Craniofacial growth following experimental craniosynostosis and craniectomy in rabbits

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Premature fusion of the coronal suture was produced in 9-day-old rabbits by immobilization of the suture area bilaterally with methyl-cyanoacrylate adhesive. The effects of suture fusion and its surgical release on suture growth and on skull morphology were evaluated by radiographic cephalometry. Immobilization resulted in significant changes in the angular dimensions in the vault toward an anteroposterior shortening. No permanent deformity was observed in the angular relationship between the cranial base and the facial skeleton. Craniectomy at 30 days, when a skull deformity had been established, resulted in rapid separation of the bones at the suture site which returned the deformed skull to a normal configuration by 90 days of age. Surgical removal of a normal suture in a control group also resulted in accelerated separation of the bones at the excised suture site, but it was less than after removal of an immobilized suture. The experimental data indicate that premature fusion of rapidly growing sutures results in consistent skull deformity. Early release of the fusion, when this is the primary abnormality, will result in spontaneous correction of the deformity.

KEY WORDS • skull growth • craniostenosis • craniosynostosis • craniotomy

Craniofacial deformities associated with craniosynostosis have resisted elucidation despite intensive investigation, and many basic questions on pathogenesis and treatment still remain. Virchow proposed a direct causal relationship between premature suture fusion and a subsequent vault deformity. This concept has been repeatedly questioned, mainly because similar deformities have been observed in the absence of suture fusion. The relationship of premature suture closure to other anomalies often coexisting with craniosynostosis also remains obscure. Some associated findings, such as neurological and ophthalmological abnormalities, have been attributed to increased intracranial pressure probably resulting from restricted brain growth. Attempts to demonstrate such a relationship in patients with isolated craniosynostosis, however, have been unsuccessful.

Finally, the correct treatment of craniosynostosis is unclear. Many neurosurgeons favor linear craniec-tomy as early as possible to release growth restriction and to allow for normalization of skull shape. Proponents of delayed surgery stress the reduced risk in older patients and the relative unimportance of the cosmetic appearance. These divergent opinions and uncertainties about pathogenesis and treatment have resulted from experimental and clinical studies in which premature suture fusion was only one facet of a complex interrelationship of craniofacial anomalies. To ascribe certain symptoms solely to suture fusion is suspect. Furthermore, since the ability to accurately diagnose sutureal closure is lacking, clinical material may include a mixture of different types and degrees of craniosynostosis.

This study presents a laboratory model of coronal suture fixation in neonatal rabbits, and documents the effect of premature suture fusion on skull development. In addition, the effect of early surgical intervention on subsequent skull growth is assessed.

Materials and Methods

Experimental Animals

Young rabbits of New Zealand White (Oryctolagus cuniculus) parents were used. The litters were limited to seven animals shortly after delivery in order to stan-

187
SUTURE IMMOBILIZATION
n=15

CRANIECTOMY
n=7

CRANIECTOMY
n=7

SHAM TREATMENT
n=19

Fig. 1. Graphic description of the experimental groups and surgical procedures.

dardize growth. All animals were maintained on a 12-hour light-dark cycle at 23 + 1° C, and a relative humidity of approximately 40%. Stock diet and water were provided ad libitum.

Model for Craniosynostosis

At 9 days of age, the baby rabbits were anesthetized by an intraperitoneal injection of sodium pentobarbital (20 mg/kg body weight). A midline scalp incision was made and the surfaces of the frontal and parietal bones bordering the coronal suture were exposed bilaterally by incision and retraction of the periosteum. The periosteum across the sutures was left intact. The exposed bone surfaces were roughened with the point of a needle.

Experimental craniosynostosis of the coronal suture was produced by immobilization of the suture with glue. Thin layers of methyl-2-cyanoacrylate adhesive* were applied bilaterally across the coronal suture in 15 animals, avoiding the sagittal suture. Radiopaque markers, consisting of dental amalgam, were inserted into the left parietal and frontal bones in holes made with a dental burr. The periosteal flaps were replaced over the markers and a topical antibiotic powder (Neomycin sulfate) was applied to the open wound. The skin incision was closed with interrupted 5-0 monofilament nylon stitches.

The procedure was repeated on 19 sham-treated animals except that no adhesive was applied. The different animal groups and experimental procedures are outlined in Fig. 1.

Experimental Craniectomy

At 30 days of age, seven animals with immobilized coronal sutures were anesthetized by intraperitoneal and intravenous administration of pentobarbital and the coronal suture area re-exposed by a midline incision. A strip of bone, 4 to 5 mm wide, including the coronal suture and extending from one parietotemporal suture to the other was removed. Care was taken to leave the underlying dura intact. The skin was closed as above and the animals were given 0.02 to 0.05 cc Crysticillin 300 A.S. (sterile penicillin G procaine suspension) daily for 5 to 7 days postoperatively.

To evaluate the effect of craniectomy alone on growth in the suture area, the same craniectomy procedure was repeated on seven animals from the sham-treated group.

Evaluation of Suture Growth and Skull Morphology

A roentgenocephalometric procedure was used to evaluate suture growth and skull development. Cephalograms were taken at Days 9, 30, 60, and 90, using a dental x-ray unit. To reveal any changes that might occur during and immediately after surgery, cephalometric recordings were additionally made on three animals with immobilized sutures and three sham-treated animals just before and after the surgical procedure on Day 30, and thereafter on Days 35 and 40. For the radiographic procedure, the animals were anesthetized by intraperitoneal or intravenous injections of sodium pentobarbital (20 to 30 mg/kg body weight) and positioned in a headholder. Lateral cephalograms were taken using Kodak No-Screen Film with a focus-film distance of 40 cm. Exposure time varied between 0.3 and 0.5 seconds at 64 kVp and 10 mA.

Growth of the coronal suture was determined by measuring on the cephalograms changes in the distance between inserted metal markers. A Vernier caliper was used to measure the distances to the nearest 0.1 mm.

Alterations in skull morphology were evaluated as angular changes between lines drawn through craniometrical points on the roentgenograms (Fig. 2). Besides the generally accepted and well defined craniometrical points basion (B), nasion (N), rhinion (Rh), and lambda (L), the following radiographic landmarks and lines were also used (the abbreviations are used in Fig. 2 and in the text below):

\[
\begin{align*}
O &= \text{a point in the center of the optic foramen} \\
Oi &= \text{the deepest point on the outer contour of the occipital bone between the foramen magnum and the external occipital protuberans} \\
Mp &= \text{the most posterior point on the marker in the parietal bone} \\
Ma &= \text{the most anterior point on the marker in the frontal bone} \\
J &= \text{the tip of the endocranial ridge (jugum limitans olfactorium) on the frontal bones separating the anterior and the middle cranial fossae} \\
S &= \text{the deepest point on the cartilaginous spheno-occipital synchondrosis} \\
PL &= \text{a line tangential to the lower border of the anterior bony palate} \\
BO' &= \text{the extension of the line through the points B and O}.
\end{align*}
\]

*Eastman 910 adhesive manufactured by Eastman-Kodak, Kingsport, Tennessee.
Experimental craniosynostosis

FIG. 2. Cephalogram (positive print) of a 30-day-old rabbit. The cephalometric landmarks, lines, and angles used for the recording of changes in cranial morphology are given (compare text). The arrow points to the coronal suture area.

The points and lines provided for the construction of the following angles:

- $BO'/PL$ (basilar-maxillary angle) = the angle formed between and below lines $BO'$ and $PL$
- $BO'/RhN$ (basilar-rhinal angle) = the angle formed between and below lines $BO'$ and through $RhN$
- $BO'/NO$ (basilar-nasal angle) = the angle formed between and above the lines $BO'$ and $NO$
- $BO'/JO$ (basilar-olfactorial angle) = the angle formed between and above lines $BO'$ and $JO$
- $BO'/MaO$ (basilar-anterior marker angle) = the angle formed between and above lines $BO'$ and $MaO$
- $BO'/MpS$ (basilar-posterior marker angle) = the angle formed between and above lines $BO'$ and $MpS$
- $BO'/LS$ (basilar-lambdoid angle) = the angle formed between and above lines $BO'$ and $LS$
- $BO'/BOi$ (basilar-foraminal angle) = the angle formed between and above lines $BO'$ and $BOi$.

All angles were recorded to the nearest one-half of a degree by direct measurements on the films with a protractor.

Histological Evaluation of Suture Fusion

Six bilateral specimens of immobilized sutures, removed by craniectomy at 30 days, were examined histologically for suture fusion. Four sets of specimens were also obtained from animals with immobilized sutures at 90 days of age and compared to specimens from sham-treated animals. The specimens were fixed in alcoholic formalin, decalcified in a formic acid/sodium formate mixture, and embedded in paraffin. Sections 7 μ thick were subsequently stained with Harris' hematoxylin-eosin and Heidenhain's azan stain.

Statistical Analysis

The mean and standard error were calculated for each dimension measured on the cephalograms and for each age group. The significance of changes between successive age groups and within and between different experimental groups was assessed by the Student's t-test.

The error of the cephalometric method was evaluated on 10 double recordings on Days 9 and 90. Between the recordings, the animals were removed...
from the headholder and re-positioned. The error of the method, $s(i)$, was calculated by the formula $s(i) = \sqrt{\frac{(x-x)^2}{2n}}$. This test showed that $s(i)$ for the eight angles studied varied between 0.47 (angle BO'/PL) and 2.06 (angle BO'/JO), the higher $s(i)$ values associated with anterior angles in young animals.

**Results**

**Growth in Suture Area after Craniosynostosis and Craniectomy**

In normal rabbits the coronal suture expanded an average of 4.4 mm from Day 9 to Day 30 (Table 1 and Fig. 3). In animals with methyl-cyanoacrylate adhesive applied to the suture, growth was significantly restricted to 1.0 mm. Growth continued in the normal animals with a total average expansion of 7.4 mm between Days 9 and 90. In contrast, only a few animals with the immobilized suture showed a slight expansion at the suture between 30 and 60 days, yielding a total average expansion for the 90-day period of 1.2 mm.

Removal of the immobilized coronal suture at 30 days by craniectomy resulted in a significantly accelerated separation of the bones in this area compared to their separation during normal growth (Table 1, Fig. 3). By 90 days of age this accelerated growth at the craniectomy site had compensated for the early restriction, and the average marker separation became identical to 90-day-old sham-treated rabbits. Except for an immediate separation of the coronal markers during surgery (0.2 mm), the expansion following craniectomy appeared to be evenly distributed over the 30 to 60-day period as judged by cephalograms taken 5 and 10 days after surgery on three of the animals.
Experimental craniosynostosis

Changes in craniofacial morphology following craniosynostosis and craniectomy

The changes in the craniofacial morphology due to normal growth and following specific manipulations of the coronal suture are recorded in Tables 2 to 6 and depicted in Fig. 5. In summary, the angular changes resulting from immobilization of the suture indicated a significant constriction of the vault, mainly by posterior shortening. At 90 days of age, all four posterior-vault angles were significantly different in the experimental animals from those of the controls. Craniectomy of the immobilized sutures at 30 days, after a significant vault deformity had already been established, resulted in compensatory angular alterations which yielded a normal morphology by 90 days of age. Removal of a non-fused suture in sham-treated animals was not accompanied by significant alterations in angular dimensions.

More detailed analysis showed that in the period immediately following immobilization of the suture

Changes in angular dimensions following the immobilization of the coronal suture in 9-day-old rabbits

<table>
<thead>
<tr>
<th>Angle</th>
<th>Days 9–30</th>
<th>Days 30–60</th>
<th>Days 60–90</th>
<th>Days 9–90</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean SE</td>
<td>p</td>
<td>Mean SE</td>
<td>p</td>
</tr>
<tr>
<td>BO'/PL</td>
<td>-0.8 0.4</td>
<td>&lt; 0.001</td>
<td>-5.8 1.4</td>
<td>NS</td>
</tr>
<tr>
<td>BO'/RhN</td>
<td>2.6 0.5</td>
<td>0.005</td>
<td>-2.0 1.1</td>
<td>NS</td>
</tr>
<tr>
<td>BO'/NO</td>
<td>-2.4 0.7</td>
<td>0.05</td>
<td>6.8 2.0</td>
<td>NS</td>
</tr>
<tr>
<td>BO'/JO</td>
<td>0.4 1.0</td>
<td>0.5</td>
<td>0.1 0.8</td>
<td>NS</td>
</tr>
<tr>
<td>BO'/MaO</td>
<td>6.9 1.1</td>
<td>&lt; 0.001</td>
<td>5.6 0.5</td>
<td>0.005</td>
</tr>
<tr>
<td>BO'/Mps</td>
<td>-1.4 0.4</td>
<td>&lt; 0.001</td>
<td>-1.6 0.5</td>
<td>0.025</td>
</tr>
<tr>
<td>BO'/LS</td>
<td>-4.7 0.5</td>
<td>&lt; 0.001</td>
<td>-3.8 0.7</td>
<td>NS</td>
</tr>
<tr>
<td>BO'/Boi</td>
<td>-4.7 0.6</td>
<td>NS</td>
<td>-5.6 1.0</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Measurements are in degrees. p = statistical comparison of immobilized animals to sham-treated animals. NS = not statistically different (p > 0.05). For definition of angles see text.
FIG. 5. Alterations in cranial morphology with age in the different experimental groups as revealed by changes in the different angular dimensions on the cephalograms. For definition of the angles, see text. Black circles = sham treated at Day 9; black squares = immobilized at Day 9; white squares = craniectomized at Day 30 following immobilization at Day 9; white circles = craniectomized at Day 30 after sham treatment at Day 9. Initial measurements are performed at Day 9, and the subsequent changes are recorded at Days 30, 60, and 90. Upper: Effect of suture immobilization (black squares) compared to sham treatment (black circles). Note the deviation of angular dimensions after immobilization, especially those of the posterior part of the vault. Center: Effect of craniectomy of an immobilized suture at Day 30 (white squares) on subsequent cranial growth. Note the catch-up growth following craniectomy of the immobilized suture by which the angles of the vault come close to those of sham-treated animals. Note also the over-correction, especially for the dimension BO/JO. Lower: Effect of craniectomy of a normal suture (white circles) on subsequent cranial growth. Note that the angular dimensions following craniectomy of a normal suture do not markedly differ from those of sham-treated controls.
Experimental craniosynostosis

**TABLE 4**

Changes in angular dimensions following linear craniectomy at 30 days of immobilized coronal sutures*

<table>
<thead>
<tr>
<th>Angle</th>
<th>Days 30-60</th>
<th>Days 60-90</th>
<th>Days 9-90</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean SE</td>
<td>p</td>
<td>Mean SE</td>
</tr>
<tr>
<td>BO'/PL</td>
<td>-7.4 0.6</td>
<td>0.010</td>
<td>-2.9 0.4</td>
</tr>
<tr>
<td>LO'/RhN</td>
<td>-2.7 0.4</td>
<td>NS</td>
<td>-1.8 0.4</td>
</tr>
<tr>
<td>BO'/NO</td>
<td>9.2 1.9</td>
<td>&lt; 0.001</td>
<td>5.4 1.0</td>
</tr>
<tr>
<td>BO'/JO</td>
<td>-5.3 1.3</td>
<td>0.005</td>
<td>-0.5 1.1</td>
</tr>
<tr>
<td>BO'/MaO</td>
<td>-2.2 0.5</td>
<td>&lt; 0.001</td>
<td>-1.1 0.4</td>
</tr>
<tr>
<td>BO'/MpS</td>
<td>2.3 0.5</td>
<td>0.010</td>
<td>0.3 0.4</td>
</tr>
<tr>
<td>BO'/LS</td>
<td>-1.1 0.4</td>
<td>0.025</td>
<td>-1.2 0.6</td>
</tr>
<tr>
<td>BO'/BOi</td>
<td>-4.3 0.8</td>
<td>NS</td>
<td>-1.7 0.6</td>
</tr>
</tbody>
</table>

*Measurements are in degrees. NS = not statistically different (p > 0.05). For definitions of angles see text.

§Statistical comparison of the total angular change for initially immobilized animals which received a craniectomy at 30 days compared to sham-treated control animals.

(9 to 30 days) all angular changes except the basilar-foraminal (BO'/BOi) changes were significantly different from those in sham-treated animals with unrestricted growth (Tables 2 and 3, Fig. 5 upper). The changes were such that the facial skeleton was slightly restricted in its normal downward rotation. In the vault, the changes were consistent with an expanding cranial base and an inhibited separation of the bones at the coronal suture. During the 30- to 60-day period, only the marker angles (BO'/MpS and BO'/MaO), which are most closely associated with the immobilized suture, showed continued significant deviation from the normal growth pattern. From Day 60 to Day 90 the anterior marker angle (BO'/MaO) persisted in this pattern. During this late stage of development a significant alteration of normal development was noted in the basilar-foraminal angle (BO'/BOi). This angle had previously been similar to sham-treated animals. Less deviation occurred with age, but at 90 days the marker angles on each side of the fused suture (BO'/MpS and BO'/MaO) and the two angles related to posterior vault structures (BO'/LS and BO'/BOi) were significantly different from normal.

The initial changes in the anterior vault angles (BO'/JO and BO'/NO) and in the relationship between the face and cranial base (BO'/PL and BO'/RhN) did not result in significant differences from sham-treated animals by the age of 90 days.

Following craniectomy of an immobilized suture at 30 days, further deviation from normal growth patterns was halted. Creation of an artificial suture allowed for a dramatic re-orientation of spatial configuration (Table 4, Fig. 5 center). All angles except BO'/RhN and BO'/BOi had significantly accelerated changes in orientation in the 30-day period following craniectomy when compared to the changes occurring from normal growth alone in sham-treated animals. The most dramatic changes occurred in the marker angles (BO'/MpS and BO'/MaO) which are closest to the artificially created suture. In these dimensions a complete reversal of direction in the angular changes toward a normal morphology occurred. During the 60- to 90-day period further changes were similar to normal animals except for the marker angle BO'/MaO. At the end of 90 days, the compensatory growth toward normal yielded a skull morphology in which the total angular changes were similar to those found in the sham-treated animals. Only the angle BO'/JO was different from normal, and this was due to an over-compensation. Similar overcorrections were measured for the other two anterior vault angles, but these differences were not statistically significant.

In contrast to the marked changes in morphology when an immobilized suture was removed, cranietomies of normal sutures in sham-treated 30-day-old rabbits did not result (except for angle BO'/JO) in angular changes that significantly differed from those due to normal growth (Table 5, Fig. 5 lower).

**TABLE 5**

Changes in angular dimensions following linear craniectomy at 30 days of normal coronal sutures*

<table>
<thead>
<tr>
<th>Angle</th>
<th>Days 30-60</th>
<th>Days 60-90</th>
<th>Days 9-90</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean SE</td>
<td>p</td>
<td>Mean SE</td>
</tr>
<tr>
<td>BO'/PL</td>
<td>-6.0 0.4</td>
<td>-2.6 0.3</td>
<td>-12.6 1.0</td>
</tr>
<tr>
<td>BO'/RhN</td>
<td>-2.2 0.7</td>
<td>-1.3 0.4</td>
<td>-3.1 0.9</td>
</tr>
<tr>
<td>BO'/NO</td>
<td>7.9 0.9</td>
<td>3.1 0.6</td>
<td>11.0 1.5</td>
</tr>
<tr>
<td>BO'/JO</td>
<td>-2.5 0.7</td>
<td>1.1 0.5</td>
<td>-3.4 1.1</td>
</tr>
<tr>
<td>BO'/MaO</td>
<td>1.3 0.7</td>
<td>-0.2 0.6</td>
<td>2.5 0.6</td>
</tr>
<tr>
<td>BO'/MpS</td>
<td>0.6 0.3</td>
<td>0.2 0.3</td>
<td>3.4 0.7</td>
</tr>
<tr>
<td>BO'/LS</td>
<td>-2.9 0.8</td>
<td>0.0 0.4</td>
<td>-5.1 0.7</td>
</tr>
<tr>
<td>BO'/BOi</td>
<td>-4.7 0.6</td>
<td>-1.4 0.7</td>
<td>-9.9 0.7</td>
</tr>
</tbody>
</table>

*Measurements are in degrees, p = Statistical comparison of 90-day-old rabbits which had cranietomies of their normal coronal sutures at Day 30 with normal 90-day-old rabbits. NS = not statistically different (p > 0.05). For definition of angles see text.
the angular changes during the immediate postoperative period (30 to 60 days) were compared for the two craniectomy groups (immobilized/craniectomized and sham-treated/craniectomized) only two angles differed significantly (Table 6). These two angles were the marker angles most closely related to the suture (BO'/MpS and BO'/MaO), which showed the most dramatic changes following release of a fused suture.

**Discussion**

This study showed that premature fusion of a cranial suture can be experimentally induced as an isolated defect. With this model the relationship between suture fusion, *per se*, and its associated anomalies can be evaluated. Although this study did not address the question of pathogenesis of premature fusion, we consider, based on the abundance of case reports on craniosynostosis, that suture fusion does not always occur secondary to a primary dyscephaly.27-28 Early suture fusion can result from factors acting at a later developmental stage, such as mechanical factors following shunting procedures for hydrocephalus,2 and metabolic factors, such as rickets41 and hyperthyroidism.29 Recognition of the multi-causal etiology of craniosynostosis is essential since the presence of other dyscephalies will influence not only the clinical picture of the deformity but also the surgical outcome. In our model the suture fusion was artificially generated and known to be the primary abnormality. Removal of the immobilized/fused suture, after a significant deformity has been established, will thus show the degree of spontaneous correction that can be anticipated from early surgical intervention. Incomplete correction cannot be attributed to dyscephalies of other origins since suture fusion is the primary anomaly.

**Craniofacial Growth Following Craniosynostosis**

The changes in skull morphology following experimental synostosis were in line with Virchow’s classical concept that premature fusion causes marked limitation on cranial growth at right angles to the abnormal suture.37 Immobilization of the coronal suture resulted in a marked inhibition of its anteroposterior growth as measured by marker separation in the frontal and parietal bones. This restriction of vault expansion, while the cranial base continued its normal growth, produced significant alterations in the angular dimensions of the posterior vault. The result was a brachycephalic skull similar to that associated with coronal synostosis in man. Hence, our results indicate that premature sutural fusion alone is a causal factor for the calvarial deformity seen in craniosynostosis.

The restriction in normal vault growth resulting from external immobilization of the coronal suture caused a significant alteration in the basilar-foraminal angle (BO'/BOi). This remote alteration may question the concept that a basicranial deformity is primary in the development of premature suture fusion.2",21 According to this concept, a basicranial deformity acts “inside-out” by transmitting abnormal tensions through the dural tissue connecting the cranial base and the suture. A direct causal relationship between cranial base deformity and sutural fusion in craniosynostosis has yet to be documented. However, the reverse situation (“outside-in”) in which a primary vault deformity results in an altered cranial base has been observed. Restriction of normal vault development in infants by head-binding results in cranial deformity similar to that seen in craniosynostosis, and has been shown to result in significant changes of the cranial base.22,28 These observations strongly suggest that the basicranial deformity seen in craniosynostosis is, in part, a manifestation of the sutural fusion.

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**TABLE 6**

Comparison of changes in angular dimensions following a linear craniectomy at 30 days in animals with immobilized and sham-treated sutures*

<table>
<thead>
<tr>
<th>Angle</th>
<th>Days 30-60</th>
<th>Days 60-90</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Immobilized</td>
<td>Sham-Treated</td>
</tr>
<tr>
<td>BO'/PL</td>
<td>-7.4 0.6</td>
<td>-6.0 0.4</td>
</tr>
<tr>
<td>BO'/RhN</td>
<td>-2.7 0.4</td>
<td>-2.2 0.7</td>
</tr>
<tr>
<td>BO'/NO</td>
<td>9.2 1.9</td>
<td>7.9 0.9</td>
</tr>
<tr>
<td>BO'/JO</td>
<td>-5.3 1.3</td>
<td>-2.5 0.7</td>
</tr>
<tr>
<td>BO'/MaO</td>
<td>-2.2 0.5</td>
<td>0.5 1.0</td>
</tr>
<tr>
<td>BO'/MpS</td>
<td>2.3 0.5</td>
<td>0.6 0.3</td>
</tr>
<tr>
<td>BO'/LS</td>
<td>-1.1 0.4</td>
<td>-2.9 0.8</td>
</tr>
<tr>
<td>BO'/BOi</td>
<td>-4.3 0.8</td>
<td>-4.7 0.6</td>
</tr>
</tbody>
</table>

*Measurements are in degrees. NS = not statistically different (p > 0.05).
†Statistical comparison of the changes in angular orientation following craniectomy of an immobilized coronal suture compared to changes after craniectomy of a normal coronal suture.
Experimental craniosynostosis

Since the deformity results from growth restriction, most of the deformity should occur during the period of rapid skull growth. This, indeed, was the case in our model since the most significant alterations occurred in the 9- to 30-day period. This period, however, occurs after the rabbit’s brain has already achieved 40% to 50% of its adult weight, a stage which in humans is reached at about 6 months of postnatal age. More profound deformities due to early suture fusion would therefore be anticipated in humans, in whom suture fusion at birth is associated with a brain that is only 25% of its adult size. The degree of deformity is also dependent on which specific suture or sutures are inhibited in their normal growth. Unfortunately, quantitative data on neurocranial sutural growth is lacking completely for humans and for rabbits during the early postnatal period. Nevertheless the most severe deformity in both humans and rabbits during the early postnatal period. The degree of deformity is also dependent on which specific suture or sutures are inhibited in their normal growth. Unfortunately, quantitative data on neurocranial sutural growth is lacking completely for humans and for rabbits during the early postnatal period. Nevertheless the most severe deformity in both humans and rabbits is considered to follow the premature fusion of the coronal suture.

Comparison between the animal model and man with regard to the effect of calvarial fusion on the nasomaxillary complex must be made with caution as different morphogenetic processes are considered to regulate the orientation of the adult facial skeleton in the two species. In man, midface distortion is often associated with coronal synostosis but is probably not a direct result. Similarly, Greene observed in a strain of rabbits with congenital coronal synostosis, that the marked calvarial defect was not always accompanied by a facial distortion. Other studies with rodents, in which normal calvarial growth was experimentally altered, failed to produce any effect in the facial area. Results from our study documented the independence of calvarial and facial growth. Although there were immediate changes in facial orientation following immobilization of the coronal suture, these changes were ameliorated with further development. This may indicate that the compensatory facial adjustment to the calvarial deformity was insufficient in the initial stages when the neurocranial growth rate far exceeded the facial growth rate.

**Craniofacial Growth Following Linear Craniectomy**

Linear release of the fused suture, after a calvarial deformity had been established, resulted in immediate and long-lasting alterations in skull shape. The changes were such that they all acted toward reversal of the existing deformity, and within 60 days after release of fusion skull morphology was not statistically different from normal litters. The results therefore strongly argue for the concept that early release of “bound” structures is important to allow growth and functional forces to operate toward normalizing the craniofacial morphology.

Normalization of the skull shape appears to have resulted primarily from a significantly accelerated expansion of the vault at the craniectomy site. As measured by marker separation, the surgical defect more than doubled its original width, although this dramatic effect was partially masked by subsequent reossification along the border of the defect. The rapid vault expansion following suture release was associated with significant changes in spatial orientation. These were most dramatic in the marker angles BO/MpS and BO/MaO, which actually reversed their direction following release of suture immobilization. These observations indicate that the effectiveness of a linear craniectomy procedure is dependent on the ability of the bones to regain normal spatial movements.

Surgical removal of a non-fused coronal suture in sham-treated animals also resulted in accelerated expansion at the suture site compared to controls. This vault expansion, however, was not associated with significant alterations in skull morphology as seen after removal of a fused suture. Growth in other sutural areas may, therefore, have adjusted to this local overgrowth to keep the spatial orientations similar to normal. This result is in accordance with other experimental studies where removal of a healthy suture has not been found to influence overall morphology. However, in our model one angle in the anterior vault (BO/JO) was significantly altered. This tendency for over-correction was also noted following craniectomy of a fused suture. Overcompensation in the anterior vault may reflect a larger capacity for adjustment in this area because of its association with the later maturing facial structures.

The accelerated growth following removal of a fused suture was significantly higher than that following craniectomy of a non-fused suture. This indicates that fusion of a suture results in a specific restraintment of normal growth in the rapidly growing vault, and this restraintment is released by early surgery. Development of abnormal stress in the fused skull or its fibrous capsules (the dura and the periosteum) is further indicated by the spring-like, although limited, separation of the bones at surgery. A similar immediate opening-up at the craniectomy site has been observed in humans. Inability to relate this opening-up to an increased intracranial pressure supports the idea that single suture fusion does not restrict brain growth but generates a biomechanical stress within the bone or its periosteal matrices.

Sutural growth in the vault is a secondary and compensatory response to forces resulting from the volumetric expansion of the neural mass. Although sutural growth is extrinsically determined, it has been suggested that intrinsic factors, such as the sutural fibers, may partially regulate the effect of external forces on sutures, thereby modifying their growth. This presumption is strongly supported by the occurrence of an accelerated separation of constituent bones when a normal suture is removed, thus indicating that sutures and connected soft tissues are a restraining component during normal growth. A large part of the catch-up of restricted growth following

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release of a fused suture may therefore consist of a simple obligatory increase in normal separative growth as a direct result of the craniectomy per se. 

Many surgeons stress the need for early surgical intervention in craniosynostosis for strictly cosmetic reasons.3,8,18,21 Our results support such a concept since the experimental data show that release of fusion will not only prevent a continuation of the induced aberrant growth pattern, but will actually reverse the existing cosmetic defect. Reports of incomplete cor-


growth as a direct result of the craniectomy early suturectomy may therefore be due to an additional restriction or dyscephaly that does not allow the freedom of bone movement necessary to permit neurocranial and other forces to act toward normaliza-


tion of skull shape.

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