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A CEPHALOMETRIC INVESTIGATION OF THE GROWTH, IN SITU, OF "ISOLATED" MANDIBULAR CONDYLES IN ADULT RATS FOLLOWING THE ADMINISTRATION OF BOVINE GROWTH HORMONE

by

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Submitted in partial fulfillment of the requirements

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A CEPHALOMETRIC INVESTIGATION OF THE GROWTH, IN SITU, OF "ISOLATED" MANDIBULAR CONDYLES IN ADULT RATS FOLLOWING THE ADMINISTRATION OF BOVINE GROWTH HORMONE

Abstract

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RAYMOND LEE BERNABEI

Today there are two opposing theories of craniofacial growth, each of which ascribes a different role to the mandibular condyle. The classical theory of mandibular growth holds that the condyle is an active growth center, is under intrinsic genetic control, and as such, effects a downward and forward translation of the mandible. In contrast, the functional matrix theory considers the condyle to be a growth site under extrinsic (environmental) control which responds compensatorily to the volumetric expansion of the oro-naso-pharyngeal capsular matrices.

The present study employed growth-hormone-treated mature rats to achieve a system (similar to acromegaly) in which translatory growth is largely restricted to the mandible. To determine the general location of the growth center(s) responsible for this bodily movement, the mandibles were dissociated into three parts: condyles and body. It was assumed that only the component associated with a growth center would still be capable of growth, and, thus, would serve to distinguish between the two theories.

The sample consisted of forty mature female rats divided equally

among the following groups:

Group I - Bilateral condylotomy, growth hormone injections, metallic implants.

Group II - Bilateral condylotomy, saline injections, metallic implants.

Group III - Bilateral sham operations, growth hormone injections, metallic implants

Group IV - Bilateral sham operations, saline injections, metallic implants.

In addition, five animals were used to assess the effect of bovine growth hormone on weight gain.

Throughout the thirty-day experimental period, all rats were weighed and injected daily with either saline or growth hormone (depending on what group they were in). Cephalometric radiographs were taken immediately after surgery and, again, thirty days later.

Implants were placed; two in the condyle-ramus area, two in the mandibular body, and one in the frontal bone. These, along with six anatomical landmarks, were used to evaluate cephelometrically treated changes in each of the four experimental groups.

It was found that isolated condyles responded to growth hormone injections by growing (translating) in a downward and forward direction. In contrast, the isolated condyles that received saline were found to rotate upward and forward. The body/ramus segment of both condylotomized groups collapsed upward and backward. Both groups of shams showed very little change in implant position.

The results of the study may be summarized:

1. Several cranial and midfacial dimensions increased during the experimental period. It is assumed that surface deposition was responsible, inasmuch as the hormone-treated animals grew more than did those injected with saline.

2. Condyles isolated in situ responded to growth hormone in a manner consistent with a growth center, while condyles without a growth promoting agent (saline) did not grow.

3. Mandibular bodies isolated in situ collapsed upward and backward irrespective of whether or not a growth promoting agent was administered. The collapse, however, was significantly greater in saline-treated animals.

4. The results of the present study conform closely to expectations generated by the classical theory and, as a result, would seem to demand a re-evaluation of the extent to which the functional matrix theory is applicable to mandibular growth.

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DEDICATED

TO

My Wife and My Parents

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INTRODUCTION

Much of the present controversy concerning the mechanisms and regulation of mandibular growth has surrounded the role of the mandibular condyle. Questions continue to be raised regarding the means by which the condyle grows and the contribution it makes to mandibular morphogenesis. The classical theory of mandibular growth assumes the condyle to be under the control of intrinsic factors, its condylar cartilage being a primary growth center. In this formulation, the proliferative activity of the condylar cartilage is responsible for bodily translation of the mandible.

A more recent view fails to credit the condylar cartilage with such primary importance. This opposing theory holds that mandibular growth occurs as a compensatory response to the function of the various components of the oro-naso-pharyngeal complex, i.e., functional matrices--muscles, teeth, glands, and "functioning" spaces regulate mandibular growth; the condyle is viewed as a growth site whose growth serves to maintain a proper relation between the condyle and glenoid fossa.

Although many of the factors influencing the condyle have been investigated, the varied results and often contradictory conclusions have left the researcher and clinician with many perplexing and unresolved problems. The general lack of concensus makes it difficult, if not impossible, for the clinician to map a rational therapeutic

strategy in the treatment of maxillo-mandibular size discrepancies.

Presumably, the opposing theories of mandibular growth can be accepted or rejected through experimentation. It is, therefore, the purpose of this investigation to determine experimentally whether the condyle acts as a growth center under the control of "intrinsic factors" or as a growth site responding only to "extrinsic factors."

REVIEW OF THE LITERATURE

The controversy associated with the condyle and its influence on mandibular growth has evolved from the frequent assumption that the mechanism of condylar growth is similar to that of epiphyseal and synchondroseal cartilage. The issue to be examined is two-fold. First, does the growth of the condyle govern growth and position of the mandible? Second, is condylar growth regulated by intrinsic (genetic) or extrinsic (environmental) factors?

Classical Theory of Mandibular Growth

The classical view of mandibular growth has as its focus the condyle, which is assumed to function in a manner similar to the "growth cartilage" of epiphyseal plates. This view emphasizes a pacemaking role of the mandibular condyle as a growth center whose volumetric and linear expansion causes downward and forward mandibular translation. The term "growth center" implies a "place of endochondral ossification with tissue separating force" (Baume, 1961).

Early studies have contributed much to a fundamental understanding of the surface changes that accompany mandibular growth. Through intravital staining pig specimens, Hunter (1771) was the first to describe the combination of surface deposition and resorption ultimately responsible for changes in mandibular proportion. It was not until almost a century later, however, that a role for the condylar cartilage in mandibular growth was first suggested by Kölliker (1853).

The classical theory of mandibular growth, however, achieved its final form from Charles' (1925) gross and histologic investigation into the growth of human fetal temporomandibular joints. Charles reported that:

1. the articular surface of the glenoid fossa and condyle is covered by fibrous tissue rather than hyaline cartilage as previously thought;
2. the growth of the mandible is largely governed by the pacemaking role of the condyle.

Following Charles' contention that "mandible growth is solely controlled by the growth which takes place at the top of the condyle," a number of later workers contributed to the evolution of the classical theory of mandibular growth. One of these men, Brodie (1941), studied serial roentgenograms of children and described mandibular growth as occurring:

1. posteriorly at the ramus;
2. upward at the alveolar process;
3. upward and backward at the condyle.

Of these, he held the condyle most responsible for dimensional change of the mandible (Brodie, 1941, 1948). He attributed to the head of the condyle "a potential and mechanism of growth not unlike that of the long bones," and added that it is the last growth center in the head to cease activity (Brodie, 1941).

Later, Rushton (1944), in his examination of histological preparations of normal human condyles and condyles gathered from individuals suffering from varied pathoses, agreed with the general conclusions of Charles. Specifically, he reaffirmed the concept of

the importance and effects of growth at the mandibular condyle in propelling the mandible downward and forward.

Sicher's (1947) observations, like those of Brodie, described bony remodeling of the mandible at:

1. the posterior border of the ramus;
2. the upper border of the coronoid process;
3. the alveolar crests.

Sicher went even further by emphasizing the role of growth of the condyle in determining the development of the whole face.

Symons (1951) and Scott (1951, 1967) expressed sentiments similar to Charles and concluded that the condyle is of primary importance to mandibular growth.

Thus, the traditional concept of mandibular growth first alluded to by Kölliker, formalized by Charles, and later supported by numerous workers (Brodie, 1941; Rushton, 1944; Sicher, 1947; Symons, 1951; Scott, 1951, 1967) assigns to the condyle the role of a primary growth center. While transformation of the mandible is accomplished by surface alteration due to bony remodeling, translation is under condylar authority. Thus, the condyle is assumed to be an active contributor to the spatial positioning and subsequent remodeling of the mandible.

The Functional Matrix Theory

> Matrix, n. . . .2) that within which, or within and from which, something originates, takes form, or develops,. . .
>
> Webster's New World Dictionary, 1968

During the past decade, a newer theory of mandibular growth has achieved wide exposure and acceptance. This theory, as enunciated by Moss and co-workers (1960, 1962, 1964, 1968, 1969, 1970, 1972) is a modification of a functional concept of cranial growth originally set forth by van der Klaaw (1945, 1948-52). According to this view, the growth of all skeletal tissues (osseous and cartilaginous) is secondary and compensatory to the primary growth of related functional matrices, i.e., the tissues, organs, and spaces related to any skeletal element. In the case of the mandible, the condyle follows in an obligatory manner the primary growth of the related matrices. In this way, the condyle contributes little to the regulation of mandibular growth; rather, it acts merely as a growth site, a "region of periosteal . . . bone formation and modeling resorption adaptive to environmental influences" (Baume, 1961).

In line with this concept, Moss views the head as a region within which a variety of functions are carried out; each function effected by a "functional cranial component." For instance, the mandible consists of a number of adjoining functional cranial components (alveolar, coronoid, angular and "basal" region), each composed of "functional matrices" and a "skeletal unit" (Moss, 1962, 1969). Functional matrices are defined by Moss as all of those soft tissues and "functioning spaces" which carry out a given function. A skeletal unit is defined as the bone or cartilage which protects and/or supports its specific functional matrix. Skeletal units are not necessarily the equivalent of individual bones. A "bone"

may in fact be formed by a number of microskeletal units completely independent of each other and related to different functional matrices (Moss, 1962). Such is the case of the mammalian mandible (Moss, 1969). These skeletal units may be singular, protecting/supporting only one functional matrix (a microskeletal unit) or they may be made up of several microskeletal units which protect/support many functional matrices (for example, the mandible--a macroskeletal unit).

In addition, Moss and Salentijn (1969) state that there are two types of functional matrices, periosteal and capsular. A periosteal matrix (muscles, blood vessels, nerves, etc.) is said to transform its adjoining skeletal unit, presumably by controlling the processes of osseous deposition and resorption. The net effect is to alter the form (size and shape) of the skeletal unit. An example of this is the presumed morphogenetic role of the temporalis in the growth of the coronoid process in the rat (Washburn, 1947).

A capsular matrix, which is defined as a functioning space or tissue mass (nasal and oral cavities or the neural and orbital tissues), is said to translate both the skeletal units and their periosteal matrices by relocating them in space (Moss, 1969, 1970). In this way, part of mandibular growth is translation in space in response to the volumetric expansion of the oro-facial functioning spaces (Moss, 1970).

Thus, according to Moss, the mandible which is a macroskeletal unit, composed of a variety of individual microskeletal units, grows by:

1. Surface alteration of skeletal units under the direction of the periosteal matrices--transformation;

2. Translation through space of the entire mandible in response to the volumetric expansion of capsular matrices (Moss, 1969).

Evidence

Many methods have been used to investigate mandibular growth in general and condylar growth in particular. Transplantation and tissue culture studies have been done to determine:

1. which cartilaginous cell-layers are responsible for proliferative activity;

2. the factors (environmental or genetic) which control this proliferation.

Condylectomies have been performed to evaluate the effect of the condyle on translation of the mandible. The sequelae of numerous pathoses in humans has been studied and interpreted to show the alteration in mandibular position associated with mandibular joints suffering such afflictions as arthritis, ankylosis, and congenitally missing condyles.

Transplantation and Organ/Tissue Culture

In an attempt to test the hypothesis that cartilaginous structures function as growth centers, investigators have employed a variety of transplantation and organ/tissue culture techniques. In such studies, it is assumed that, when placed in a "neutral" site, growth centers will grow and growth sites will not.

Unfortunately, such studies have led to markedly dissimilar conclusions regarding condylar growth. In some instances, it has

been concluded that the condylar cartilage lacks an independent growth potential (Baker, 1937; Koski et al., 1963, 1964, 1965; Rönning, 1966; Duterloo, 1967) while in others cartilaginous structures appear to have an intrinsic growth-potential (Duterloo, 1967; Meikle, 1973; Bremers, 1973).

For example, a variety of workers (Murray, 1926; Felts, 1961; Duterloo, 1967) have shown that long bones transplanted in vivo in a nonfunctioning environment (brain, subcutaneously, etc.) grow approximately as in situ (Meikle, 1973). Such growth is generally assumed to be due to proliferation of the epiphyseal cartilage and is thought to be mostly under genetic control (van Limborgh, 1971). Similar studies have been conducted with the mandibular condyle but the results have shown, at the very least, marked quantitative differences vis-à-vis epiphyseal cartilage.

Koski and associates (1971) transplanted into a nonfunctioning environment (subcutaneously and intracerebrally) three components of condylar cartilage:

1. condylar cartilage proper;
2. condylar cartilage plus adjacent spongiosa;
3. condylar cartilage plus adjacent ramus.

The components were implanted in 3 to 5 day old littermates and left for periods of 30, 60, and 90 days. Upon recovery, the first component, i.e., condylar cartilage proper, displayed no typical structural change. Recovery of the second and third components showed a small amount of growth. In none of the three components did the

growth approach that of the condyle *in situ*. It was concluded, therefore, that condylar cartilage lacks an independent growth potential and is not comparable to epiphyseal cartilage as a growth center. These findings support the functional matrix concept of condylar growth.

With regard to such transplantation studies, Meikle (1973) has questioned whether the cells of the proliferative zone in a transplanted condyle retain the capacity to differentiate. To investigate this, he transplanted complete mandibular joints as an isograft between 7 day old littermate rats and recovered them at from 1 to 21 days. By administering tritiated thymidine at different intervals, he was able to evaluate cellular differentiation. There was evidence that the proliferative zone differentiated into osteoblasts and not chondroblasts as *in situ*. But the cellular proliferation appeared to be relatively independent of any functional environment (Meikle, 1973).

A similar conclusion was reached by Duterloo (1967), from an examination of intracerebral, autologous condylar transplants. The hosts were 4 day old rats injected with tritiated thymidine. He interpreted the presence of labeled cells over a 4 to 6 day period of time in both the proliferative zone and the cartilage as a response to intrinsic factors. He concluded that condylar cartilage is capable of a limited amount of growth in ectopic, nonfunctional sites.

Bremers (1973) conducted a condylar organ-culture investigation to attempt to eliminate uncontrollable factors as much as possible, i.e., loss of the transplant *in vivo*, insufficient blood

supply, etc. The results of this study on rat condyles showed that the condylar cartilage is able to grow independent of normal environmental factors (pressure, tension, etc.).

Although many workers have concluded that chondrogenesis in the condylar cartilage is under intrinsic (genetic) control, the proliferation generally seen was of short duration. Whether environmental factors are necessary to achieve prolonged growth remains to be seen.

An important issue to be considered in evaluating the condyle are the unproven and sometimes loosely drawn analogies linking condylar growth to synchondroseal and epiphyseal growth. As Baume (1961) has noted:

1. condylar cartilage is a secondary cartilage and, as such, develops differently from "true" endochondral growth centers (Symons, 1951);

2. condylar cartilage is covered by a thin fibrous layer, variously described as fibrocartilage (Charles, 1925; Sicher and Weinmann, 1955) or perichondrium (Baume, 1961), and this is able to grow either appositionally or interstitially;

3. condylar cartilage is not totally replaced by bone and, therefore, never loses the ability to grow;

4. condylar cartilage is more responsive to mechanical stimuli than is the cartilage of an epiphysis (Baume, 1961; Duterloo, 1972; Belhobek, 1974).

Condylectomy--Condylotomy

A number of investigators have studied the effect of condylectomy on mandibular growth in an attempt to determine whether or not the condyle is a primary growth center. When condylectomy is unilateral (Sarnat and Engel, 1951; Sarnat, 1957; Walker, 1960;

Skuble et al., 1970; Sarnat and Muchnic, 1970; Castelli et al., 1971) the general observation has been that growth of the mandible is distorted. In bilateral condylectomy experiments (Jarabak and Graber, 1951; Jarabak and Thompson, 1951; Jarabak and Thompson, 1953; Jolly, 1961; Das et al., 1965; Gianelly and Moorrees, 1965; Sanghani, 1965; Skuble et al., 1970; Pimenidis and Gianelly, 1972), the findings are comparable (i.e., some mandibular growth occurs), although the conclusions are different. For example, Gianelly amd Moorrees (1965) assessed the contribution of the condyle to the growth of the mandible by performing bilateral condylectomies on young rats. They reported that the mandibles of the condylectomized group were 2 mm shorter than those of the controls, while the maxillo-mandibular dental relationship was unaffected. The experimental differences, however, were small enough--perhaps in comparison to their expectations--to cause them to conclude that condylar growth is secondary and compensatory, much like that seen in the cranial sutures.

Das, Meyer and Sicher (1965), presented findings similar to those of Gianelly and Moorrees, but reached very different conclusions, namely that the enlargement of the mandible in the experimental group was due to an adjustment in position (in contrast to normal developmental growth), and that growth seen in the absence of condyles would not necessarily rule out a primary role for the condyle in mandibular growth. As Das et al. (1965) point out, "Though the condylectomized mandible may attain nearly normal size, its shape and proportions differ from those of the normal rat mandible."

Moreover, in addition to the controversy surrounding the conclusions drawn from condylectomy experiments, considerable criticism has been leveled at condylectomy experiments, per se. Apropos of this criticism Meikle made two interesting observations. Firstly, he criticized the age of the animals used in the condylectomy experiments (Gianelly and Moorrees, 1965; Das et al., 1965), saying they were too old and thus had expressed upwards of 66% of their growth prior to the condylectomy procedure. Pimenidis and Gianelly (1965) attempted to overcome this problem by performing bilateral condylectomies on rats at the age of one day. Since their findings and conclusions were similar to those of their earlier study (Gianelly and Moorrees, 1965), they concurred with Moss' contention that condylar growth is adaptive.

Secondly, Meikle observed that it is difficult to draw inferences about the role of the condyle in normal growth from preparations which lack condyles. The fact that a mandible without condyles appears to achieve a relatively normal position, does not mean that it mimics normal physiologic growth in arriving there. Indeed, it is difficult to imagine how (in the absence of ankylosis) condylectomy could prevent a mandible from being carried downward and forward by the growth of the maxilla, occlusal interdigitation, gravity, etc.

Thus, condylectomy experiments could, at best, be expected to give only a "rough indication" of the role of the condyle in mandibular growth (Meikle, 1973).

Experiments of Nature

An important source of evidence and hypothesis in the field of craniofacial biology has always been the study of a variety of pathoses which produce alterations in facial growth. Indeed, the constellation of signs associated with one disease--acromegaly--has, until recently, served to focus attention on the condyle as a "prime mover" in mandibular growth.

Acromegaly is a disorder in adults caused by hyperfunction of the anterior pituitary, characterized--in part--by a marked overgrowth of the mandible (Sarnat, 1964; Tieke, 1965; Pindborg, 1968; Gorlin and Goldman, 1970; Shafer, Hine and Levy, 1974). With Minkowski's (1887) recognition of enlargement of the pituitary gland as the cause of acromegaly came an appreciation of the relation between the pituitary gland and somatic growth. Evans and Long (1921) first induced gigantism experimentally in the rat by the injection of crude bovine pituitary extracts. Changes resembling acromegaly were later produced experimentally by the action of pituitary extracts (or growth hormone) in various animals (Putman et al., 1929; Evans et al., 1933--dog; Des Enfants, 1966--rabbit; Silberberg and Silberberg, 1943--guinea pig; Silberberg and Silberberg, 1943--mouse; Mackenzie and Avery, 1958--hamster; Handelsman and Gordon, 1938; Becks et al., 1946; Collins et al., 1946; Becks et al., 1948; Collins et al., 1949; Evans et al., 1949; Baume et al., 1959; Asling et al., 1961; Asling et al., 1965; Meyer et al., 1967--rat). The acromegalic response in these animals, and more specifically in the rat, displayed

the typical mandibular enlargement along with many of the associated body changes seen in human acromegalics. Although there is no doubt that mandibular over-growth occurs, there is growing controversy concerning the mechanisms involved.

Classically, most pathology texts hold that the elevated level of growth hormone (somatotrophin) acts directly on the condyle, causing an increase in the proliferation of cartilage and, as a result, a marked downward and forward translation of the mandible (Sarnat, 1964; Tiecke, 1965; Pindborg, 1968; Gorlin and Goldman, 1970; Shafer, Hine and Levy, 1974). This is a remarkably "tidy" explanation which, until recently, has enjoyed general acceptance.

The newer functional matrix theory, however, holds that growth hormone causes an expansion of various functional matrices (e.g., tongue), and that this expansion is primarily responsible for translating the mandible (Moss, 1970). Although the tongue and other soft tissues are known to enlarge with hyperpituitarism (Sarnat, 1964; Tiecke, 1965; Pindborg, 1968; Gorlin and Goldman, 1970; Shafer, Hine and Levy, 1974), this behavior, although necessary, is not sufficient to prove the functional matrix hypothesis.

As with other avenues of investigation, the problem reduces to a question of whether or not the condyle responds directly to the influence of the growth hormone or whether the growth hormone acts on a functional matrix, the expansion of which serves to alter the spatial position of the mandible.

In order to resolve the question of condylar influence on

mandibular growth, a recent approach in which the condyles are isolated and their growth potential evaluated, in situ, by means of radiographs and metallic implants was developed. This method was introduced by Fuller (1974), who investigated condylar growth in 20 guinea pigs by sectioning the neck of the condyle (condylotomy) so as to divide the mandible into two separate parts: condyle and ramus and body. The animals ranged from 21 to 32 days of age and, therefore, still had a considerable amount of growth remaining. The condyle on one side of the mandible was surgically isolated and stripped of all muscle attachments but left in situ; the condyle on the other side was subjected to a sham operation. The growth of the two parts over a 30 day period was evaluated by way of implants and cephalograms.

The results showed that the isolated condyle not only grew downward and forward but also did so at a greater rate than that of the sham. Fuller concluded that his results were best explained by the assumption that condyles serve as growth centers.

The concept of studying the mandible under physiologic conditions, but in parts, presents an interesting approach to condylar investigation. There are, however, some basic problems with Fuller's approach:

1. since the condylotomy was unilateral, there is the possibility of interaction between the control and experimental sides;

2. the whole head is growing; therefore, the growth of the mandible is probably influenced by the growth of other structures, most notably the midface.

To overcome these shortcomings, performance of a bilateral

condylotomy should eliminate an interaction effect between experimental and control sides. To eliminate the effect of midfacial growth on the mandible, it would be desirable to find a system in which the only thing growing to any great extent is the mandible.

Since growth hormone has a potent effect on mandibular growth (Asling, 1961; Baume, 1961; Cimasoni et al., 1963; Roche, 1967; Bremers, 1973) and since the potential for growth (either primary or secondary) of the mandibular condyle persists throughout life in rats--and humans--(Collins et al., 1946; Becks et al., 1948; Asling, 1961; Baume and Derichsweiler, 1961; Baume, 1961; Sarnat, 1964; Meyer et al., 1967; Silbermann and Frommer, 1972), bilateral condylotomies in an adult rat would seem to constitute an excellent model for determining whether or not the condyle has an intrinsic growth potential.

STATEMENT OF THESIS

Much of our present attitude toward mandibular growth ascribes a growth potential to the condyle. A divergence of opinion becomes apparent, however, when the question arises whether this condylar growth is a primary response to genetic factors or a secondary, adaptive response to environmental influence. As a primary respondent, the condyle would be instrumental in propeling the mandible downward and forward. If however, the other view holds true, the condyle serves merely to maintain the integrity of the temporomandibular articulation, and the growth center would, instead, be the oropharyngeal airspace associated with the mandibular body.

It will be the purpose of this study to analyze mandibular growth in an experimental system where the only thing growing to any great degree is the mandible. Since the hypothesized--but indistinguishable--growth centers and growth sites are connected, i.e., the condyles are connected to the body of the mandible, it is necessary to divide the mandible into its component parts, condyles and body, so that each is able to act alone if capable of doing so--in the absence of interaction among, or interference from, the other parts. This scheme can be termed a "Site-center dissociation" design and is depicted schematically in Figure 1.



Figure 1

A. S and C move. Some say C pushes S; others say S pulls C. To determine which is the growth center, the entire complex is dissociated into its component parts.

B. If C propels the entire C-S complex, then only C will move. If, however, S is responsible for pulling C, then only S will move. A third possibility exists in which both C and S move separately.

The relationship between this model and mandibular growth can be seen by calling C the condyle and S the body of the mandible. We have seen previously that growth hormone makes the mandible grow. By performing a bilateral condylotomy, the two condyles and the mandibular body are "free" to respond to growth hormone injections. With each part (condyles and mandibular body) able to respond alone--if capable of doing so--the growth center-growth site argument can be resolved. If the condyles grow downward and the body does not, the result would favor the classical theory. If the body grows and the condyles do not, the functional matrix theory will gain experimental support. If both segments (condyles and body) grow, some combination of the two theories will constitute a tenable hypothesis.

MATERIALS AND METHODS

Sample

Forty-five adult female rats (Sprague-Dawley) supplied by Zivic-Miller Laboratories Inc., Allison Park, Pennsylvania were employed in this investigation. The rats weighed approximately 300 grams and were 200 days old at the start of the experiments. The animals were weighed upon receipt from the supplier and only those animals which gained no more than 10 grams in 10 days were used.

Rats were chosen for this study because:

1. they are hardy beasts and thus, are able to survive extensive surgical manipulation;
2. they are the animal most frequently used in hormone experiments (Becks et al., 1946; Becks et al., 1948; Asling et al., 1965);
3. they respond well to growth hormone extracted from many species, especially bovine hormone (Papkoff and Li, 1962).

Experimental Design

Forty rats were divided into four groups of ten as follows (Figure 2):

Group I - Bilateral condylotomy, growth hormone injections, metallic implants.

Group II - Bilateral condylotomy, saline injections, metallic implants.

Group III - Bilateral sham operations, growth hormone injections, metallic implants.

Group IV - Bilateral sham operations, saline injections, metallic implants.

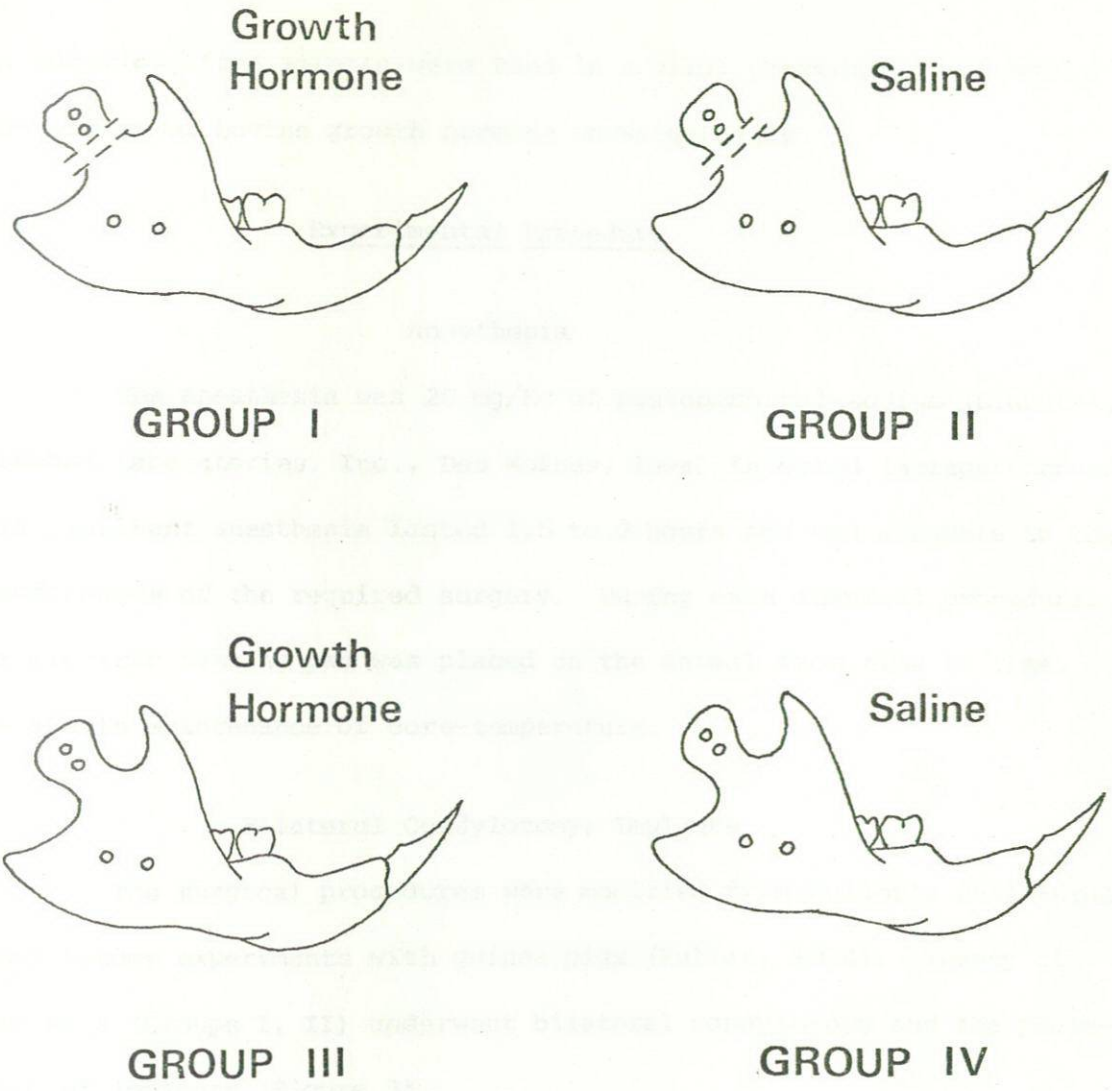


Figure 2.--Experimental Design

In addition, five animals were used in a pilot procedure to assess the effect of bovine growth hormone on weight gain.

Experimental Procedure

Anesthesia

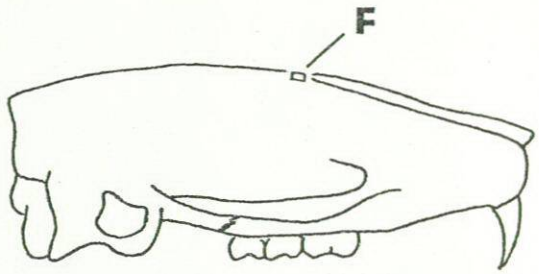
The anesthesia was 20 mg/Kg of pentobarbital sodium (Diabutal, Diamond Laboratories, Inc., Des Moines, Iowa) injected intraperitoneally. The resultant anesthesia lasted 1.5 to 2 hours and was adequate to the performance of the required surgery. During each surgical procedure, an electric heating pad was placed on the animal from time to time, to assure maintenance of core-temperature.

Bilateral Condylotomy; Implants

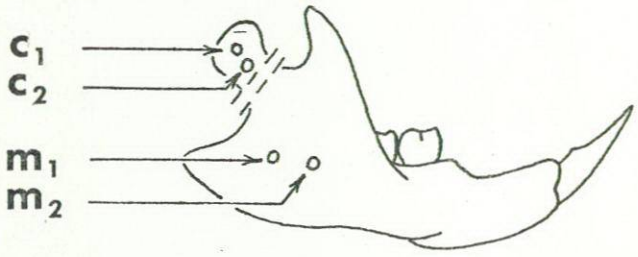
The surgical procedures were modified from Fuller's unilateral condylotomy experiments with guinea pigs (Fuller, 1974). Twenty of the rats (Groups I, II) underwent bilateral condylotomy and the placement of implants (Figure 3).

Once anesthesia was attained, the surgical field was clipped and shaved. The animal was placed on its side on a surgical board, and the head immobilized with a standard head holder (Plate I). The field was then painted with a tincture of nitromersol (Metaphen, Abbott Laboratories, North Chicago, Illinois), and a vertical incision approximately 2 cm long was made from just above the zygomatic arch midway between the eye and ear to the lower border of the mandible. Care was exercised as not to injure the transverse facial veins, the

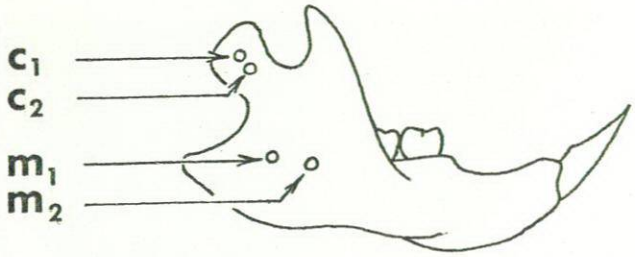
FRONTAL IMPLANT



CONDYLAR IMPLANTS



EXPERIMENTAL (GROUP I & II)



SHAM (GROUP III & IV)

Figure 3.--Location of Implants

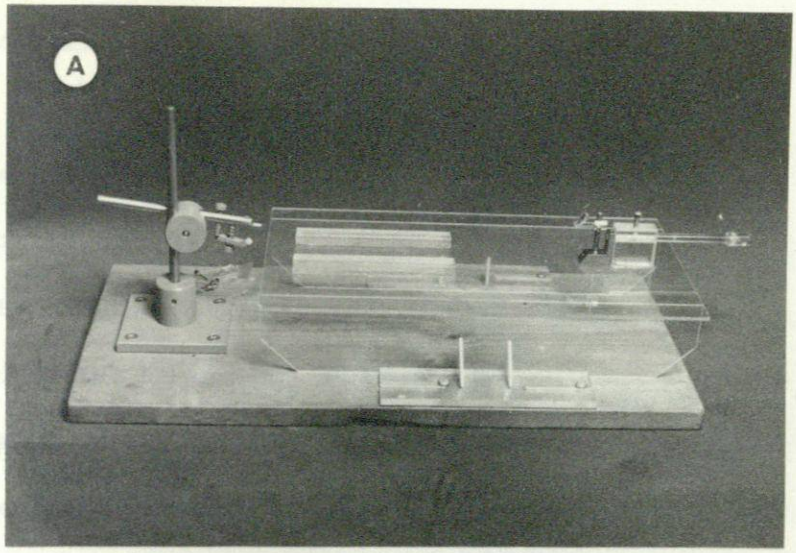
PLATE 1.--Surgical Board and Headholder.

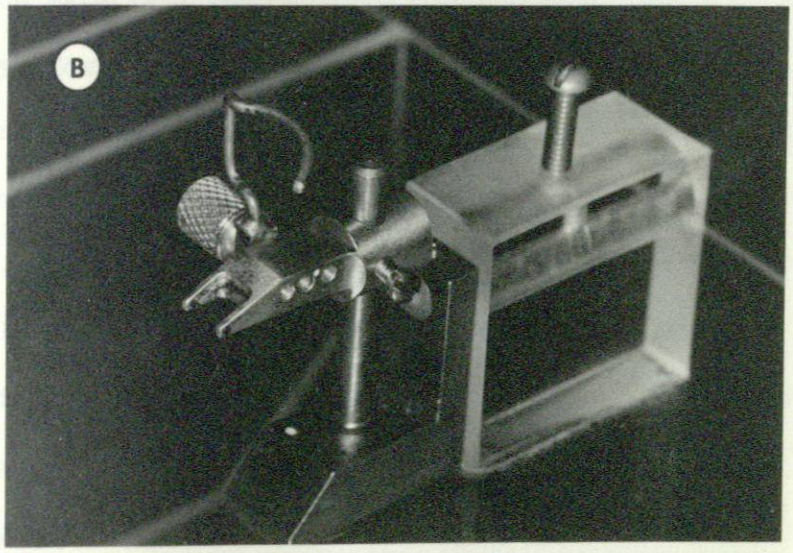
Figure a.--Surgical Board

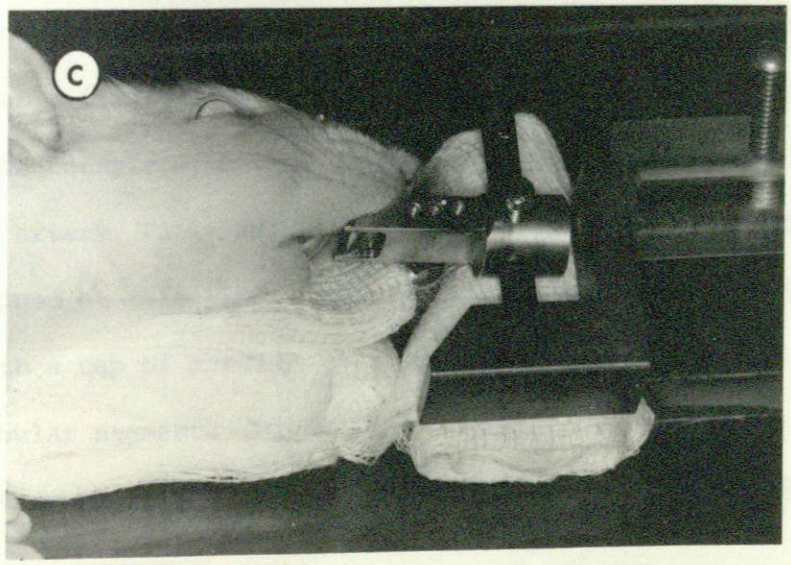
Figure B.--Headholder

Figure c.--Head-fixation.

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A


B


C

zygomatico-maxillary division of the seventh nerve, or the anterior extension of the parotoid gland (Plate IIA). The superficial fascia was incised and retracted, and the condyle approached by blunt dissection of the superficial and deep bellies of the masseter muscle (Plate IIB). With a 33 1/2 inverted cone dental bur in an air-driven high-speed dental handpiece, two holes were placed in both the condyle ramus portion of the mandible and in the body of the mandible (Plate IIC). The field was then dried and the holes packed with one of two radioopaque materials (Plate IID): on one side, zinc-free amalgam (Spheraloy, Kerr, Romulus, Michigan), and on the other, a mixture of amalgam powder and acrylic (Cranial Resin Powder, Batch #36448; Cranioplastic Liquid, Batch #637898; L. D. Caulk Company, Milford, Delaware). By using materials of different densities, right and left sides could be differentiated on radiographs (see below). The choice of sides into which one or the other type of implant is placed was made at random. In addition, an amalgam marker was placed in the frontal bone.

Once the markers were placed, condylotomies were performed one side at a time. They were effected by making a cut across the neck of the condyle with a #6 round bur, taking care not to cut the maxillary artery (Plate IIE). All muscle attachments to the condyle were stripped at this time. The cut end of the condyle was then coated with a cap of acrylic to retard bony union of the condylar and mandibular segments (Plate IIF). Tissue overlying the zygomatic arch was then reflected and an implant placed in the zygomatic arch.[1]

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[1]This implant proved unreliable and was not used in the subsequent analysis.

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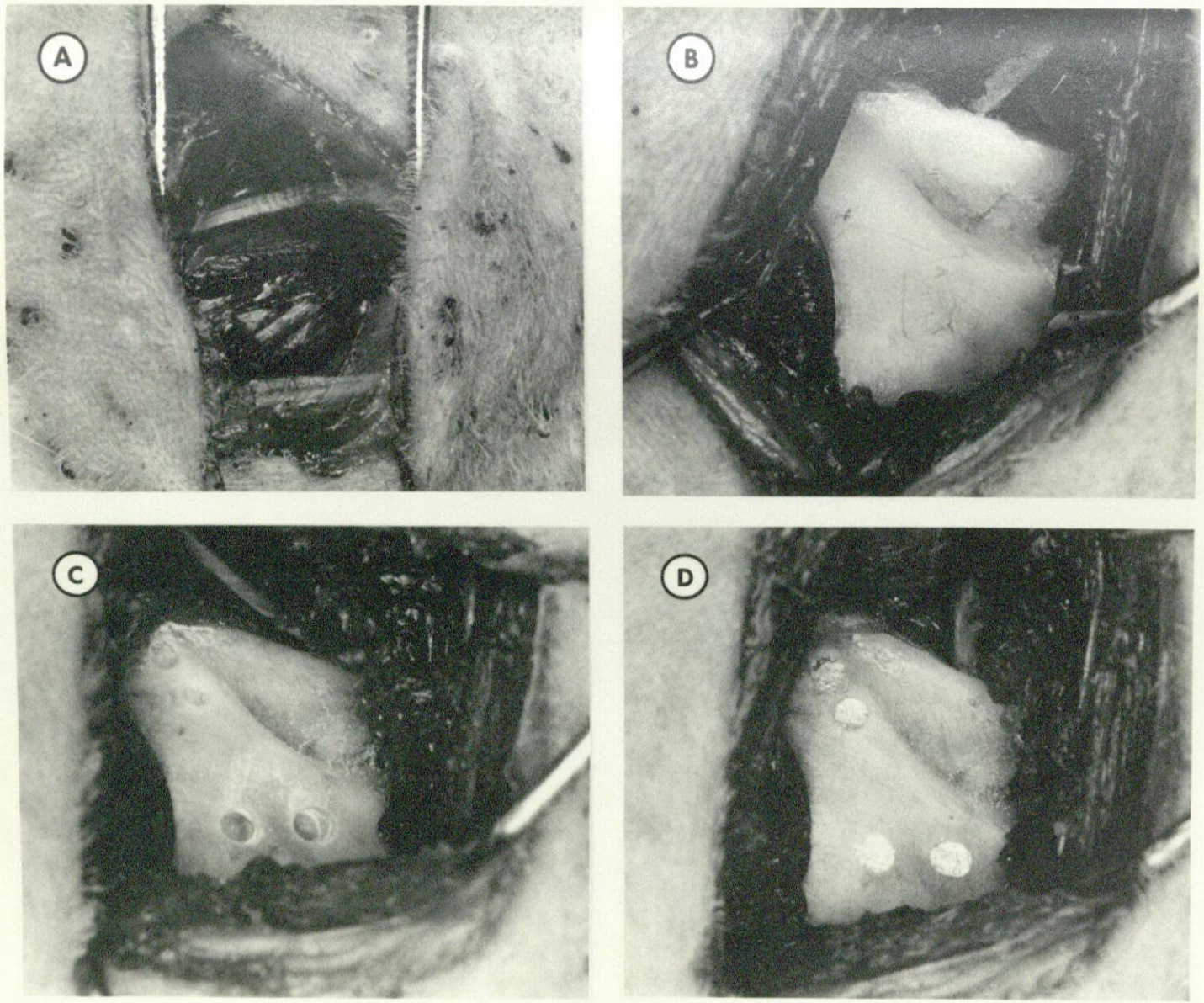
PLATE II.--Condylotomy Procedure.

Figure A.--Surgical Entry.

Figure B.--Condylar Exposure--
Blunt dissections of masseter.

Figure C.--Placement of Implant Holes.

Figure D.--Implant Placement.


A
B
C
D

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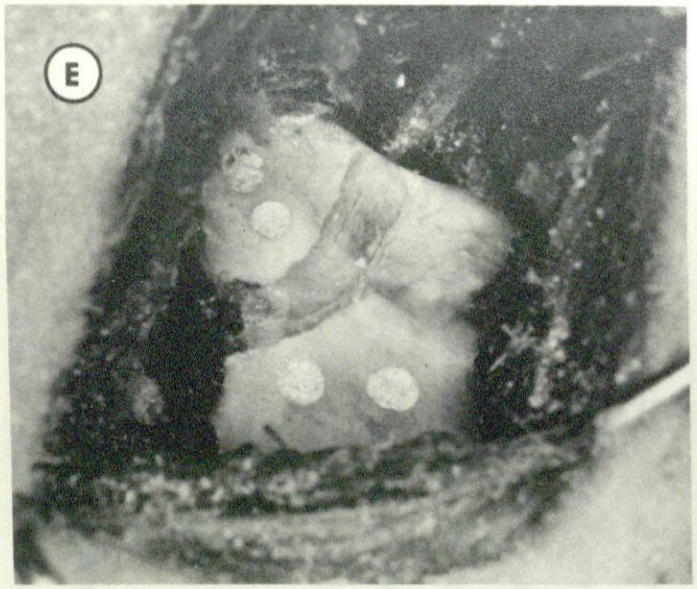
PLATE II.--Continued

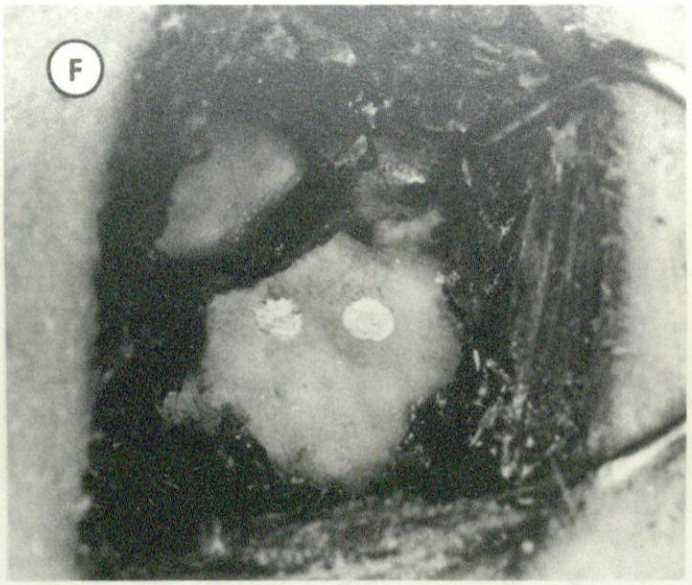
Figure E.--Condylotomy--Initiation of Surgical Cut.

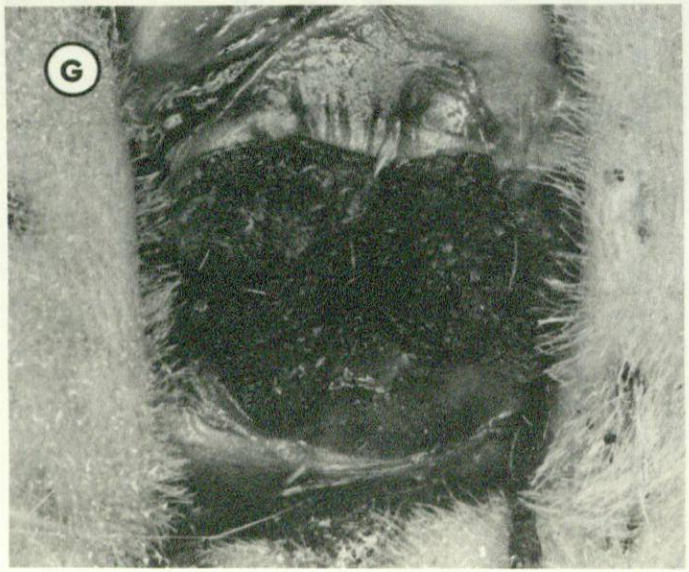
Figure F.--Acrylic Cap Covering Condylar Portion.

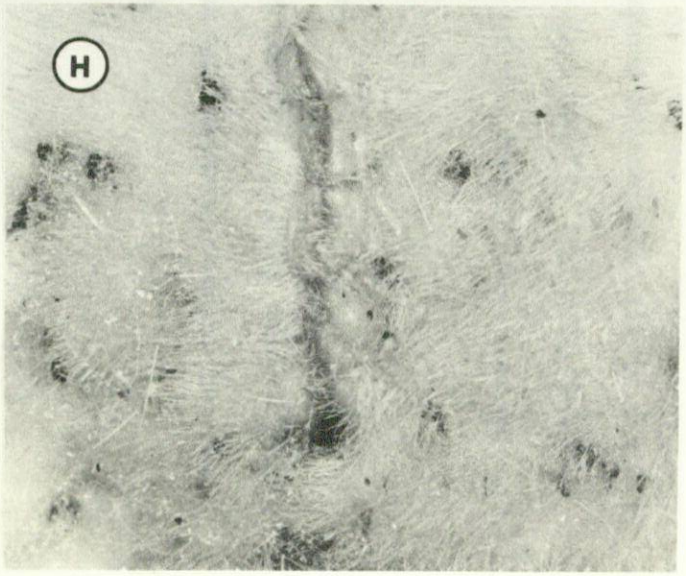
Figure G.--Approximation and Suturing of Overlying Musculature.

Figure H.--Surgical Closure Completed.


E


F


G


H

The incisions were then closed by layers using 4-0 plain gut suture (Ethicon, Inc., Somerville, New Jersey) (Plate IIG, H).

All condylotomies were performed bilaterally (14 in one sitting; 6 in separate procedures, two days apart); the only between-side difference was the composition of the implant (amalgam vs amalgam acrylic).

Sham Surgery

Twenty of the rats underwent sham procedures, that is, bilateral soft tissue incisions were made, implants placed, but the condyles were left intact (Figure 3).

Postoperative Care

Postoperatively, the rats were returned to their individual cages and were permitted to recover from the anesthetic. The rats were fed a soft feed in cake form (Tube Feeding Diet--Modified Rat, ICN Pharmaceuticals, Cleveland, Ohio) to stimulate the recovery of masticatory function subsequent to surgery. After three to four days of the soft diet, the rats were able to ear harder rat pellets (Purina Laboratory Chow, Ralston Purina Company, St. Louis, Missouri) for the remainder of the experimental period. Both diets and water were supplied ad libitum.

Growth Hormone

Growth hormone injections (Bovine, Somatotropin, Miles Laboratories, Inc., Kankakee, Illinois; Activity: 0.8-1.0 U.S.P. units/mg) were begun the day of surgery. On this and on each

successive day, growth hormone was injected intraperitoneally into half of the 20 condylotomized rats, and half of the 20 sham rats, as well as the 5 unoperated "assay" rats.

The daily dosage of 1 mg/100 gr body weight was administered for a 30 day period. Since the growth hormone was supplied in powder form, the exact amount of growth hormone was weighed daily and suspended in normal saline for injection. This was done daily to assure that the growth hormone did not lose its activity by being in suspension over an extended period of time.[2] Change in body weight was used to assay the effect of the growth hormone and was monitored daily to determine any needed increase in hormone dosage over the 30 day period (Figure 4).

The remaining 10 condylotomized and 10 sham rats received normal saline injections for the same 30 day period as the hormone-injected rats and were also weighed daily.

Data Collection

Using a rat cephalostat devised by Gange (1973) and modified by Fuller (1974), lateral cephalograms (Kodak Occlusal Film, DF-46; Eastman Kodak Company, Rochester, New York) were taken immediately after surgery and after the 30 day experimental period (Plate III). At each sitting, cephalograms were taken with the animal first facing right and then facing left. This was done to obtain separate radiographs having minimal magnification for both the right and left sides. The films were exposed for 0.12 seconds at 90kV and 15mA with the

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[2]Personal communications with chemists at Miles Laboratories.

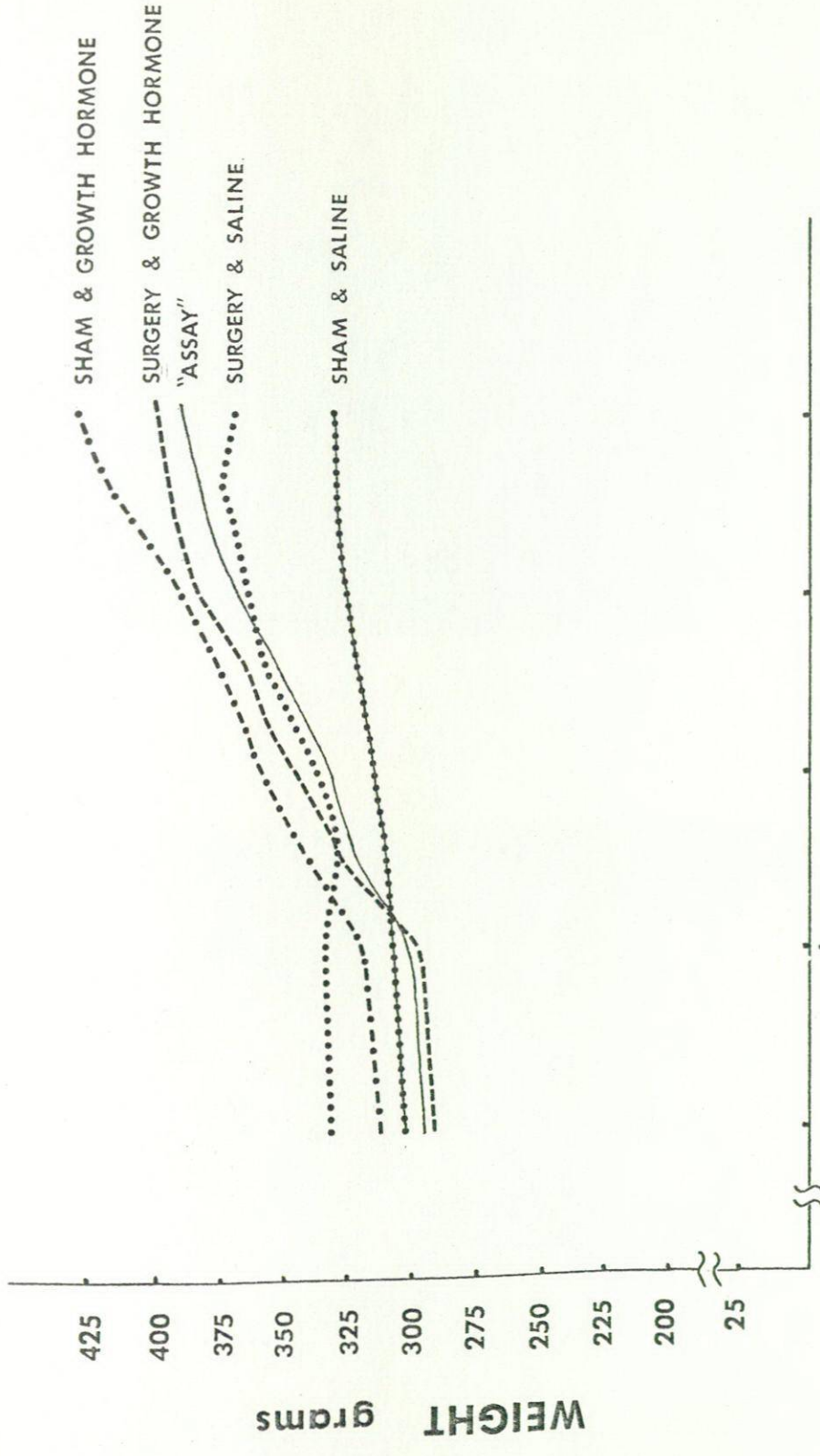


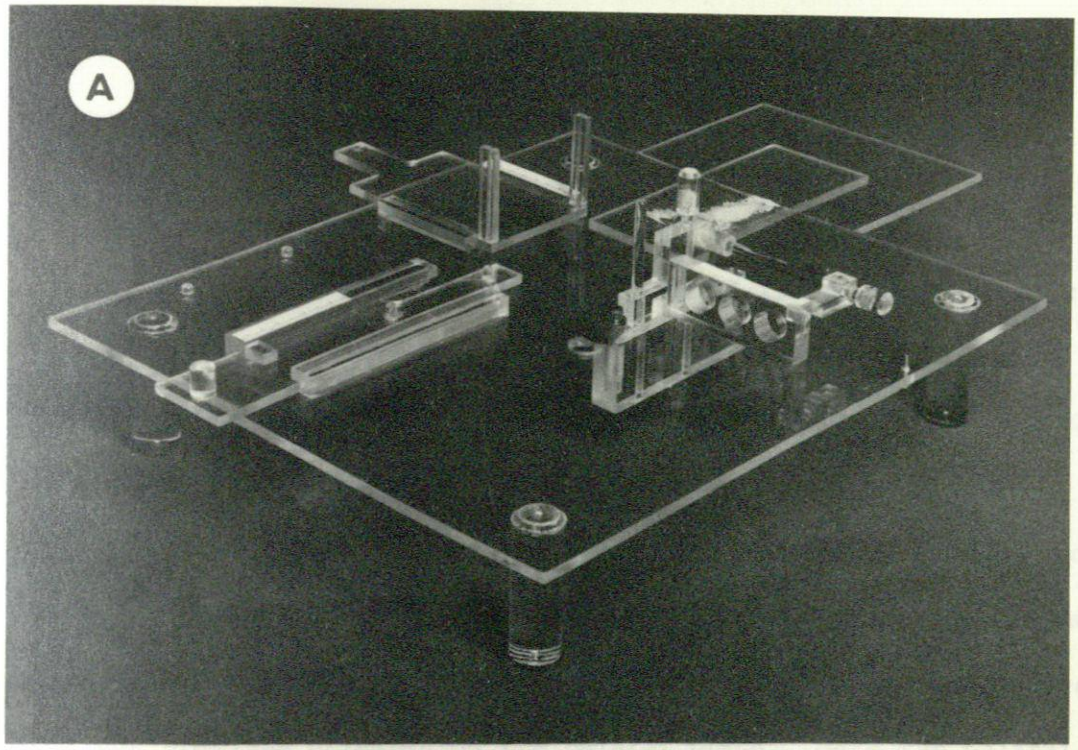
Figure 4.--Weight Gain of Sample

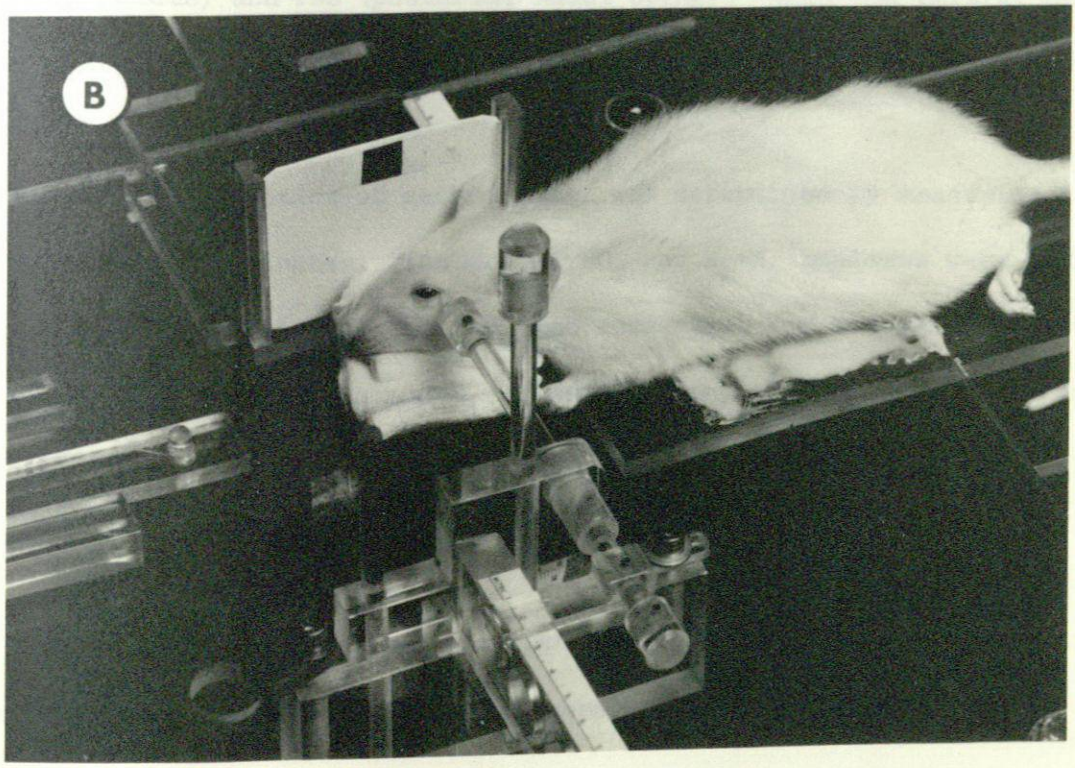
PLATE III.--Rat Cephalostat

Figure A.--Cephalostat

Figure B.--Radiographic Technique

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A


B

central ray directed perpendicular to the film through the external auditory meatus at a constant distance of 26 cm.

Cephalometric Analysis

Radiographs were mounted on a pane of glass which was placed on a cephalometric view box. The landmarks, summarized in Figure 5, were punched directly on the radiographs with a fine needle with the aid of a magnifying glass.

The "punched" radiographs (first day and thirtieth day) were mounted side-by-side on a piece of graph paper and placed on a view box for measurement. The analysis employed an X-Y coordinate system with the abscissa oriented on the palatal plane. Here the palatal plane is defined as the line passing through i (the intersection of the lingual periodontal ligament of the maxillary incisors and the bony palate) and PNS (posterior nasal spine). With the palatal plane oriented on the X axis, the Y axis is registered on the frontal implant (Plate IV).

The position of each implant was determined by measuring its Cartesian Coordinates. The dual C_1-C_2 and M_1-M_2 implants were employed to measure rotation of the isolated segments. The angular orientation of implant-lines C_1-C_2 and M_1-M_2 were determined by using the formula:

$$\text{arc tan } \frac{(YC_2 - YC_1)}{(XR_2 - XR_1)} = \theta$$

The entire analysis is depicted in Figures 6 and 7. All measurements were made with dial vernier calipers (Helios Dial

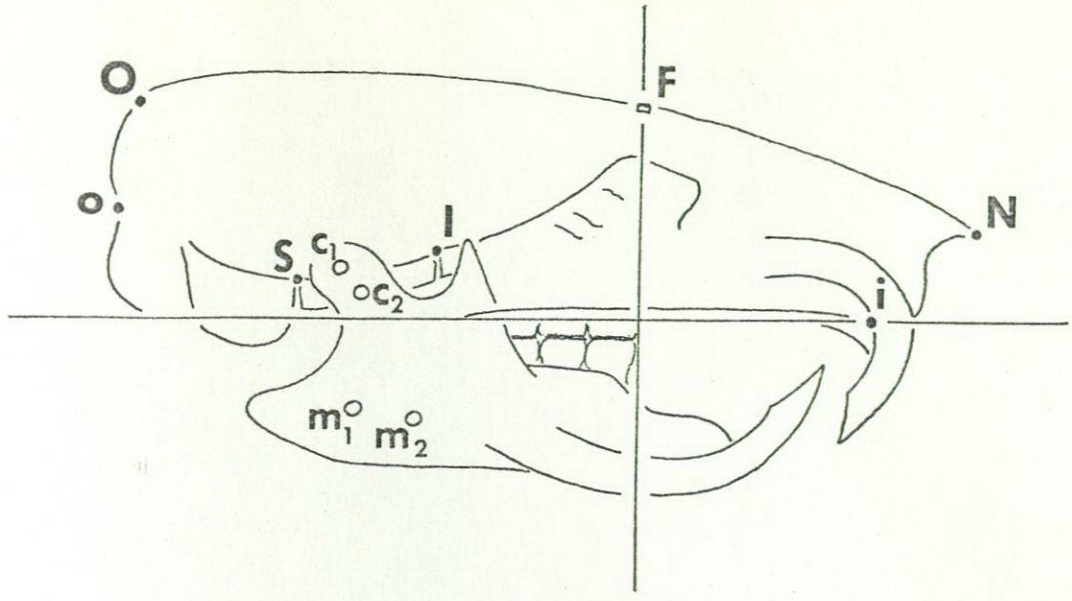


Figure 5.--Cephalometric Landmarks

A: Implants

F, midsagittal implant in the frontal bone; C_1, superior ramal implant; C_2, inferior ramal implant; M_1, posterior mandibular body implant; M_2, anterior mandibular body implant.

B: Anatomic Points

N, the tip of the nasal bone; S, the highest point of the sphenooccipital synchondrosis; I, the highest point of the interspheroidal synchondrosis; i, the intersection of the lingual periodontal ligament of the maxillary incisors and the bony palate; O, most posterior, superior aspect of the occipital bone; o, most posterior, inferior aspect of the occipital bone.

PLATE IV.--Cephalometric Analysis

Implants:

F = Frontal

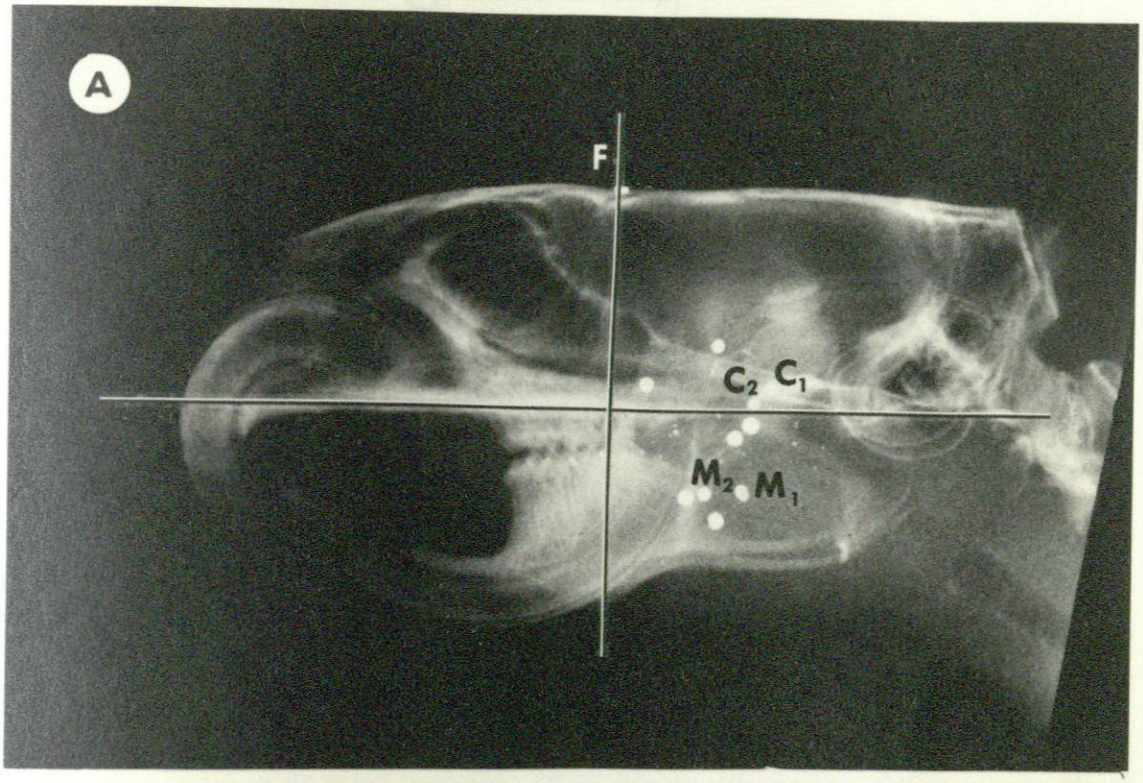
C_1, C_2 = Condyle

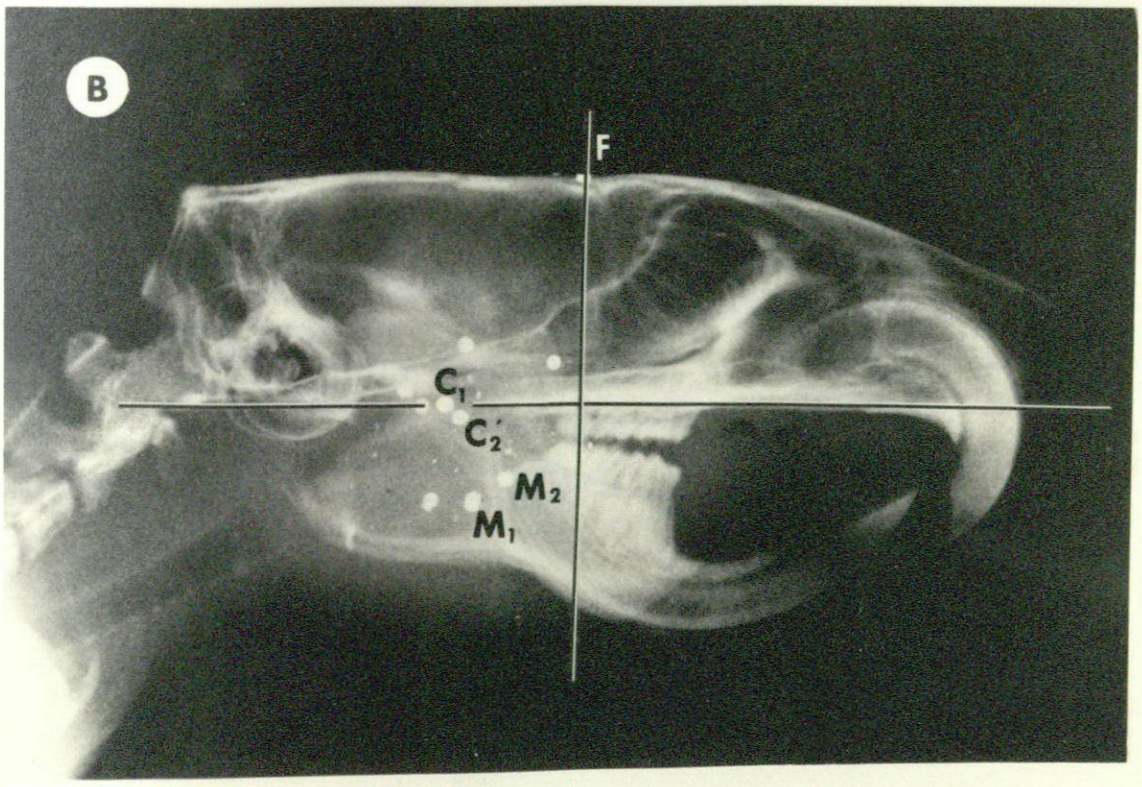
M_1, M_2 = Mandible

Figure A.--Right Side Analysis

Figure B.--Left Side Analysis

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A
F
C2 C1
M2 M1


B
F
C1
C2
M2
M1

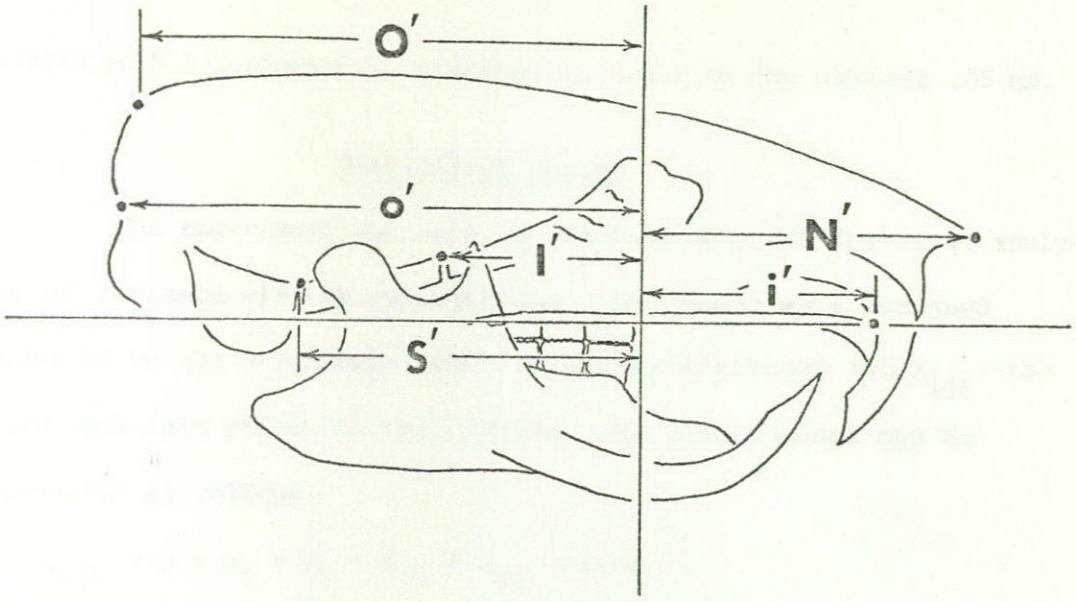


Figure 6.--Linear Measures; Anatomic Points

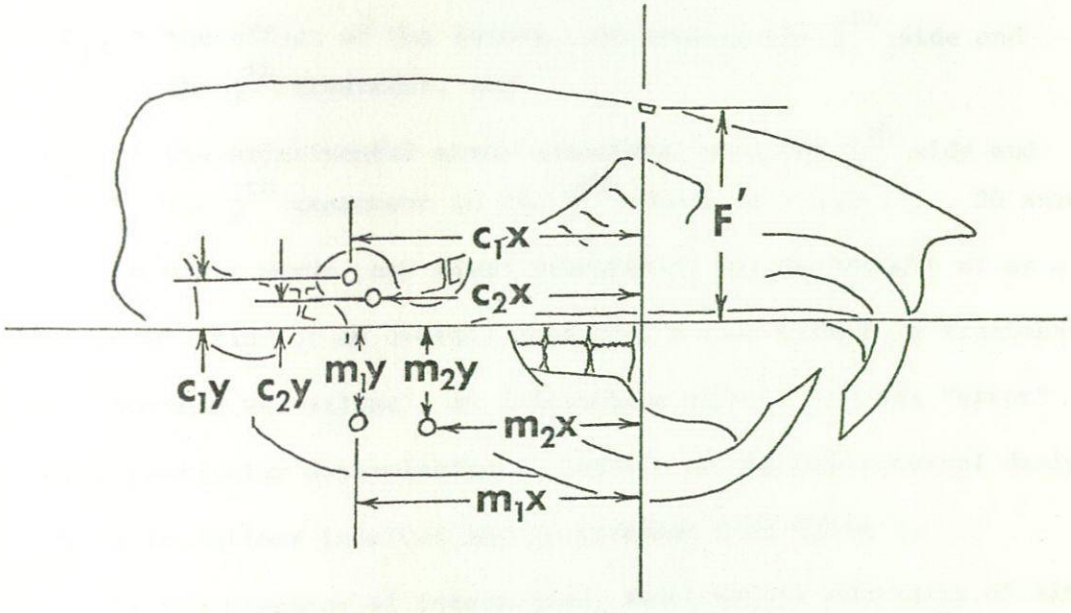


Figure 7.--Linear Measures; Implants

Calipers; DCA Corporation, Washington, D.C.) to the nearest .05 mm.

Statistical Design

The experiment was cast in the form of a 2X2 factorial analysis of variance with 20 replications. Treatments were assigned randomly to the 40 animals, each of which contributed two X_{ijk}--the right and left sides--to the outcome. The linear model may be expressed as follows:

$X_{ijk} = \mu + \alpha_i + \beta_j + \sigma_{ij} + \varepsilon_{ijk}$ where,

X_{ijk} = any measurement of the $\underline{i}^{th}$ side, $\underline{j}^{th}$ treatment, in the $\underline{k}^{th}$ animal,

μ = the population mean,

α_i = the effect of the $\underline{i}^{th}$ side (i = 1,2--right and left side),

β_j = the effect of the $\underline{j}^{th}$ treatment (j = 1,2--hormone or saline),

σ_{ij} = the effect of the interaction between the $\underline{i}^{th}$ side and the $\underline{j}^{th}$ treatment, and

ε_{ijk} = the experimental error associated with the $\underline{i}^{th}$ side and the $\underline{j}^{th}$ treatment in the $\underline{k}^{th}$ animal (k = 1,2 . . . 20 animals).

In other words, any given measurement may be thought of as a linear combination of an overall mean plus a side effect, a treatment effect (hormone vs. saline), an interaction effect, and the "error" for that particular determination. Details of the experimental design and the calculations involved may be inferred from Table I.

In the presence of interaction, supplemental contrasts of simple effects were performed. All calculations were performed on an electronic calculator (Model 9100A, Hewlett-Packard, Loveland, Colorado).

TABLE I

ANALYSIS OF VARIANCE DESIGN

Source	Degrees of Freedom df	Sum of Squares (SSQ)	Mean Squares (MSQ)
Surgery (side)	i - 1 = 1	$\sum_{ijk}^{2220} (\bar{X}_{i..} - \bar{X}...)^2$	$\frac{SSQ_{tr.}}{1}$
Treatment (Hormone)	j - 1 = 1	$\sum_{ijk}^{2220} (\bar{X}_{.j.} - \bar{X}...)^2$	$\frac{SSQ_{arches}}{1}$
Interaction	3 - 2 = 1	Subtotal - (Surg. + Treat.)	$\frac{SSQ_{intr.}}{1}$
Subtotal	i (j-1) = 3	$\sum_{ijk}^{2220} (\bar{X}_{ij.} - \bar{X}...)^2$	. .
Error	79 - 3 = 76	Total - Subtotal	$\frac{SSQ_{error}}{76}$
Total	IJK - 1 = 79	$\sum_{ijk}^{2220} (\bar{X}_{ijk} - \bar{X}...)^2$	. .

RESULTS

Descriptive Statistics

Means ($\bar{d}$) and standard deviations ($S.D._d$) for the change in the X-Y coordinates of the five implants, six anatomical landmarks, along with weight-change in each of the four groups and five "assay" animals are presented in Table II.

It may be noted from the means that there was downward and forward movement of the Group I (condylotomy and growth hormone) condyles (C_1 and C_2) over the thirty day experimental period. The vertical change was greater than the horizontal change. The Group II condyles (condylotomy and saline) displayed some horizontal change but in an upward and forward rotation. The Group III and IV condyles (sham surgery) displayed only very slight movement (Figure 8).

The mandible (M_1 and M_2) in both Groups I and II collapsed upward and backward while the Groups III and IV mandibles (sham surgery) showed only negligable change (Figure 9). Cranial and midfacial (O, o, i, and N) landmarks displayed some change in a horizontal direction in Groups I and II. The I and S landmarks and F implant showed little change in any group.

Inferential Statistics

The results of the analysis of variance contrasting the change in the X and Y coordinates for the implants and anatomical

TABLE II

DIFFERENCES OF MEANS AND STANDARD DEVIATIONS
(30 day experimental period)

	Group I Bilateral + Growth Hormone		Group II Bilateral + Saline		Group III Sham + Growth Hormone		Group IV Sham + Saline	
Measure	$\bar{d}$	$S.D._d$	$\bar{d}$	$S.D._d$	$\bar{d}$	$S.D._d$	$\bar{d}$	$S.D._d$
Implants: Condylar								
C_1X	+0.61	0.58	+0.30	0.79	+0.04	0.42	-0.20	0.47
C_1Y	-0.46	0.46	+0.26	0.32	-0.10	0.51	+0.02	0.39
C_2X	+0.44	0.54	+0.21	0.67	+0.05	0.45	-0.23	0.57
C_2Y	-0.42	0.57	+0.26	0.46	-0.02	0.42	+0.05	0.46
Implants: Mandibular Body								
M_1X	-0.47	0.64	-0.60	0.83	+0.18	0.63	-0.26	0.50
M_1Y	+0.22	0.69	+0.59	0.45	-0.06	0.45	-0.15	0.32
M_2X	-0.53	0.62	-0.58	0.79	+0.07	0.48	-0.30	0.49
M_2Y	+0.08	0.60	+0.44	0.43	-0.01	0.44	+0.02	0.32
Cranial and Midfacial								
O'	-0.31	0.27	-0.16	0.12	-0.41	0.28	-0.27	0.39
o'	-0.35	0.27	-0.23	0.21	-0.63	0.30	-0.38	0.44
I'	-0.14	0.23	-0.17	0.19	-0.19	0.23	-0.11	0.25
S'	-0.36	0.25	-0.23	0.24	-0.49	0.30	-0.37	0.36
i'	+0.61	0.31	+0.09	0.21	+0.50	0.34	+0.36	0.44
N'	+0.65	0.25	+0.15	0.28	+0.74	0.36	+0.50	0.58
F'	+0.03	0.11	+0.07	0.24	+0.22	0.21	+0.17	0.30
Weight								
Weight	83.55	17.86	7.40	29.58	98.35	25.71	14.70	13.59

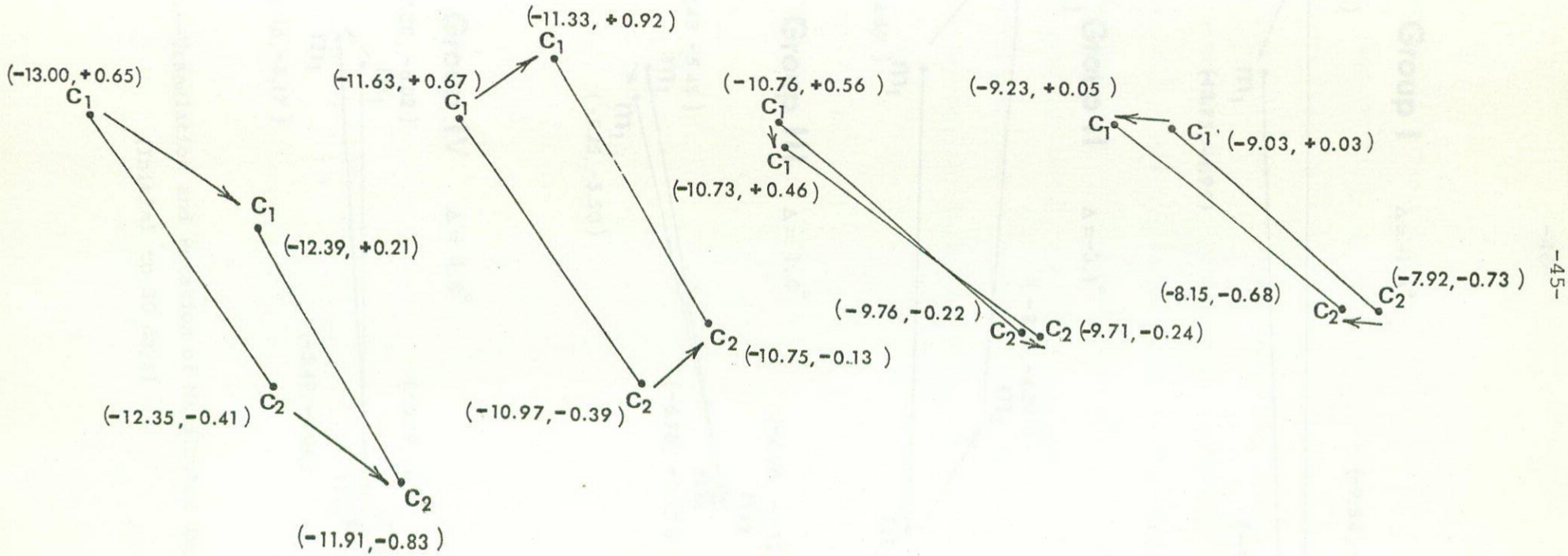


Figure 8.--Translation and Rotation of Condylar Implants
(Initial to 30 days)

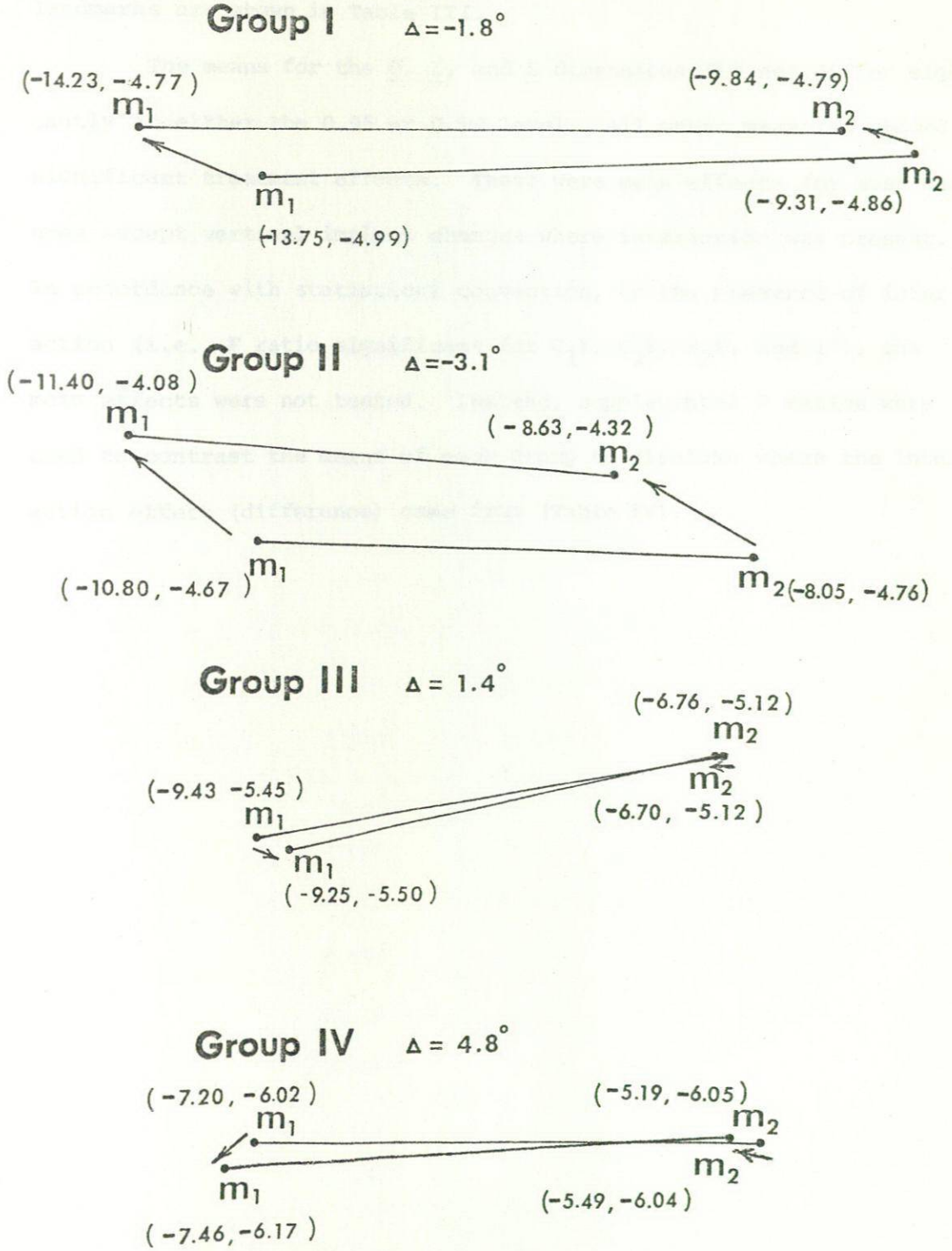


Figure 9.--Translation and Rotation of Mandibular Implants (Initial to 30 days)

landmarks are shown in Table III.

The means for the O, I, and S dimensions did not differ significantly at either the 0.95 or 0.99 level. All other measures showed significant treatment effects. These were main effects for most measures except vertical implant changes where interaction was present. In accordance with statistical convention, in the presence of interaction (i.e., F ratio significant for C_1Y, C_2Y, M_2Y, and i´), the main effects were not tested. Instead, supplemental F ratios were used to contrast the means of each group to disclose where the interaction effect (difference) came from (Table IV).

TABLE III

ANALYSIS OF VARIANCE

Measure	Variance Ratios (F)		
	Interaction	Surgery	Hormone
Implants: Condylar			
C_1X	0.074	17.124**	4.342*
C_1Y	8.846**	See Table IV	
C_2X	0.041	10.801**	3.994*
C_2Y	7.792**	See Table IV	
Implants: Mandibular Body			
M_1X	1.122	11.209**	3.572
M_1Y	4.537*	See Table IV	
M_2X	1.440	10.637**	2.253
M_2Y	2.899	6.192*	3.611
Cranium and Midfacial			
O'	2.106	0.300	0.595
o'	0.859	9.121**	7.293**
I'	2.897	0.010	0.093
S'	2.118	0.493	0.389
i'	6.446*	See Table IV	
N'	2.152	6.411*	17.887**
F'	0.940	8.560**	0.000
Weight			
Weight	0.276	2.395	125.206**

*Significant at .95 level ($F_{.95(1,76)} = 3.99$)

**Significant at .99 level ($F_{.99(1,76)} = 7.08$)

TABLE IV

SIMPLE EFFECTS

(Supplemental Contrasts Required by the Presence of Interaction)

Treatment Comparisons	df	Measure							
		C_1Y		C_2Y		M_1Y		i´	
		MSQ	F	MSQ	F	MSQ	F	MSQ	F
Hormone/Saline within Condylotomy	1	4.761	26.159**	4.489	19.43**	1.406	5.717*	2.704	24.143**
Hormone/Saline within Sham	1	0.150	0.825	0.049	0.212	0.095	0.386	0.196	1.750
Condylotomy/Sham within Hormone	1	1.122	6.166*	1.541	6.669*	0.743	3.019	0.121	1.080
Condylotomy/Sham within Saline	1	0.541	2.970	0.431	1.864	5.550	22.562**	0.729	6.509*

*Significant at 0.95 level ($F_{.95(1,76)} = 3.99$

**Significant at 0.99 level ($F_{.99(1,76)} = 7.08$

DISCUSSION

Introduction

The purpose of this study was to test the two prevailing theories of mandibular growth. The primary question to be examined was whether or not the condyle can grow independently (and thus act as a primary growth center) or whether it can only respond secondarily to the growth of the various functional matrices.

The experimental design (termed here, "site-center dissociation") involved the use of bilateral condylotomy to divide the mandible into separate parts which could then be challenged by growth hormone and whose individual response could be measured. Thus, the growth of each isolated element--condyles and body--were studied *in situ* in the relative absence of extraneous, uncontrolled variables associated with condylectomy, transplantation, and tissue/organ culture studies. In addition, since a bilateral approach was used in mature animals, variables such as interaction between sides and the influence of translatory midfacial growth were minimized.

Technical Details

Pilot procedures disclosed a number of obstacles which had to be overcome. At first, the surgery was a prolonged procedure; it was only after a number of animals were completed (in two stages) that the surgery could be done in one operation. For ease of implant

placement, a retrograde amalgam carrier (3/64" KG Retrograde Amalgam Carrier, Union Broach Company, Long Island City, New York) was found both to expedite implant placement and to minimize the number of extraneous amalgam fragments in the surgical area. At first, the animals would eat only a soft diet, but after three to four days they could be switched to the harder diet. This was an important transition since the continual growth of the incisors could interfere with mandibular closure if they are not worn down by masticatory function.

In preliminary work, the growth hormone had little effect. The lack of activity was attributed to deterioration in solution and too small a dosage. In the experiment, proper, the hormone solution was prepared daily and the dosage was increased so that an effect on weight was clearly evident.

Experimental Design

Although a 2 X 2 factorial design was employed, the results from one particular combination, bilateral condylotomy and growth hormone, were assumed from the beginning to be of prime importance in testing the two contemporary theories of mandibular growth. By inference from Fuller (1974), two mutually exclusive outcomes may be listed--one consistent with the functional matrix theory and the other consistent with the condylar growth center theory (Table V).

With respect to the mandible, the data appeared to be highly reliable. Condylar and ramus/body implants provided a relatively

TABLE V

EXPECTED VERTICAL CHANGES,[a]
CONDYLOTOMY AND
GROWTH HORMONE

	Theory	
Isolated Segment	Functional Matrix	Condyle
Condyle	No Growth	Growth
Ramus/Body	Growth	No Growth or Collapse

[a]See Figures 8 and 9 and Table II--for the relevant implants. Translatory growth is indicated by a negative (downward) change; collapse by a positive (upward) change.

precise indication of bodily movement and rotation for each mandibular segment and none were lost throughout the experimental period. Although the frontal implant was placed to assure a fixed registration point, the rhinal ridge was found to be stable relative to the frontal implant and thus could be substituted for an implant in future investigations. The cephalometric technique employed here had previously been shown to be reliable by Gange (1973) and was used successfully by Fuller (1974). To minimize errors each radiograph was measured twice with the correct measurement being recorded and any discrepancies rechecked prior to recording.

In Fuller's unilateral study (1974), a bony fusion was found between the condyle and mandibular segment. In the present study, all of the experimental animals were sacrificed after a thirty day period and only a soft tissue attachment was seen bridging the gap between the acrylic on the condyle and the ramus. Thus, whatever effects any tissues might have had, they are assumed to be similar for all four groups.

Findings

For purposes of discussion, the significant findings may be discussed under two headings: 1) cranium and midface, and 2) mandibular segments.

Cranium and Midface

The hormone-treated rats presumably underwent surface changes (deposition) similar to those seen in "acromegalic" rats (Collins

et al., 1949). In the present study, a significant "hormone effect" is attested to by the enlargement of the O', o', and N' measures, presumably due to surface deposition. The forward advancement of the incisor (i) in the shams was quite similar to the i' change in Group I (condylotomy-hormone), while in Group II (condylotomy-saline), advancement of i was much less pronounced. The relatively normal masticatory function of the shams might cause a mesial migration of the incisors, thus explaining the increase in Groups III and IV. It is interesting, that i' increases in the condylotomy-hormone group also. Growth hormone is known to accelerate eruption (Collins et al., 1949), a fact which might explain the increase seen here. Moreover, masticatory function is probably altered in this group, a fact which might also contribute to the increase.

Although the synchondroses appear radiographically to be "open," there was no appreciable synchondroseal growth as evidenced by a general lack of change for measures I' and S'.

Mandibular Segments

Horizontal Changes

In the horizontal dimension there was no interaction for the mandibular segments and, as a result, only main treatment effects are of interest. The condylotomy effect (compared to sham) was a forward rotation of the condyle in conjunction with a posterior collapse of the ramus/body segment. The hormone was associated with an increased forward growth (rotation?) of the condyle, while the mandibular segment displayed little change.

Vertical Changes

The changes in three of the four implants showed a significant interaction, and, as a result, simple effects (rather than main effects) must be examined (see Tables II and IV). It is interesting that the M_2 implant displayed a non-significant change. A levering action of the distal mandibular portion upward can be logically responsible for the seemingly small amount of M_2 vertical change.

In looking at the significant difference between hormone and saline, within condylotomy, it may be noted that hormone caused a significant downward growth of the condylar implants (the normal direction of growth), while saline was associated with a vertical change (rotation) opposite to the normal vector. The mandibular segment collapses with both hormone and saline, albeit significantly less when hormone was administered. There is, therefore, reason to suspect some effect from soft tissues, i.e., the tongue--a known target organ of growth hormone.

Moss (1960) has attributed mandibular elongation (as seen in acromegaly) to an enlargement of, among other things, the tongue. Although the effect seen here is much smaller than would be expected of a major growth center (capsular matrix), the present findings would seem to indicate that soft-tissue enlargement may exert some influence.

A comparison of condylotomy to sham, within hormone, makes it apparent that both condylar implants grew downward but that the isolated condyle grew more than the sham. This difference could be

due to a "release" from functional pressures associated with the body and ramus, and is, in fact, in accord with Fuller's (1974) finding that actively growing, isolated condyles grew faster than intact condyles.

It is interesting to note that the translation of isolated condyles in rats treated with a growth hormone (see Figure 8, Group I) was qualitatively almost identical to that reported by Fuller (1974, Figure 3, p. 35) for isolated condyles in growing guinea pigs.

The comparison between condylotomy and sham, within saline, shows a significant collapse of the distal mandibular implant. This finding poses an interesting question: If soft tissues and spaces caused the mandible to grow downward and forward in the first place, why would it collapse after condylotomy? That is, if there was once enough force to overcome muscle pull and translate the mandible downward and forward, it would seem that these matrices should be capable of maintaining the advanced position--if, as is claimed, the condyle is only a site of secondary, compensatory growth.

SUMMARY AND CONCLUSIONS

Today there are two opposing theories of craniofacial growth, each of which ascribes a different role to the mandibular condyle. The classical theory of mandibular growth holds that the condyle is an active growth center, is under intrinsic genetic control, and as such, effects a downward and forward translation of the mandible. In contrast, the functional matrix theory considers the condyle to be a growth site under extrinsic (environmental) control which responds compensatorily to the volumetric expansion of the oro-naso-pharyngeal capsular matrices.

The present study employed growth-hormone-treated mature rats to achieve a system (similar to acromegaly) in which translatory growth is largely restricted to the mandible. To determine the general location of the growth center(s) responsible for this bodily movement, the mandibles were dissociated into three parts: condyles and body. It was assumed that only the component associated with a growth center would still be capable of growth, and, thus, would serve to distinguish between the two theories.

The sample consisted of forty mature female rats divided equally among the following groups:

Group I - Bilateral condylotomy, growth hormone injections, metallic implants.

Group II - Bilateral condylotomy, saline injections, metallic implants.

Group III - Bilateral sham operations, growth hormone injections, metallic implants.

Group IV - Bilateral sham operations, saline injections, metallic implants.

In addition, five animals were used to assess the effect of bovine growth hormone on weight gain.

Throughout the thirty-day experimental period, all rats were weighed and injected daily with either saline of growth hormone (depending on what group they were in). Cephalometric radiographs were taken immediately after surgery and, again, thirty days later.

Implants were placed; two in the condyle-ramus area, two in the mandibular body, and one in the frontal bone. These, along with six anatomical landmarks, were used to evaluate cephalometrically treated changes in each of the four experimental groups.

It was found that isolated condyles responded to growth hormone injections by growing (translating) in a downward and forward direction. In contrast, the isolated condyles that received saline were found to rotate upward and forward. The body/ramus segment of both condylotomized groups collapsed upward and backward. Both groups of shams showed very little change in implant position.

The results of the study may be summarized:

1. Several cranial and midfacial dimensions increased during the experimental period. It is assumed that surface deposition was responsible, inasmuch as the hormone-treated animals grew more than did those injected with saline.

2. Condyles isolated in situ responded to growth hormone in a manner consistent with a growth center, while condyles without a growth promoting agent (saline) did not grow.

3. Mandibular bodies isolated *in situ* collapsed upward and backward irrespective of whether or not a growth promoting agent was administered. The collapse, however, was significantly greater in saline-treated animals.

4. The results of the present study conform closely to expectations generated by the classical theory and, as a result, would seem to demand a re-evaluation of the extent to which the functional matrix theory is applicable to mandibular growth.

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