

Effects of Rigid Plate Fixation and Subsequent Removal on Craniofacial Growth in Rabbits

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Objective: To examine the effects of rigid plate fixation (RPF) and subsequent removal on craniofacial growth in rabbits.

Design: Randomized controlled experiment.

Subjects: Thirty-two 6-week-old male New Zealand white rabbits.

Interventions: Group 1 underwent exposure of the left nasofrontal suture and midzygomatic arch; group 2, RPF of the left nasofrontal suture and midzygomatic arch areas; group 3, single osteotomy at left nasofrontal suture and double osteotomies at midzygomatic arch with RPF of osteotomies; and group 4, controls. At 11 weeks of age, the RPF was removed. Animals were killed at 20 weeks of age. Linear and 3-dimensional measurements (euclidean distance matrix analysis) were used to evaluate craniofacial regions.

Results: In comparison with control animals, linear data showed shortening of the left nasal bone in group 3. Groups 1 through 3 also exhibited shortening of the left zygomatic arch, orbital diameter, and anterior midfacial height. Euclidean distance matrix analysis showed significant restrictive shape alterations on both the ipsilateral and contralateral sides in groups 1 through 3. In comparison with animals in which RPF was left in place, linear data showed significant shortening of the orbital diameter in groups 1 through 3 and of anterior midface height in groups 2 and 3. Euclidean distance matrix analysis showed significant restrictive shape alterations on both contralateral and ipsilateral sides.

Conclusion: Rather than preventing restrictive growth disturbances to the growing midface in rabbits, RPF with subsequent removal produces a greater amount of restrictive shape alteration than RPF that is left in place.

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ADVANCEMENTS in rigid plate fixation (RPF) techniques and materials have led to their widespread use in the treatment of facial fractures and craniofacial anomalies in the pediatric population. There is increasing evidence that RPF of the growing craniofacial regions produces marked restrictive shape alterations at the site of application, as well as to contralateral craniofacial regions.¹⁻⁵ An earlier study demonstrated that RPF, bony trauma, and soft tissue trauma make independent contributions to restriction of the growing midface of rabbits.⁶ Linear data showed that RPF with osteotomy also had more effect on midfacial growth than RPF, bony trauma, or soft tissue trauma alone. The purpose of the present study was to determine whether removal of RPF would reduce or prevent the restrictive growth effects induced by their application. Linear and 3-dimensional analysis of craniofacial

landmarks and regions by euclidean distance matrix analysis (EDMA) was used to analyze facial growth.

RESULTS

Gross examination of group 1 animals showed slight leftward deviation of the snout and leftward curvature of the nasal bones. In group 2 and 3 animals, there was notable leftward deviation of the snout, leftward curvature of the nasal bones, shortening of the left zygomatic arch, and a smaller left orbital diameter. All osteotomy sites were well healed with no retained screws or plates.

Comparison of the left- and right-sided linear measurements disclosed sev-

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MATERIALS AND METHODS

SURGICAL PROCEDURE

The experimental protocol is similar to that previously described.⁶ Thirty-two 6-week-old male New Zealand white rabbits (*Oryctolagus cuniculus*) were obtained and randomly divided into 4 groups as follows: group 1, surgical approach with periosteal elevation over the left nasofrontal suture and left midzygomatic arch; group 2, application of RPF at the left nasofrontal suture and midzygomatic arch; group 3, single osteotomy at left nasofrontal suture and double osteotomies at left midzygomatic arch with application of RPF; and group 4, unoperated-on controls. The rabbits in groups 1 through 3 were anesthetized via an intramuscular injection of ketamine hydrochloride (40 mg/kg), xylazine hydrochloride (10 mg/kg), and acepromazine maleate (1 mg/kg). The left nasofrontal and zygomatic arch areas were shaved and prepared aseptically with povidone-iodine, and 2-cm parasagittal incisions were made to expose the underlying periosteum. Subperiosteal elevation was carried out for a distance of approximately 2 cm at each site. At this point, the procedure was terminated in group 1 animals. In group 2 animals, microplates (AO/Synthes 1.0, Synthes Inc, Paoli, Pa) with 4.0×0.8-mm self-tapping screws were placed across the left nasofrontal suture and midzygomatic arch. In group 3 animals, a single osteotomy was made at the left nasofrontal suture and double osteotomies were made at the left midzygomatic arch before RPF was applied as in group 2 animals. In all groups, wounds were closed by means of simple interrupted 3-0 plain chromic sutures without closing the periosteum. At 11 weeks of age, a second procedure was performed. After induction of anesthesia and preparation as described above, in group 1 animals the left nasofrontal suture and midzygomatic arch areas were exposed; in group 2 and 3 animals, the RPF was removed. All incisions were closed with 3-0 plain chromic suture.

Animals were cared for in the University of Iowa Animal Research Facility, Iowa City, until they were killed at 20 weeks of age. Two animals died during the study, 1 in group 3 of an anesthetic complication and another in group 2 secondary to a wound infection. The Institutional Review Board for Animal Research at the University of Iowa

approved all procedures. Institutional guidelines for animal experimentation were strictly followed.

DATA ACQUISITION

With the use of cleaned skulls, a database of 3-dimensional coordinates corresponding to each of 34 craniofacial landmarks was recorded from which 23 linear distances were calculated, as described previously by Lorenzo et al⁶ (Figure 1 and Table 1 from their article). A single investigator (S.M.C.) performed all data acquisition by means of a digitizer (3Space, Polhemus Navigation, Colchester, Vt) interfaced with an IBM-compatible computer. Investigator technique was validated by comparison of 10 sets of measurements from 1 randomly selected skull. Statistical analysis of these measurements found no significant differences between these sets. A simple mathematical program was used to calculate linear distances between points in each database.⁶

STATISTICAL ANALYSIS

All distance measurements were normalized for differences in scale by means of a calculated cranial module defined as $1/3 \times (\text{maximum height} + \text{maximum width} + \text{maximum length})$ of the skull.^{2,7} A 1-way analysis of variance was used to compare data across all groups. The mean square error from each analysis of variance was used to perform the Dunnett *t* test to compare differences between left- and right-sided measurements in experimental groups with controls. Dunnett *t* test also was used to make raw comparisons of left- and right-sided measurements within groups.

Euclidean distance matrix analysis was applied to the database to permit objective comparison of geometric shapes. Multiple linear measurements between landmark coordinates were used to define 10 craniofacial regions, and for specimens in each group, data were averaged to create a form matrix. The resulting regional matrixes were used to compare 3-dimensional shapes between experimental groups and controls in this study, and with animals from our previous study in which RPF was left in place.⁶ The compared craniofacial regions and corresponding landmarks are given in Table 2 and Figures 2 and 3 in the article by Lorenzo et al.⁶

eral statistically significant linear differences (left compared with right nasal bones in group 3; left compared with right zygomatic arch length in groups 1 and 3; left compared with right orbital length in groups 2 and 3; left compared with right orbital height and anterior midface height in groups 1 through 3) (**Table 1**). Comparison of the differences between left- and right-sided measurements within groups vs controls disclosed that the discrepant length of the nasal bones in group 3, the orbit in groups 2 and 3, and the orbital and midface height in groups 1, 2, and 3 were statistically asymmetrical when compared with control animals. However, the statistically significant difference noted between left and right zygomatic arch length in group 1 and 3 animals was not significant after comparison with measurement differences between sides in control animals (**Table 2**). The EDMA data from several craniofacial regions showed sig-

nificant growth restriction in all craniofacial regions we examined except the midsnout region (**Table 3**).

Data comparing left- and right-sided linear differences in groups 1 through 3 animals with animals in which RPF was applied and left in situ (data from Lorenzo et al⁶) showed that discrepant lengths in orbital and anterior midface height existed but that there were no significant differences in lengths of the nasal bones, zygomatic arches, or orbits (**Table 4**). The EDMA data of several craniofacial regions show that group 1 animals exhibited significant growth restriction in the bifrontal, left orbital, left total frontal, left anterior frontal, and right anterior frontal regions (**Table 5**). Groups 2 and 3 animals exhibited significant growth restriction in all craniofacial regions except the midsnout region, and in group 3, the right lateral maxilla.

Table 1. Selected Left- vs Right-Sided Linear Measurements in Groups 1 Through 4*

Measurement (Landmarks)	Group			
	1	2	3	4
Nasal bone length (4-1 vs 6-3)	0.010	0.022	0.054 (<i>P</i> <.001)	0.004
Zygomatic arch length (32-33 vs 30-31)	0.054 (<i>P</i> <.02)	0.021	0.064 (<i>P</i> <.005)	-0.003
Orbital length (23-26 vs 17-20)	-0.005 (<i>P</i> <.005)	0.068 (<i>P</i> <.001)	0.086 (<i>P</i> <.001)	-0.006
Orbital height (8-25 vs 9-19)	0.058 (<i>P</i> <.001)	0.068 (<i>P</i> <.001)	0.073 (<i>P</i> <.001)	-0.014
Anterior midface height (24-28 vs 18-22)	0.068 (<i>P</i> <.001)	0.116 (<i>P</i> <.001)	0.122 (<i>P</i> <.001)	0.009

*All measurements were normalized; table shows measured differences and significant *P* values. See Lorenzo et al⁶ for definition of landmarks.

Table 2. Left-Right Linear Differences in Experimental Groups vs Controls*

Measurement	Group		
	1	2	3
Nasal bone length	0.005	0.017	0.050 (<i>P</i> <.05)
Zygomatic arch length	0.058	0.025	0.068
Orbital length	0.008	0.081 (<i>P</i> <.05)	0.099 (<i>P</i> <.05)
Orbital height	0.0646 (<i>P</i> <.001)	0.075 (<i>P</i> <.001)	0.08 (<i>P</i> <.001)
Anterior midface height	0.058 (<i>P</i> <.05)	0.107 (<i>P</i> <.001)	0.112 (<i>P</i> <.001)

*All measurements were normalized; table shows calculated differences and significant *P* values. See Lorenzo et al⁶ for definition of landmarks.

COMMENT

The techniques and technology of RPF have advanced substantially during the past 20 years. With this advancement has come a revolution in the treatment of pediatric craniomaxillofacial trauma and anomalies. Rigid plate fixation facilitates direct bone healing, allows improved stability at fracture and reconstructive sites, is associated with decreased risk of infection, and permits an earlier return to function.⁸ In addition, RPF is particularly appealing in the pediatric population because of the relative ease and quickness of its application. Despite these attributes, however, RPF is not innocuous.

A growing body of evidence has shown that RPF produces significant growth alterations in the cranial and midfacial regions in animal models.^{1-5,9} Several studies also have shown that disruption of bony and soft tissue elements without application of RPF produces significant alterations in craniofacial growth.¹⁰⁻¹³ Experimental evidence that correlates with these clinical studies has been provided by the often-cited work of Sarnat and Wexler.^{9,14,15} The presumption from these studies has been that bony trauma, soft tissue trauma, and RPF each act as independent factors to produce growth alterations in the craniofacial regions. This hy-

Table 3. Selected Results of Euclidean Distance Matrix Analysis*

Anatomical Region	Group		
	1	2	3
Midsnout	1.25	1.17	1.20
Bifrontal	2.41 (<i>P</i> <.001)	2.16 (<i>P</i> <.001)	2.40 (<i>P</i> <.001)
Biparietal	1.14 (<i>P</i> <.01)	1.17 (<i>P</i> <.001)	1.21 (<i>P</i> <.001)
Left lateral maxilla	1.17 (<i>P</i> <.01)	1.23 (<i>P</i> <.001)	1.15 (<i>P</i> <.05)
Left orbital area	7.33 (<i>P</i> <.001)	6.59 (<i>P</i> <.001)	7.64 (<i>P</i> <.001)
Left total frontal	2.44 (<i>P</i> <.001)	2.21 (<i>P</i> <.001)	2.52 (<i>P</i> <.001)
Left anterior frontal	2.44 (<i>P</i> <.001)	2.21 (<i>P</i> <.001)	2.52 (<i>P</i> <.001)
Left posterior parietal	1.09 (<i>P</i> <.01)	1.12 (<i>P</i> <.001)	1.21 (<i>P</i> <.001)
Right lateral maxilla	1.13 (<i>P</i> <.001)	1.14 (<i>P</i> <.001)	1.1 (<i>P</i> <.03)
Right anterior frontal	2.13 (<i>P</i> <.001)	1.98 (<i>P</i> <.001)	2.24 (<i>P</i> <.001)

*Ratios of the control matrix (numerator) to the experimental matrix (denominator). See Lorenzo et al⁶ for definition of regions.

Table 4. Left-Right Linear Differences in Experimental Groups vs Rigid Plate Fixation-Only Groups*

Measurement	Groups		
	1	2	3
Nasal bone length	0.008	-0.014	0.0096
Zygomatic arch length	0.0487	0.0008	-0.0035
Orbital length	0.0112	0.0645	0.0538
Orbital height	0.0537 (<i>P</i> <.001)	0.0612 (<i>P</i> <.001)	0.0698 (<i>P</i> <.001)
Anterior midface height	0.0456	0.0551 (<i>P</i> <.05)	0.0613 (<i>P</i> <.05)

*All measurements were normalized; table shows calculated differences and significant *P* values. See Lorenzo et al⁶ for definition of landmarks.

pothesis was verified experimentally by Lorenzo et al in 1995.⁶

The present study was identical in all aspects of design to the Lorenzo et al study⁶ with one exception: the RPF was removed at 11 weeks of age. The New Zealand white rabbit was selected as the experimental animal on the basis of precedent and a well-defined pattern of craniofacial growth. Data have shown that a 6-week-old rabbit is comparable with a 2-year-old human with respect to brain development and detailed roentgenocephalometric analyses.^{3,16} In both studies, the nasofrontal region and zygomatic arch were chosen as operative sites to simulate complex fractures or craniofacial reconstructive procedures; suture lines were selected for osteotomies and fixation because of their frequent involvement in fractures or reconstructive procedures. The experimental groups were designed to compare the effects of RPF and subsequent removal with and without osteotomies with those of the surgical approach only (soft tis-

Table 5. Selected Results of Euclidean Matrix Analysis Results in Rigid Plate Fixation vs Experimental Groups*

Anatomical Region	Groups		
	1	2	3
Midsnout	1.299	1.3708	1.1819
Bifrontal	2.47 (<i>P</i> <.001)	2.5406 (<i>P</i> <.001)	2.9304 (<i>P</i> <.001)
Biparietal	1.1031	1.1579 (<i>P</i> <.001)	1.2195 (<i>P</i> <.002)
Left lateral maxilla	1.384	1.3098 (<i>P</i> <.001)	1.1192 (<i>P</i> <.001)
Left orbital area	7.3157 (<i>P</i> <.001)	7.8796 (<i>P</i> <.001)	10.4704 (<i>P</i> <.001)
Left total frontal	2.5193 (<i>P</i> <.001)	2.694 (<i>P</i> <.001)	3.0059 (<i>P</i> <.001)
Left anterior frontal	2.4065 (<i>P</i> <.001)	2.694 (<i>P</i> <.001)	3.0059 (<i>P</i> <.001)
Left posterior parietal	1.096	1.1243 (<i>P</i> <.001)	1.2195 (<i>P</i> <.001)
Right lateral maxilla	1.0964	1.1927 (<i>P</i> <.001)	1.0093
Right anterior frontal	1.9313 (<i>P</i> <.001)	2.2623 (<i>P</i> <.001)	2.6071 (<i>P</i> <.001)

*Ratios of rigid plate fixation matrix (numerator) to experimental group matrix (denominator). See *Laurenzo et al*⁶ for definition of regions.

sue trauma) and with data from unoperated-on controls. We also compared the results of both studies to determine whether removal of RPF was beneficial.

Our linear data show that RPF with subsequent removal, with or without osteotomy, produces significant restriction on local bone growth compared with unoperated-on controls. In comparison with animals in which RPF is left in situ, there also is greater growth restriction and asymmetry, implying that RPF with subsequent removal does not prevent the untoward growth-restrictive effects of its initial application; it produces a restrictive effect similar to, and in some regions greater than, that with RPF alone.

The EDMA data provide a more thorough evaluation of the global growth effects of RPF. Compared with controls, all experimental groups in this study showed significant growth-restrictive effects in all craniofacial regions measured except the midsnout region. Compared with the animals of the earlier study treated with RPF, group 1 animals in this study showed greater growth restriction at the bifrontal, left orbital, left total frontal, left anterior frontal, and right anterior frontal regions, suggesting that a second approach to the growing pediatric craniofacial region in the attempt to remove RPF would, by itself, produce deleterious effects with regard to craniofacial growth. In groups 2 and 3 animals, there was significant growth restriction in all craniofacial regions

compared with those animals in the RPF study. (For a review of EDMA, see the 2 articles by Lele and Richtsmeier.^{17,18})

These data imply that RPF with subsequent removal actually produces more global growth restriction than RPF left in situ. On this basis, we would not recommend removal of RPF to prevent growth disturbances to craniofacial regions in children. Furthermore, when RPF techniques are required, to minimize growth alteration, only the minimal amount of dissection should be used to expose fracture sites.

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