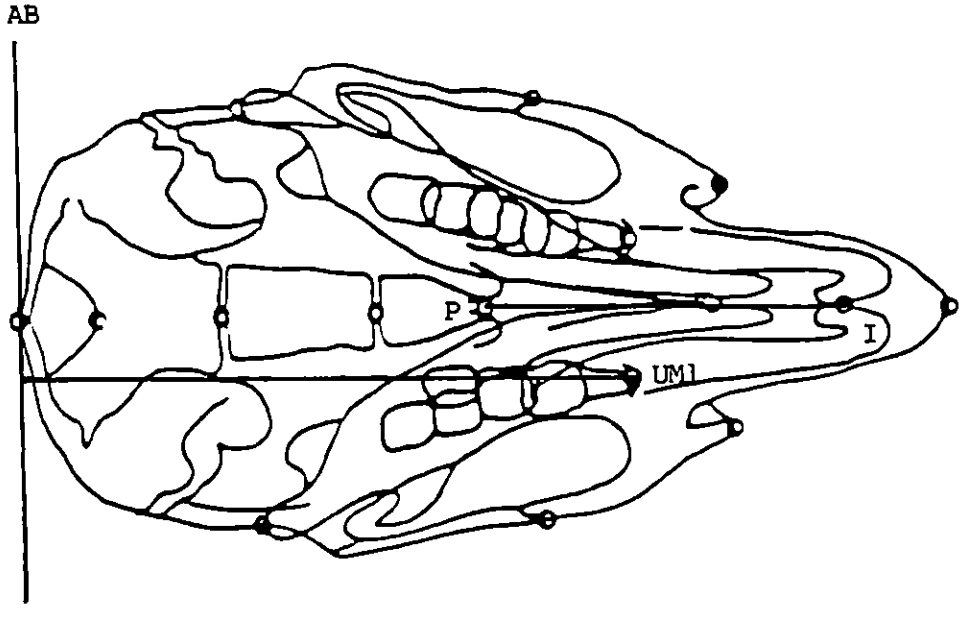
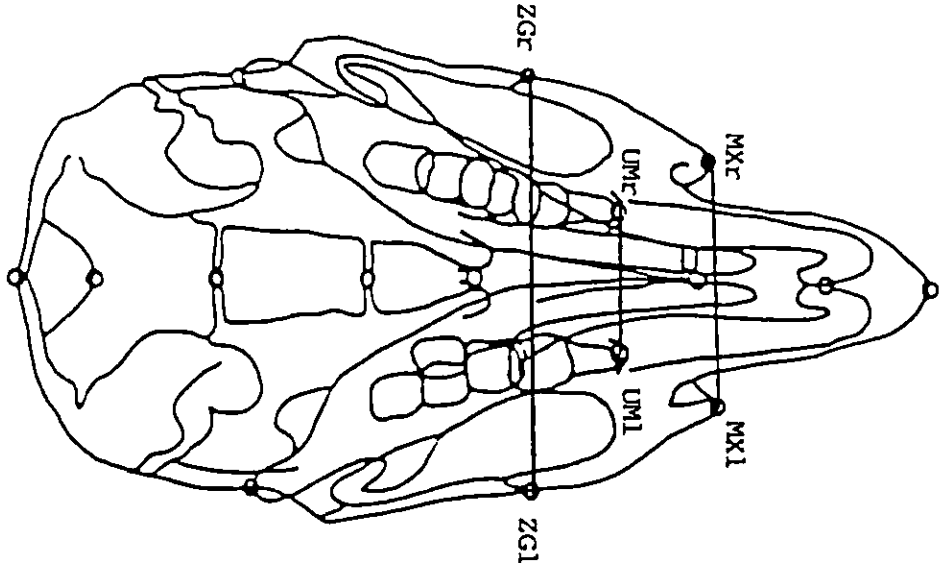

AB
P
I
UM1

Figure 19 Significant Variables (transverse measures)



## DISCUSSION

The objective of this investigation was to examine the maxillary growth in the Sprague Dawley rat during and after passive restraint of the maxillary complex. A schematic representation of the experimental design is illustrated in Figure 4. Animal age at the start of the experiment was twenty days. This age corresponds to an age of nine to ten years in human subjects (Baer et al., 1984; Stutzman and Petrovic 1985). The experimental time period also encompasses the equivalent of the mixed dentition phase of development which has been suggested to be the most susceptible to environmental factors that might limit transverse maxillary growth (Fletcher 1975; Brickbauen 1984; Hannuksela 1967; Bresolin 1984). A passive restraint appliance was bonded to maxillary molars of rats belonging to the experimental groups for three weeks in order to limit transverse maxillary growth. The forty-first day after birth, when the restraint phase of the experiment was ended is analogous to age twelve or thirteen in human subjects (Stutzmann and Petrovic 1977).

Following the removal of the restraining appliances, both experimental and control groups were divided into two subgroups. In one subgroup ($E_1$, $C_1$) maxillary molars were

totally reduced, while in the other subgroup ($E_2$, $C_2$) maxillary molars were left intact and dental interferences were eliminated by reducing the mandibular molar cusps. Unrestrained growth was allowed to take place for all subgroups for four more weeks (physiologic rebound phase). The sixty-ninth day after birth, when the animals were sacrificed, is analogous of sixteen to seventeen years of age in human subjects.

This experimental design facilitates the examination of the degree of input that intrinsic growth potential and environmental factors have on the transverse maxillary growth. During the restraint phase of the experiment an effort was made to override the intrinsic potential for maxillary transverse growth using a controlled environmentally imposed factor (restraint appliance) in the experimental group. Comparison between experimental and control groups during the restraint phase of the experiment demonstrated the effect of mechanical restraint on the genetic potential for transverse maxillary growth. It was thought that during the physiologic rebound phase lateral tongue forces against the lingual surface of maxillary molars might influence growth rate. Therefore, the experimental design included elimination of the clinical crowns of maxillary molars in half the control ($C_1$) and half the experimental ($E_1$) animals.

By using a block design, the relative effects of environmental (mechanical restraint) and genetic factors on transverse maxillary growth during the physiologic rebound phase, could be studied. By comparing experimental versus control groups during the physiologic rebound phase, we can determine if the growth rate is different following the restraint phase. By comparing differences among subgroups, we can detect the amount of input that functional matrices (Moss 1969) and mastication forces (Vinkka 1989) have in the transverse maxillary growth. The results of this study will be dicussed according to the block design as follows:

A) CHANGES IN TRANSVERSE DIMENSION (SNOUT WIDTH)

B) CHANGES IN VERTICAL DIMENSION (SNOUT HEIGHT)

C) CHANGES IN ANTEROPOSTERIOR DIMENSION (SNOUT LENGTH)

A) CHANGES IN THE TRANSVERSE DIMENSION

Variables significantly different between groups and among subgroups, representing changes in transverse dimension were

(I) UMr-UMl, (II)ZGr-ZGl, (III)MXr-MXl

UMr-UMl was measured both cephalometrically and directly from dental impressions. The remaining variables were measured only on the cepholometric radiograph.

(I) UMr-UMl. The variable UMr-UMl represents maxillary dental arch development. Bar line plots for the mean and

standard deviation of maxillary dental arch width measured from the dorsoventral radiographs (see Figures 16a, 16b) are parallel with the ones measured from dental impressions (see Figures 10a, 10b). Differences between groups and among subgroups for the variable UMr-UMl are exagerated in the bar line plots of measurements taken from dorsoventral radiographs due to technical enlargment during tracing (3X). The results of the same variable (UMr-UMl) measured in two different ways varyfies the reliability of the cephalometric technique. Bar line plots in Figures 10 and 16 for the mean and standard deviation demonstrated the following:

During the restraint phase the rate of increase in dental arch width for the control group was gradual throughout the restraint phase of the experiment. In the experimental group the rate of increase in maxillary arch width during the restraint phase was minimal. These findings indicate that the intrinsic potential for transverse growth can be overridden by environmentally imposed factors (palatal restraint appliance).

During the physiologic rebound phase increases in maxillary dental arch width were slower for the control subgroups with maxillary molars reduced ($C_1$) and did not achieve the same growth potential as

control animals with molars intact ($C_2$). This indicates that an intact maxillary dention is necessary for normal maxillary growth. The standard deviation for subgroup $C_2$ was greater than $C_1$. One possible explanation for the increased variability is that the influence of the functional matrix on transverse arch development shows more individual variability among different rats.

Differences between the experimental subgroups ($E_1$ and $E_2$) were identical to those observed for control subgroups ($C_1$, $C_2$). The $E_1$ transverse dental arch development was reduced compared with the $E_2$ subgroup. The similarity among subgroups supports the previous finding that an intact dentition is necessary for normal tranverse arch development.

Comparison between experimental and control animals by subgroups ($C_1$, $E_1$) reveals that growth rate in arch width was much higher in subgroup $E_1$. This indicates that, even if the expression of growth is temporarily limited by mechanical restraint, the potential remains and is expressed after the restraining factor is removed. Growth rate was excelerated and width of the maxilla was near normal at the conclusion of the experiment.

Similar to the previously compared subgroups, growth rate in subgroup $E_2$ was higher than that observed in subgroup $C_2$. This difference was presumed to be due to the influence of oral function on the intact maxillary dentition.

In summary, the results from the variable UMr-UMl indicate that experimental animals generally "caught up" to the control animals during the post restraint phase. Those experimental animals with molars intact had greater arch width when compared to animals without teeth. One possible expanation for the observed increase in the amount of rebound growth in animals with teeth is the effect of multiple assurances (Latham and Scott 1970). The combination of local environmental effects (tongue or teeth), with intrinsic growth factors, results in the greatest growth response.

The standard deviation for subgroups $E_2$, $C_2$ was also greater than for subgroups $E_1$, $C_1$ during the physiologic rebound phase. This indicates that animals with no teeth grew slower, but at a more constant rate, compared with animals with intact maxillary teeth. Several possible explanations exist for the aforementioned results. Each of these explanations is based on the principle factors that control transverse maxillary growth.

First, according to the counterpart principle of craniofacial growth (Enlow 1973), the growth of any given facial or cranial part relates specifically to other structural and geometric "counterparts". The counterpart for the maxilla is the anterior cranial fossa. The cranial base is the template upon which the face developes. Growth in the cranial base is due to expansive forces generated by neural growth and due to endochondral growth in the midline of the cranial fossa (spneno-occipital synchondrosis). Expansion of the middle cranial fossa displaces the anterior cranial fossa and the nasomaxillary complex. Thus, according to Enlow, epigenetic factors set the limits for anteroposterior and transverse growth of the anterior cranial fossa. The anterior cranial fossa defines the anatomic limits for its counterpart, the maxilla. In the present experiment no attempt was made to alter the epigenetic limits for transverse growth determined by the anterior cranial base. Therefore, our results are in agreement with Enlow's counterpart analysis which suggests that rebound growth will occur until epigenetic limits are reached.

The second principle factor controlling transverse maxillary growth is the volumetric capacity of the airway (Moss 1969, Enlow 1970). According to the Functional Matrix Theory, the whole nasomaxillary complex developes in

order to fullfil functional demands. One of the most significant functional demands necessary for species survival is airway volumetric capacity. Nasomaxillary growth developes according to the demands placed on it by the "airway". It has been shown that impaired nasal breathing reduces transverse maxillary growth (Hannuksela 1987, Enlow and Cheng 1988). In the present experiment, there was no attempt to interfere with the nasal airway capacity of the animal. However, the appliance did produce an open bite during the restraint phase of the experimental period and may have forced the animals to breath through their mouth. The effect of the change from nasal to oral breathing was not quantitated, but could account for some of the observed variability in post-restraint growth.

Finally, intraoral and perioral local environmental factors control maxillary width development by stimulating growth on the midpalatal suture and bone deposition along the lateral areas of the alveolar ridge. In the young, rapidly growing rat the midpalatal suture is unusual in that it is composed of a secondary type of cartilage on each side of the median line. There are some basic differential biologic features between primary and secondary types of cartilage. In primary cartilages (epiphyseal, spheno-ocipital synchondrosis, nasal septal, etc.) the chondroblasts divide and synthesize intercellular

matrix. In secondary-type cartilages (condylar, coronoid, augular, and in the rat the midpalatal suture), the cells that divide (i.e., the prechondroblasts) are not yet surrounded by cartilaginous matrix. When the secondary-type prechondroblast begins synthesizing, the specific cartilaginous matrix, it usually stops dividing. Emphasis is placed on the following point. In primary cartilages, the cartilaginous matrix seems to isolate the dividing chondroblasts from local factors able to restrain or stimulate the cartilage growth rate, whereas in secondary-type cartilages, the dividing cells are not isolated from the influence of local factors. In other words, local extrinsic factors may modulate (stimulate or restrain) the growth rate of secondary-type cartilages. Experiments conducted since 1968 (Petrovic) and followed later (Stockli and Willert 1971; McNamara et al., 1973; Graber 1975; Komposch 1976) have clearly shown the influence of intrinsic or local extrinsic factors on secondary cartilage morphology. Mohamed (1957) was the first to demonstrate this pleomorphic nature of the rats' intermaxillary suture. According to Mohamed, as early as nineteen days in utero cartilage forms in the suture. However, the appearance of cartilage is transient and is not present at birth. Around the time the first maxillary molars erupt (three weeks), the cartilage is again present. At this time, the suture

presents as a bilateral epiphyseal plate. Later on, at approximately nine weeks, the suture reverts to a syndesmosis. Stutzmann et al., (1983) have shown that function can stimulate cartilage formation in the rat midpalatal suture even after the suture has become a bony-type suture. It is likely that this cartilage can then be stimulated by mastication resulting in increased transverse growth of the maxilla.

The above mentioned studies on the rat midpalatal suture give the following model for the results observed in the present study. During the restraint phase of the experiment, animals in the control groups were growing normally. Transverse growth was taking place by growth in the midpalatal suture and by bone deposition on the lateral areas of the alveolar ridges. In the experimental groups, the restraint appliance had a direct effect on the mid-palatal suture by slowing down the rate of secondary cartilage growth. The precondroblast cells did not progress to the chondroblast stage. In addition, the progenitor cells, from which the precondroblasts originate, started to produce preosteoblasts which matured to osteoblasts and a slow rate of bone formation took place.

Previous experimental work (Hall 1969, 1972, 1978; Stutzmann and Petrovic 1970; Mura 1973) has shown that intermittent rather than constant forces elicit

preferential differentiation of the chondroblasts over osteoblasts.

Vinkka (1989) has suggested that the molars of the rat, by their intermittent masticatory forces are responsible for secondary cartilage formation.

These previous experiments suggest that the restraint appliance used in the present study could have affected midpalatal sutural growth both directly and indirectly. The direct effect was due to mechanical limitation of transverse and maxillary growth. The indirect effect may have been due to the occlusal coverage that the restraint appliance provided for the maxillary molars. Because most of the mastication forces were absorbed by the restraint appliances, these forces could not have a stimulating effect on the secondary cartilage formation and growth at the midpalatal suture.

The restraint appliance also contacted the lateral aspect of the alveolar ridges. This design may have also contributed to the decrease in transverse growth by inhibition bone deposition in this area.

During the physiologic rebound phase, normal function may have stimulated growth in the midpalatal suture. This could occur in the following ways:

1) Maxillary molars were uncovered and intermittent masticatory forces were transmitted through them and acted as a stimulating factor for secondary cartilage growth.

2) The tongue had a direct effect via the teeth on transverse maxillary expansion.

3) Because rats do not have buccal musculature, there was no restraining effect due to buccal musculature to transverse growth.

The following senario is another reason why both subgroups $E_1$ and $C_1$ ($E_1$, $C_1$ maxillary molars reduced) did not develope the same palatal width seen in subgroups $E_2$ $C_2$. The restraint appliance occupied the palatal vault of the animals' oral cavity. This induced an open bite in the experimental animals. Because of the position of the appliance, it is possible that restrained animals ($E_1$, $E_2$), developed a lower tongue position and were forced to breathe through their mouth. Upon removal of the restraint appliance, some of the animals may have retained these alterations of normal function (mouth breathing - low tongue position). Dental compensations during the experimental period (over-eruption of upper and lower incisors due to induced open bite) may also have helped retain these abnormal functions throughout the physiologic rebound period. If a lower tongue position was retained, this would lead to decreased response during the physiologic rebound phase.

Differences in oral function during the rebound phase may explain the low rate of transverse growth observed in rat #9 during the physiologic rebound phase. This animal showed very little "catch up" growth even though the

maxillary molars remained intact.

Another unexpected finding was the individual variability in response to transverse maxillary restraint in the experimental group. Even though the cause of the transverse deficiency was controlled, Sprague Dawley rats are an inbred strain and thus have similar genetic information, different rats responded differently. This suggests that the post-restraint response is not solely under genetic influence. Rather, environmental or epigenetic factors must be responsible for a portion of the observed variability. Because variability in "treatment response" was observed in this controlled experimental animal model, clinicians can expect greater variability in human "catch up growth" because often the precise etiology of transverse maxillary deficiency is unknown and human genetic information is not uniform.

II. Bizygomatic Width (ZGl-ZGr)

The variable ZGr-ZGl which measures bizygomatic width was also significantly different between groups (E, C). Bar line plots of means of ZGr-ZGl (see Figure 15) demonstrated the following:

There was very little change between experimental and control groups during the restraint phase of the experiment.

However, during the physiologic rebound phase, the control subgroup without teeth ($C_1$) demonstrated decreases in transverse growth rate of the bizygomatic width during the physiologic rebound phase compared to the control group with teeth ($C_2$).

The difference between experimental subgroups was not as great as between the control subgroups. Comparison of subgroups $E_1$ vs. $C_1$ and $E_2$ vs. $C_2$ did not show any significant difference in bizygomatic width during the physiologic rebound phase for these subgroups.

Zygomatic arch growth in the rat correlates with growth of the masseter and temporal muscles (Bear et al., 1984). The masseter originates at the zygomatic arch and the temporal muscle lies beneath the arch. In this experiment altering oral function by removing the maxillary molars presumably altered masticatory muscle activity tending to an adaptive change in skeletal morphology. Although the appliance produced a transient open bite in the rats during the restraint phase, there was no apparent bizygomatic width between experimental and control groups. Musculature adaptation should also have had an effect on periosteal growth of bone into areas of muscle attachments (Oyen 1982). Our results did not demonstrate differences between control and experimental groups during the restraint or physiologic rebound phase. This may be

because the amount of change was too small t be detected by our methods. Alternatively, it may be that only a dramatic change in function (teeth/no teeth) effectively causes a change in form.

III. Bimaxillary Width (MXr-MXl)

The variable MXr-MXl represents maxillary width development. The analysis of covariance (ANCOVA) for the cephalometric measurement MXr-MXl (maxillary width) showed a significant difference among groups. Bar line plots in Figure 17 for the mean and the standard deviation demonstrated the following:

During the restraint phase, the rate of increase in maxillary width for the control groups was gradual. In contrast, the experimental group showed a slower increase in maxillary width during the restraint phase.

During the physiologic rebound phase, the control subgroup with maxillary molars reduced [$C_1$] showed an increase in maxillary width that was much slower during the physiologic rebound phase and did not achieve the same growth potential compared with the control subgroup with teeth ($C_2$).

Differences among experimental subgroups ($E_1$, $E_2$) were similar to those observed for the control subgroups ($C_1$ $C_2$).

Comparison between subgroups $C_1$, $E_1$, revealed that growth rate in maxillary width was much higher in subgroup $E_1$ during the physiologic rebound phase.

Similar to previously compared subgroups, comparison between $C_2$ and $E_2$ subgroups revealed that the growth in subgroup $E_2$ accelerated during the physiologic rebound phase and reached the same potential of growth as the $C_2$ group.

The same concepts discussed earlier regarding the transverse alveolar development apply to maxillary skeletal development. However, it is interesting to note that, although the types of effects were similar, the degree of effects was more pronounced at the alveolar level. This is probably due to the fact that morphologic boundaries have a greater influence on skeletal dimensions. This may explain why some types of human transverse maxillary deficiency can be treated by archwire expansion and others respond more favorably to rapid or slow palatal expansion.

B). CHANGES IN VERTICAL DIMENSION

Visual observation of initial, intermediate and final dental impressions revealed the following:

During the restraint phase palatal depth gradually increased in the control groups throughout the experiment.

The experimental group showed a dramatic increase in palatal depth during the restraint phase creating the typical high arch palate normally associated with human transverse arch deficiency.

During the physiologic rebound phase, the dental modification in the control subgroup ($C_1$) did not seem to have any effect on palatal depth.

In the experimental subgroups there was a decrease in palatal vault depth during the physiologic rebound phase. The decrease observed in the subgroup without teeth ($E_1$) was smaller than that observed for the subgroup with teeth ($E_2$).

Comparison of experimental and control subgroups showed a decrease in palatal depth for both experimental subgroups during the physiologic rebound phase.

Scotese (1981), using the rabbit as an experimental animal, observed similar changes in palatal depth. He reported that palatal depth in the experimental groups increased dramatically during the restraint phase and, when the appliances were removed, there was a decrease in the palatal depth with regression towards normality. It has also been demonstrated in human subjects that factors restraining transverse maxillary growth also cause an increase in palatal vault depth. (Larson 1967; Brickbauer

1988). Vertical development of the maxilla was presumably not restrained by our appliance. Therefore, one can assume that downward palatal movement and remodeling was normal. If growth in the vertical dimension proceeds normally while the transverse arch dimension is limited, a deepening of the palatal vault would result. The observed deepening of the palatal vault in the restrained group could also result from the redirection of maxillary alveolar growth in a vertical direction. If the genetic potential for maxillary growth could not be expressed in a transverse direction due to the restraint appliance a compensatory vertical increase could have resulted. This intertissue tension could also work as a negative feedback mechanism to slow down midpalatal suture growth. Therefore, transverse maxillary deficiency may be accomanied by increased maxillary vertical development. This may explain the relationship between transverse deficiency and increased lower vertical facial height often seen in human subjects. Further investigation of this relationship between transverse and vertical arch development will be explored in future studies.

C) CHANGES IN ANTEROPOSTERIOR DIMENSION

The cephalometric analysis used was designed to assess compensatory changes that occurred in both the anteroposterior and transverse dimensions of the maxillary

complex. Previous experimental work (Scotese 1981) showed that rabbits (during the restraint phase) developed a longer snout in comparison to the control animals. Scotese suggested that this increase in length was a compensatory response to inhibition in the transverse dimension. In the present experiment, variables representing anteroposterior changes (I-N, P-I, AB-UM1, SO-UM1, IS-UM1) showed statistically significant differences between experimental and control animals. Studying the bar line plots of the means of these variables, (See Figures 11 through 14) demonstrates that variable I-N (anterior nasal position) showed the greatest decrease.

A more detailed analysis (See Figure 14) of variable I-N revealed the following:

During the restraint phase, the experimental group showed a significant increase in anterior nasal position.

During the physiologic rebound phase, there was a constant increase for both control subgroups. However, the subgroups with maxillary molars totally reduced ($C_1$) were slightly longer than subgroups with teth ($C_2$).

During the physiologic rebound phase of the experiment, both experimental subgroups showed a decrease in anterior nasal position. Growth rate in

the subgroup with maxillary molars totally reduced ($E_1$) showed a larger decrease in anterior nasal growth rate during the physiologic rebound phase.

During the physiologic rebound phase there was a constant increase in anterior nasal position for the control subgroup $C_1$ whereas the experimental subgroups $E_1$ showed a decrease in anterior nasal growth rate. This combination of responses between control and experimental groups resulted in no significant difference in anterior nasal position between the groups at the end of the experiment ("reverse" catch up growth).

Changes among the subgroups $C_2$, $E_2$ during the physiologic rebound period were identical with those seen for subgroups $C_1$ and $E_1$.

Surprisingly, variable P-I which represents the overall palatal length, showed no differences among control and experimental subgroups during any phase.

Increased anterior nasal position for the experimental group during the restraint period could be explained as a result of altered function due to the restraint appliance. The occlusal coverage of the restraing appliance, as previously discussed, induced an anterior open bite and increased the vertical height of the lower third of the animal's face. Labionarinary muscles (perioral musculature

and muscles attached to the nose) in experimental groups were much more active during the restraint period compared with analogous musculature of the control group. This is suggested because in the experimental group, perioral musculature during swallowing had to be stretched more than normal in order to provide a satisfactory seal for the oral cavity due to induced open bite. This increased tension in the perioral musculature may have stimulated growth of the snout in the experimental group. During the physiologic rebound phase removal of the restraint appliance allowed the animals to swallow normally. A change in functional demands and decreased tension in perioral musculature may have led to a decreased rate of forward nasal growth.

Regression towards normality ("reverse" catch up growth) of initially increased forward nasal growth can also be inferred from the counterpart principles of Enlow (1975). According to Enlow, the anterior cranial fossa is the template for the nasomaxillary complex. That defines the borders of the growth compartment occupied by the nasomaxillary complex. As previously stated, these growth boundaries can be violated by environmental factors. If the overriding extrinsic factors are removed, the normal balance of the functional and intrinsic forces work to greater or lesser degrees to return skeletal parts to their "normal" positions.

A study of human fetuses led Latham (1970) to formulate the hypothesis that forward growth of the nasal septal cartilage pulls the premaxilla forward via the septopremaxillary ligament. Based on Latham's hypothesis, an analagous increase in overall palatal length should have been observed in our animals. In the present study there was no evidence of differences in overall palatal length between groups. Our findings agree with those of Stutzmann and Petrovic (1975). After resection of the septomaxillary ligament in the young rat they concluded that a stimulating action on the growth of the premaxillomaxillary suture is not caused by septopremaxillary ligament pull.

Increased tension in the perioral muscalature during the experimental phase of the experiment should also have had some effect on forward growth of the premaxilla. Reports on experimental investigations in young rats on the mechanisms of action of the Frankel FRIII appliance (Stutzmann 1973) have suggested that the superior labial frenum and the labionarinary muscles are the biologic receptors for the so-called superior retrolabial "lip pads". Stretching of the labionarinary muscles presumably stimulates sagittal growth of the maxilla. In the present study, similar observations were not documented.

The variables SO-UM1, IS-UM1, AB-UM11 all represent anterior maxillary dental development. Bar line plots of

means of these vaiables (see Figures 11 through 13) are very similar and they indicate the following:

During the restraint phase there was no significant difference in anterior maxillary dental development between control and experimental groups.

During the physiologic rebound phase the control subgroups ($C_1$, $C_2$) showed a significant difference in anterior maxillary dental development. Subgroup $C_1$ (maxillary totally reduced molars) showed a decrease, compared with $C_2$ (teeth intact).

No other differences among subgroups was seen during the physiologic rebound phase. ANCOVA for the aforementioned variables indicated that a statistically significant difference existed only on the left side of the animal's face. Although skeletal and dental asymmetries are a common clinical finding in orthodontic patients, the etiology of these asymmetries is not know. It is possible that asymmetric development occurs in response to factors which restrain growth in one dimension. This hypothesis would be supported by our data. It is also interesting to note that, once established, the asymmetry remained during the entire experimental period. Another possible explanation for the observed asymmetries is unequal reduction of the right and left maxillary molars during dental modification. This was observed in rat #2, seen in

Plates 8a,8b. The difference in molar height between right and left sides could have created an asymmetry by increasing mastication forces on one side of the animal's face. Regardless of the extrinsic factor that caused the asymmetry, it is important to note that asymmetries do occur: This is important clinically because asymmetric orthodontic mechanotherapy is more complex. This finding suggests that orthodontists treating transverse maxillary deficiency should be aware of underlying asymmetries that may modify their treatment plan.

The changes in function, (e.g. mastication) caused by the restraint appliance might be expected to have an effect on the mandible. However, no differences were observed between control and experimental animals. In the case of the mandible, there are practical difficulties in orienting the mandible in sacrificed animals with the consistency needed to produce cephalometric radiographs of diagnostic quality. In addition, lateral radiographs may reveal mandibular changes that were not seen on the dorsoventral view. Therefore, no conclusions about the restraint appliance effects on mandibular growth and form can be made from this study.

In addition, cephalometric analysis revealed no significant differences between treatment and control groups for measures that represent the cranial base. This

was expected because cranial base dimensions are established early in postnatal life. Therefore, they are not susceptible to modification by external stimuli during the time period studied.

## SUMMARY AND CONCLUSIONS

Compensatory responses to experimentally induced alterations of craniofacial structures by the application of active or passive force systems has received little attention in the literature. Results of previous studies (Tuenge 1974, Henry 1976, Scotese 1981) indicate that post restrained compensatory responses are varied.

The present study was performed to examine the nature of compensatory responses during and after passive, tranverse restraint of the maxillary complex of young growing rats. The sample consisted of thirty-nine rapidly growing female Sprague Dawley rats. The sample was initially divided into experimental (21 rats) and control groups (18 rats). A passive restraining appliance was placed in the experimental group for three weeks. The restraining appliance was removed after twenty-one days and physiologic rebound was studied during the subsequent four weeks. At the end of the restraint phase the experimental and control animals were subdivided into two groups. Subgroups in both experimental and control animals, ($E_1$, $C_1$) received total reduction of maxillary molars. The rationale behind maxillary molar reduction was to eliminate

lateral tongue pressure and mastication forces, which are factors believed to stimulate transverse maxillary growth. Subgroups in the experimental and control animals, ($E_2$, $C_2$) recieved reduction of only the tips of the lower molar crowns. This was done to eliminate cusp interference during the rebound phase.

Data was collected from all groups and analyzed using two methods.

1. Dental impression measurements which assessed structural compensatory responses of the maxillary complex;

2. Cephalometric measurements which assessed the compensatory responses of surrounding structures in the anteroposterior and transverse dimensions.

Results of the present study may be summarized as follows:

1) Dental impression measurements, and visual observations.

   a) Maxillary dental arch width increase was minimal to none ($p \leq 0.0117$) during the restraint phase of the experiment, while during the physiologic rebound phase, there was regression towards normality.

      Animals whose maxillary dentition remained intact expressed in full their potential for transverse maxillary growth (during the rebound phase). Animals with totally reduced maxillary molars did not totally overcome the effects of the restraint during the rebound phase.

   b) Palatal vault depth was increased in the experimental animals during the restraint phase. During the physiologic rebound phase, there was regression towards normality. Palatal vault depth decrease was slower for animals with reduced maxillary molars.

2. Cephalometric Measurements

a) Maxillary dental arch width was significantly ($p \leq 0.0001$) different between treatments. Changes between groups during the experimental phases were similar to measures taken from the dental impressions.

b) Maxillary skeletal width (MXl-MXr) was significantly reduced ($P \leq 0.0112$) for both experimental groups during the restraint phase of the experiment. During the physiologic rebound phase there was an acceleration in maxillary transverse growth and both experimental groups reached the same potential of growth as the control groups.

Transverse growth rate in the experimental group with retained maxillary molars ($E_2$) was slightly increased compared with the experimental group which had maxillary molars reduced ($E_1$).

c) Bizygomatic width was significantly ($p \leq 0.0128$) reduced in animals with reduced maxillary molars ($E_1$, $C_1$) but no significant difference could be demonstrated between control and experimental groups.

d) Anterior nasal position was significantly increased ($p \leq 0.0001$) in experimental animals during the restraint phase of the experiment. During the physiologic rebound phase, anterior nasal position advancement was slowed down. Dental modifications in groups did not seem to play a crucial role to anterior nasal position.

e) Anterior maxillary dental development on the left side was significantly decreased ($p \leq 0.089$) for rats that had maxillary molars reduced, while there was no difference between control and experimental groups during the different experimental phases.

Based on the above results, the following conclusions can be drawn.

1) An intact maxillary dentition is necessary for

maximum transverse development of the maxilla.

2) On average, the constricted maxilla rebounds during the post-restraint phase. During this phase, growth rate is accelerated for the experimental group and there was no significant difference between control and experimental groups in the final width of the maxilla.

3) Even with an experimental animal population, there was considerable variability in individual response during the rebound phase.

4) Modification of the maxillary dentition caused noticeable asymmetry in the snout of the rat.

5) In addition to transverse deficiency, an increase in A-P length of the snout was observed for the experimental group.

Based on these conclusions, the following clinical implications can be drawn:

1) Because transverse deficiencies are often accompanied by vertical and A-P changes as well as asymmetries, clinicians should plan treatment based on a three dimensional diagnosis. 2) Human subjects will show greater variability in rebound (catch up growth) because of a more varied genetic pool, dental interferences, and the multifactorial etiology of transverse arch deficiencies.

# APPENDIX A

## Animal weight over time

TABLE V

ANIMAL WEIGHT OVER TIME
(grams)

| EXPERIMENTALS | | | | CONTROLS | | | |
|---|---|---|---|---|---|---|---|
| | $E_1$ group N = 10 | | | | $C_1$ group N = 9 | | |
| | T1 | T2 | T3 | | T1 | T2 | T3 |
| # 2 | 51.0 | 178 | 277 | # 1 | 53.0 | 182 | 255 |
| # 6 | 59.0 | 173 | 261 | # 4 | 46.0 | 176 | 254 |
| # 7 | 53.5 | 162 | 247 | #13 | 57.5 | 177 | 243 |
| #16 | 54.0 | 170 | 254 | #22 | 58.0 | 175 | 263 |
| #20 | 58.5 | 187 | 248 | #25 | 51.5 | 179 | 265 |
| #27 | 53.5 | 160 | 250 | #34 | 53.0 | 173 | 250 |
| #30 | 56.0 | 158 | 227 | #41 | 58.0 | 193 | 267 |
| #40 | 61.0 | 200 | 270 | #44 | 56.5 | 194 | 288 |
| #42 | 55.0 | 181 | 259 | #47 | 59.0 | 209 | 288 |
| #43 | 51.0 | 167 | 260 | | | | |
| Average | 55.3 | 173 | 258 | | 54.7 | 184 | 263 |
| | $E_2$ group N = 11 | | | | $C_2$ group N = 9 | | |
| | T1 | T2 | T3 | | T1 | T2 | T3 |
| # 3 | 52.0 | 156 | 266 | # 5 | 46.0 | 158 | 233 |
| # 8 | 47.0 | 141 | 223 | #11 | 46.5 | 165 | 241 |
| # 9 | 55.5 | 144 | 213 | #15 | 55.5 | 169 | 240 |
| #12 | 54.5 | 145 | 257 | #21 | 56.0 | 170 | 251 |
| #19 | 60.0 | 178 | 276 | #26 | 54.5 | 169 | 256 |
| #23 | 56.0 | 168 | 251 | #32 | 49.0 | 160 | 257 |
| #24 | 52.0 | 140 | 241 | #33 | 43.5 | 140 | 225 |
| #28 | 48.0 | 140 | 233 | #37 | 54.0 | 178 | 250 |
| #29 | 48.0 | 159 | 246 | #39 | 55.0 | 177 | 257 |
| #45 | 58.0 | 164 | 270 | | | | |
| #46 | 54.0 | 152 | 231 | | | | |
| Average | 53.7 | 154 | 246 | | 51.1 | 165 | 246 |

# APPENDIX B

## Means and standard deviations of measured variables over time

TABLE VI

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING ANTEROPOSTERIOR CHANGES IN MIDFACIAL BONY SIZE OR DISPLACEMENT OF THE MIDFACIAL COMPLEX FOR EACH RAT GROUP AT TIME 1

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| MXr-N | 32.0 | 1.9 | 30.7 | 2.0 | 31.9 | 1.7 | 32.8 | 2.3 |
| MXl-N | 31.9 | 1.5 | 30.3 | 2.3 | 32.5 | 1.8 | 32.2 | 2.4 |
| SO-UMr | 40.8 | 2.2 | 40.4 | 2.1 | 41.8 | 2.0 | 41.7 | 1.6 |
| *SO-UMl | 40.9 | 2.1 | 39.7 | 1.9 | 42.1 | 1.6 | 41.2 | 1.0 |
| IS-UMr | 27.0 | 3.0 | 26.4 | 2.4 | 27.5 | 2.2 | 28.4 | 2.1 |
| *IS-UMl | 27.2 | 2.6 | 25.2 | 2.4 | 27.7 | 2.8 | 27.8 | 2.1 |
| *P-I | 43.9 | 1.9 | 42.0 | 1.5 | 44.8 | 1.7 | 44.6 | 1.4 |
| BA-MXr | 65.1 | 2.1 | 64.6 | 1.4 | 65.6 | 1.2 | 64.4 | 1.4 |
| BA-MXl | 66.3. | 2.5 | 65.9 | 1.3 | 65.8 | 1.2 | 65.2 | 1.4 |
| AB-ZGr | 43.4 | 4.3 | 44.2 | 3.7 | 44.2 | 3.5 | 44.9 | 4.0 |
| AB-ZGl | 43.8 | 2.3 | 44.0 | 2.8 | 43.5 | 3.2 | 45.1 | 2.1 |
| AB-UMr | 54.7 | 2.1 | 54.2 | 2.5 | 55.2 | 2.6 | 55.7 | 2.1 |
| *AB-UMl | 54.5 | 2.4 | 53.3 | 2.4 | 55.3 | 2.1 | 55.1 | 1.5 |
| AB-MXr | 64.2 | 2.1 | 63.9 | 1.5 | 64.7 | 1.3 | 63.4 | 1.4 |
| AB-MXl | 64.9 | 2.6 | 64.5 | 1.3 | 64.3 | 1.2 | 63.9 | 1.4 |
| SO-MXr | 51.2 | 1.8 | 50.8 | 1.0 | 52.1 | 1.5 | 50.5 | 1.6 |
| SO-MXl | 52.4 | 2.3 | 52.1 | 1.2 | 52.5 | 1.4 | 51.1 | 1.8 |
| IS-MXr | 37.7 | 1.7 | 37.0 | 0.9 | 38.0 | 1.9 | 37.4 | 1.7 |
| IS-MXl | 39.0 | 1.3 | 38.8 | 0.8 | 38.4 | 1.7 | 38.0 | 2.4 |
| *I-N | 11.3 | 1.1 | 11.3 | 1.5 | 10.7 | 1.1 | 10.8 | 1.1 |
| 0-MXr | 76.5 | 2.0 | 75.5 | 1.3 | 76.9 | 1.4 | 75.5 | 1.1 |
| 0-MXl | 77.3 | 2.8 | 76.4 | 1.3 | 76.9 | 1.7 | 76.1 | 1.7 |

* Statistically significant difference ($p \leq 0.05$) assessed by analysis of covariance with weight as the covariate.

TABLE VII

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING ANTEROPOSTERIOR CHANGES IN MIDFACIAL BONY SIZE OR DISPLACEMENT OF THE MIDFACIAL COMPLEX FOR EACH RAT GROUP AT TIME 2

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| MXr-N | 35.6 | 2.7 | 35.3 | 0.9 | 37.9 | 1.3 | 37.1 | 1.5 |
| MXl-N | 35.8 | 2.3 | 36.4 | 1.8 | 38.3 | 1.21 | 37.1 | 1.4 |
| SO-UMr | 50.6 | 2.5 | 48.1 | 1.6 | 48.4 | 1.2 | 48.0 | 2.0 |
| *SO-UMl | 51.9 | 2.2 | 48.8 | 2.7 | 48.5 | 1.7 | 48.0 | 1.9 |
| IS-UMr | 32.2 | 2.9 | 30.4 | 2.0 | 30.2 | 1.5 | 30.9 | 2.6 |
| *IS-UMl | 33.1 | 2.2 | 30.9 | 2.7 | 30.0 | 1.9 | 30.5 | 3.1 |
| *P-I | 57.4 | 2.1 | 56.5 | 1.7 | 55.4 | 1.8 | 55.0 | 2.3 |
| BA-MXr | 83.0 | 1.8 | 81.9 | 2.1 | 83.1 | 1.9 | 82.0 | 1.3 |
| BA-MXl | 84.4 | 1.0 | 82.4 | 2.4 | 83.5 | 2.0 | 82.6 | 1.5 |
| AB-ZGr | 53.4 | 1.3 | 54.2 | 2.4 | 54.4 | 2.7 | 54.3 | 2.2 |
| AB-ZGl | 52.8 | 1.9 | 54.4 | 2.3 | 53.3 | 3.3 | 53.2 | 2.1 |
| AB-UMr | 67.9 | 2.5 | 65.0 | 2.0 | 67.7 | 1.7 | 65.5 | 2.0 |
| AB-MXr | 82.1 | 1.9 | 81.0 | 2.2 | 82.2 | 1.8 | 81.2 | 1.4 |
| AB-MXl | 82.6 | 1.9 | 80.6 | 2.5 | 81.9 | 2.2 | 81.1 | 1.4 |
| SO-MXr | 65.5 | 1.9 | 64.8 | 1.7 | 65.7 | 1.5 | 64.4 | 1.0 |
| SO-MXl | 67.0 | 0.9 | 65.2 | 2.0 | 66.3 | 1.3 | 65.1 | 1.2 |
| IS-MXr | 47.4 | 1.5 | 47.3 | 1.4 | 47.7 | 1.3 | 47.6 | 1.6 |
| IS-MXl | 48.5 | 1.3 | 47.7 | 1.7 | 48.1 | 1.2 | 48.0 | 1.9 |
| *I-N | 10.6 | 0.9 | 10.9 | 1.3 | 14.5 | 0.9 | 13.8 | 1.3 |
| O-MXr | 92.9 | 2.2 | 91.8 | 1.8 | 92.3 | 1.5 | 90.6 | 1.4 |
| O-MXl | 93.8 | 1.3 | 92.1 | 1.9 | 92.6 | 1.5 | 90.9 | 1.4 |

* Statistically significant difference ($p \leq 0.05$) assessed by analysis of covariance with weight as the covariate.

TABLE VIII

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING ANTEROPOSTERIOR CHANGES IN MIDFACIAL BONY SIZE OR DISPLACEMENT OF THE MIDFACIAL COMPLEX FOR EACH RAT GROUP AT TIME 3

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| MXr-N | 39.8 | 1.8 | 39.6 | 1.6 | 41.3 | 1.8 | 40.7 | 1.9 |
| MXl-N | 39.4 | 2.1 | 39.6 | 1.2 | 41.4 | 1.3 | 41.0 | 1.9 |
| SO-UMr | 52.8 | 8.7 | 55.4 | 1.9 | 54.8 | 2.2 | 54.7 | 2.4 |
| *OS-UMl | 51.7 | 7.9 | 55.3 | 2.3 | 55.7 | 1.8 | 55.5 | 3.3 |
| IS-UMr | 34.0 | 7.1 | 35.4 | 2.8 | 34.6 | 2.2 | 35.0 | 2.9 |
| *IS-UMl | 32.5 | 5.8 | 35.1 | 2.9 | 35.6 | 2.4 | 35.5 | 2.9 |
| *P-I | 62.7 | 1.6 | 69.4 | 1.9 | 62.8 | 2.5 | 61.0 | 2.3 |
| BA-MXr | 94.1 | 3.0 | 92.6 | 2.6 | 93.6 | 1.7 | 92.8 | 2.5 |
| BA-MXl | 95.2 | 2.2 | 93.0 | 2.9 | 93.5 | 2.0 | 93.1 | 2.3 |
| AB-ZGr | 59.5 | 2.9 | 57.0 | 3.6 | 59.2 | 2.5 | 60.4 | 3.3 |
| AB-ZGl | 60.5 | 3.4 | 57.3 | 2.8 | 58.5 | 3.3 | 59.2 | 3.7 |
| AB-UMr | 74.2 | 2.6 | 73.9 | 2.3 | 73.9 | 2.5 | 74.2 | 2.2 |
| *AB-UMl | 72.9 | 2.8 | 73.9 | 2.6 | 74.6 | 1.8 | 74.9 | 3.3 |
| AB-MXr | 93.0 | 2.9 | 91.3 | 2.5 | 92.3 | 1.8 | 91.5 | 2.6 |
| AB-MXl | 93.7 | 2.3 | 91.4 | 2.9 | 91.9 | 1.9 | 91.5 | 2.2 |
| SO-MXr | 72.6 | 6.8 | 73.6 | 2.2 | 74.5 | 1.6 | 73.0 | 1.7 |
| SO-MXl | 73.5 | 6.6 | 74.0 | 2.5 | 74.3 | 2.0 | 73.5 | 2.2 |
| IS-MXr | 54.0 | 4.7 | 53.7 | 1.9 | 54.7 | 2.5 | 53.7 | 1.1 |
| IS-MXl | 54.4 | 4.6 | 54.1 | 2.1 | 54.5 | 2.6 | 53.8 | 1.6 |
| *I-N | 13.2 | 1.4 | 12.7 | 1.7 | 14.3 | 1.5 | 14.6 | 1.0 |
| O-MXr | 102.8 | 3.1 | 101.7 | 2.0 | 102.3 | 1.2 | 100.3 | 1.7 |
| O-MXl | 103.8 | 2.4 | 102.1 | 2.1 | 101.3 | 1.5 | 100.7 | 1.9 |

* Statistically significant difference ($p \leq 0.05$) assessed by analysis of covariance with weight as the covariate.

TABLE IX

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING TRANSVERSE CHANGES IN MIDFACIAL DIMENSION FOR EACH RAT GROUP AT TIME 1

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| ZGr-ZGl | 45.8 | 1.5 | 44.5 | 1.2 | 45.3 | 1.0 | 45.0 | 1.4 |
| UMr-UMl | 11.6 | 1.0 | 11.9 | 1.0 | 11.7 | 1.0 | 11.8 | 0.6 |
| MXr-MXl | 24.1 | 1.5 | 23.5 | 1.6 | 24.2 | 1.7 | 24.0 | 1.7 |
| ZGr-MXr | 24.2 | 4.9 | 23.0 | 4.5 | 23.8 | 3.9 | 21.9 | 4.3 |
| ZGl-MXl | 23.9 | 3.7 | 22.4 | 2.7 | 22.7 | 2.6 | 21.0 | 2.2 |

TABLE X

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING TRANSVERSE CHANGES IN MIDFACIAL DIMENSION FOR EACH RAT GROUP AT TIME 2

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| *ZGr-ZGl | 56.6 | 1.3 | 54.5 | 1.5 | 54.1 | 1.0 | 53.7 | 1.4 |
| *UMr-UMl | 16.2 | 1.0 | 15.6 | 0.9 | 12.1 | 1.0 | 11.7 | 1.0 |
| *MXr-MXl | 29.2 | 1.1 | 29.4 | 1.0 | 28.1 | 0.8 | 27.4 | 0.9 |
| ZGr-MXr | 32.7 | 2.7 | 30.3 | 1.0 | 31.6 | 3.2 | 30.7 | 1.7 |
| ZGl-MXl | 32.2 | 1.7 | 28.3 | 1.4 | 30.7 | 2.9 | 30.9 | 1.4 |

* Statistically significant difference ($p \leq 0.05$) assessed by analysis of covariance with weight as the covariate.

TABLE XI

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING TRANSVERSE CHANGES IN MIDFACIAL DIMENSION FOR EACH RAT GROUP AT TIME 3

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| ZGr-ZGl | 62.9 | 1.3 | 62.4 | 1.4 | 62.4 | 1.3 | 61.4 | 2.2 |
| *UMr-UMl | 17.0 | 1.4 | 18.6 | 1.3 | 15.3 | 1.6 | 16.4 | 2.0 |
| *MXr-MXl | 31.0 | 1.3 | 31.8 | 1.5 | 32.2 | 1.1 | 32.3 | 1.4 |
| ZGr-MXr | 37.5 | 2.3 | 38.0 | 2.9 | 36.6 | 1.7 | 34.9 | 2.4 |
| ZGl-MXl | 36.6 | 1.5 | 37.1 | 2.0 | 36.5 | 3.0 | 35.0 | 3.1 |

* Statistically significant difference ($p \leq 0.05$) assessed by analysis of covariance with weight as the covariate.

TABLE XII

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING CHANGES IN THE CRANIAL BASE OR CRANIUM FOR EACH RAT GROUP AT TIME 1

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| O-BA | 11.5 | 0.9 | 11.0 | 0.9 | 11.5 | 1.3 | 11.2 | 0.7 |
| BA-SO | 14.2 | 0.9 | 14.2 | 1.5 | 13.7 | 0.8 | 14.4 | 1.1 |
| IS-P | 14.0 | 1.9 | 14.6 | 1.5 | 14.6 | 1.1 | 13.7 | 1.4 |
| BA-IS | 39.6 | 2.4 | 39.6 | 1.6 | 39.7 | 1.5 | 39.2 | 1.7 |

TABLE XIII

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING CHANGES IN THE CRANIAL BASE OR CRANIUM FOR EACH RAT GROUP AT TIME 2

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| O-BA | 9.9 | 1.1 | 9.9 | 0.9 | 9.4 | 1.2 | 8.6 | 1.3 |
| BA-SO | 17.8 | 0.6 | 17.6 | 0.6 | 17.7 | 0.9 | 17.8 | 0.9 |
| IS-P | 18.9 | 1.0 | 18.1 | 0.8 | 18.6 | 0.6 | 17.6 | 1.5 |
| BA-IS | 46.6 | 1.7 | 45.6 | 0.6 | 45.6 | 1.2 | 43.9 | 1.3 |

TABLE XIV

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING CHANGES IN THE CRANIAL BASE OR CRANIUM FOR EACH RAT GROUP AT TIME 3

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| O-BA | 8.8 | 0.8 | 9.3 | 1.1 | 9.0 | 1.4 | 7.7 | 1.5 |
| BA-SO | 22.0 | 7.2 | 19.3 | 0.7 | 19.5 | 0.5 | 20.1 | 1.5 |
| IS-P | 19.5 | 2.8 | 20.6 | 2.2 | 20.5 | 2.2 | 20.2 | 1.9 |
| BA-IS | 50.2 | 5.4 | 49.1 | 1.4 | 48.9 | 2.5 | 47.9 | 1.6 |

TABLE XV

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING CHANGES IN MANDIBULAR DIMENSION FOR EACH RAT GROUP AT TIME 1

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| AB-COr | 15.6 | 1.8 | 15.6 | 1.5 | 16.0 | 1.7 | 16.1 | 1.8 |
| AB-COl | 13.8 | 1.3 | 13.6 | 2.6 | 15.1 | 2.4 | 14.7 | 1.9 |
| COr-COl | 46.1 | 1.7 | 45.4 | 1.2 | 45.3 | 1.0 | 45.8 | 1.3 |
| O-COr | 35.8 | 1.2 | 35.2 | 1.4 | 35.9 | 1.2 | 35.5 | 1.8 |
| O-COl | 33.9 | 1.6 | 33.2 | 1.6 | 34.7 | 1.9 | 34.7 | 1.8 |
| COr-LI | 54.4 | 3.0 | 54.5 | 1.6 | 54.9 | 2.6 | 55.3 | 2.2 |
| COl-LI | 57.4 | 1.6 | 58.1 | 2.7 | 57.5 | 2.2 | 57.6 | 2.3 |

TABLE XVI

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING CHANGES IN MANDIBULAR DIMENSION FOR EACH RAT GROUP AT TIME 2

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| AB-COr | 17.9 | 2.8 | 19.0 | 2.0 | 18.8 | 2.2 | 20.1 | 2.1 |
| AB-COl | 18.9 | 1.5 | 18.7 | 1.2 | 18.8 | 1.9 | 18.4 | 3.7 |
| COr-COl | 49.1 | 0.8 | 48.2 | 1.0 | 49.0 | 1.0 | 48.2 | 1.3 |
| O-COr | 37.4 | 2.0 | 37.9 | 1.2 | 37.6 | 1.4 | 37.8 | 0.9 |
| O-COl | 37.5 | 1.6 | 37.2 | 0.9 | 36.9 | 1.1 | 35.8 | 2.5 |
| COr-LI | 70.7 | 4.6 | 67.2 | 3.7 | 66.6 | 1.7 | 64.1 | 3.6 |
| COl-LI | 71.3 | 2.3 | 68.7 | 2.6 | 67.8 | 2.5 | 67.6 | 5.9 |

TABLE XVII

MEAN VALUES (IN MM.) AND STANDARD DEVIATIONS (S.D.) FOR VARIABLES REFLECTING CHANGES IN MANDIBULAR DIMENSION FOR EACH RAT GROUP AT TIME 3

| | $C_1$ | | $C_2$ | | $E_1$ | | $E_2$ | |
|---|---|---|---|---|---|---|---|---|
| VARIABLE | M | S.D. | M | S.D. | M | S.D. | M | S.D. |
| AB-COr | 20.2 | 2.5 | 18.8 | 2.7 | 19.9 | 3.5 | 19.4 | 2.5 |
| AB-COl | 19.9 | 2.2 | 20.0 | 1.6 | 20.5 | 2.4 | 21.5 | 3.9 |
| COr-COl | 50.9 | 1.1 | 49.5 | 2.2 | 50.4 | 2.0 | 50.0 | 1.3 |
| O-COr | 38.6 | 2.1 | 37.3 | 1.5 | 38.4 | 2.9 | 36.5 | 1.5 |
| O-COl | 38.3 | 1.8 | 38.6 | 1.0 | 38.7 | 1.3 | 38.4 | 2.4 |
| COr-LI | 78.8 | 2.1 | 77.6 | 5.3 | 78.9 | 3.8 | 76.5 | 5.1 |
| COl-LI | 79.7 | 3.0 | 77.5 | 4.1 | 77.9 | 3.3 | 75.5 | 4.7 |

TABLE XVIII

RESULTS OF ANALYSIS OF COVARIANCE FOR SIGNIFICANT ($p \leq 0.05$) VARIABLES

| Variable | Reliability * | Reliability ** | F ANCOVA | Significance |
|---|---|---|---|---|
| SO-UM1 | 85.5 | 99.95 | 3.93 | 0.0020 |
| IS-UM1 | 85.7 | 99.86 | 2.59 | 0.0253 |
| P-I | 91.1 | 99.83 | 4.49 | 0.0007 |
| AB-UM1 | 80.0 | 99.86 | 3.13 | 0.0089 |
| I-N | 71.0 | 99.51 | 7.23 | 0.0001 |
| ZGr-ZG1 | 81.2 | 99.84 | 2.95 | 0.0128 |
| UMr-UM1 | 96.8 | 98.76 | 12.26 | 0.0001 |
| MXr-MX1 | 92.0 | 98.85 | 3.02 | 0.0112 |

* Reliability of the trace data

** Digitizer system reliability

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