Condylar Adaptation after Alteration of Vertical Dimension in Adult Rhesus Monkeys, Macaca Mulatta

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ABSTRACT: Remodeling in the cartilage of the mandibular condyle was investigated in young adult monkeys after an increase in vertical dimension of the midface through the use of a tooth-borne intraoral appliance. Six young adult male rhesus monkeys had bite-splints of 5 mm, 10 mm or 15 mm cemented to their maxillary dentition for 48 weeks. Five age- and sex-matched monkeys were used as controls. The thickness of the articular tissue and of the prechondroblastic and chondroblastic layers of the condylar cartilage in the superior, posterosuperior and posterior regions was measured from parasagittal sections of the temporomandibular joint (TMJ). It was found that articular tissue thickness was reduced in the superior region; the prechondroblastic layer, absent in control animals, was very distinctive (30-75μm) in experimental animals; and there was a 62% increase in the thickness of the chondroblastic layer in the experimental animals. These findings indicate that chronic alteration of mandibular posture via increase in vertical dimension stimulates progressive remodeling of the mandibular condyle in young adult monkeys.

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Introduction

The temporomandibular joint (TMJ) is an important subject of investigation by craniofacial biologists and clinicians because of its role in growth of the mandible and in the function of the craniofacial complex. However, there is no general agreement regarding the potential for adaptive condylar growth and remodeling of the TMJ in response to alterations of its structural and functional environment, especially in adult subjects.

Experimental animals provide an excellent model for analysis of the development and growth of the TMJ and as a model for experimental investigation of the factors controlling TMJ adaptation. Previous studies indicate that all mammals possess complete morphophysiologic similarity of the tissues comprising the TMJ despite significant differences between the specific anatomy of the TMJ of humans and certain experimental animals such as rodents and non-human primates.[1,2]

Previous experimental studies have indicated that mandibular posture can affect condylar growth in young growing animals;[3-6,9] however, many of these studies have suggested that similar condylar adaptations do not occur in adults.[4,6-9] In fact, some studies have concluded that altered mandibular posture may cause pathology and regressive remodeling in the TMJ of adults.[7,8] In contrast, Schneiderman and Carlson[10] reported small, but biologically significant, compensatory condylar growth after displacement of the mandible using adult monkeys in their cephalometric studies.

The growth-related cartilage of the TMJ is a special form of secondary cartilage that arises from a cellular blastema distinct from the developing ramus and body of the mandible.[11] The condylar cartilage is characterized by growth that is largely, though not completely, secondary, compensatory and adaptive to the biomechanical environment of the TMJ. The underlying reason for the fact that the growth of the condylar cartilage is largely compensatory and adaptive is related to the nature of secondary cartilage and to the phylogenetic origin of the articulation between the lower jaw and the cranium.[12] Remodeling may be necessary for the maintenance of congruity between apposing articular surface in all joints. In typical joints of the appendicular skeleton, this remodeling is mediated through the proliferative activity of articular cartilage. However, the TMJ does not possess a true articular cartilage. Therefore, it is likely that adaptation associates with articular function in the TMJ are characterized by cellular proliferation in the layer of undifferentiated prechondroblasts located just deep to the articular tissue of the mandibular cartilage.

The purpose of this study was to investigate microscopic cellular changes in the mandibular condyle of young adult rhesus monkeys after lowering of the mandible via chronic alteration of interincisal vertical dimension. The vertical dimension of the face was increased through the use of a tooth-borne intraoral bite-opening appliance. Based on previous studies of condylar adaptation in adult animals, we hypothesized that the experimental alteration of mandibular posture would result in histologic evidence for progressive remodeling of the condyle, characterized by an increase in condylar cartilage thickness and growth.

Materials and Methods

Eleven young adult male rhesus monkeys (Macaca mulatta), six experimental and five control, were used. The animals ranged in age from 6 to 9 years, based on the presence of complete permanent dentitions and occlusal wear.[13,14]

An intraoral occlusal appliance made of tantalum was cemented to the maxillary dentition of each experimental animal for a period of 48 weeks. Bite-splints were designed to create 5 mm (n=3), 10 mm (n=2), and 15 mm (n=l) openings interincisally. Despite the change in jaw position, the animal had no apparent difficulty in eating a normal diet of commercial monkey chow and fruit and exhibited normal agonistic display behavior.[15] Appliances were worn continuously throughout the 48-week experimental period.

Following perfusion with saline and phosphate-buffered formalin, the right and left TMJs and surrounding tissue were removed and placed in neutral buffered formalin. The tissue blocks were washed and demineralized with EDTA. After radiographic verification of demineralization, the tissue blocks were dehydrated, embedded in paraffin and sectioned serially in the parasagittal plane at a thickness of 10 to 12 micrometers using a Leitz microtome. Hemotoxylin and eosin stain was used to show basic cellular structure. Masson trichrome also was used to emphasize the structure of the connective tissues associated with the joint.

Histomorphologic analysis of parasagittal sections of the TMJ was performed using the BIOQUANT image analysis system. Quantitative measurements of the thickness of each layer were made using a Hi-Pad digitizer interfaced with a video camera and Leitz microscope, projected onto a high resolution video monitor (Sony) and microcomputer. All data were recorded simultaneously in the computer for statistical analysis.

The mandibular condyle may be perceived as containing two distinct tissue layers. The articular tissue layer is composed of dense fibroelastic connective tissue whose collagen fibers are oriented parallel to the articular surface of the condyle. This layer is continuous with the fibrous layer of the periosteum. The thickness of the articular tissue varies along the condyle, increasing posteriorly.

The subarticular cartilaginous region of the condyle is the site of the major growth-related adaptation of the condyle. This region can be divided further into two layers, i.e., a prechondroblastic layer and a chondroblastic layer. The prechondroblastic layer, which lies immediately inferior to the articular layer, is continuous with the osteogenic layer of the periosteum. The prechondroblastic layer gives a very distinctive basophilic color with hematoxylin and eosin stain, indicating the major chondrocytic proliferative site. The chondroblastic layer contains the maturing and hypertropic chondrocytes and lies above the endosteal surface of the condyle.

Thicknesses of the articular tissue, prechondroblastic and chondroblastic cartilage layer were measured perpendicular to the articular surface at the superior, posterosuperior and posterior region around the circumference of the condyle according to previous methods (**Figure 1**).[5,17] Maximum condylar length was used as a covariate to compensate for individual variations in tissue area and thickness due to general body size. A total of 10 middle sections, five from the left and five from the right TMJ of each animal, were selected and analyzed qualitatively for evidence of regressive bone remodeling and joint pathology.

Data were subjected to analysis of variance and analysis of covariance, using condylar length as a covariate in

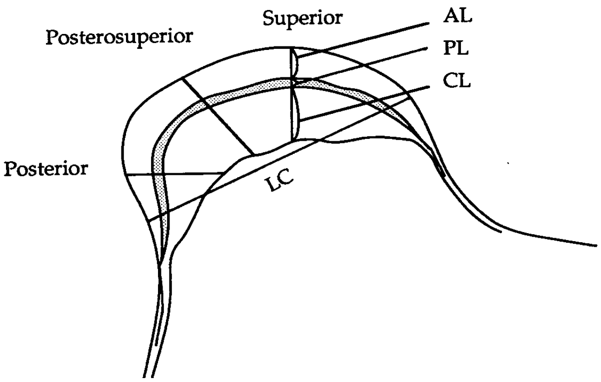

Figure 1
Length of the mandibular condyle (LC) and thicknesses of the articular (AL), prechondroblastic (PL) and chondroblastic (CL) cartilage layers were measured perpendicular to the articular surface at the superior, posterosuperior and posterior regions around the circumference of the mandibular condyle. (Adapted from McNamara and Carlson: Quantitative analysis of temporomandibular joint adaptations to protrusive function. *Am J Orthod* 1979; 76:593-611)

order to determine any differences between groups. The grand mean and standard deviation for each measurement were used in group comparison at different regions of the condyle.

Results

Articular layer thickness was reduced an average of 67% in the experimental animals compared to that in the control group ($p < 0.01$). With respect to the prechondroblastic layer, typically absent in the control group (**Figure 2**), the 15 mm experimental animal exhibited the largest increase in thickness ($p < 0.01$); however, splint size was not correlated with layer thickness in the other experimental groups. Thickness of the chondroblastic layer of cartilage was more than 100% greater in the 15 mm group, with an overall mean increase of 60.5% compared to control group (**Figure 3**).

Figure 2
Right temporomandibular joint of monkey, the control group. No distinctive subarticular cartilage layers are noticeable. (Hemotoxylin & eosin; parasagittal section; x8)

The 15 mm group had the smallest increase in the thickness of the articular layer, 12.7%, ($p < 0.05$); however, this group also had the largest increase in both prechondroblastic ($p < 0.01$) and chondroblastic layer thickness (196%) compared to the control group (**Figure 4**). The thickness of the prechondroblastic layer was more pronounced in this region than in others.

In the articular layer, the 10 mm group had the largest increase in thickness, 53%, with the 5 mm group being the smallest ($p < 0.01$) (**Figure 5**). The 10 mm group had the smallest increase in prechondroblastic layer of all three regions ($p < 0.01$). The 15 mm group had the largest increase in chondroblastic layer of all three regions (**Figure 6**). Even though it was not possible to show statistical significance, the articular layer had the largest increase, and the chondroblastic layer had the smallest increase in the posterior region of the condyle in experimental animals.

It should be noted that there was no evidence of pathology and regressive remodeling (abnormal bone loss) within the condyle and TMJ during the experimental period. Articular tissue thickness was reduced in the superior region where the condyle came into contact with the articular eminence in experimental animals, most likely because of repositioning of the condyle anteriorly. The prechondroblastic layer, which typically is absent in control groups, was very distinctive (30-75µm) in all experimental animals, indicating reactivation of cellular proliferation. The chondroblastic layer had more than

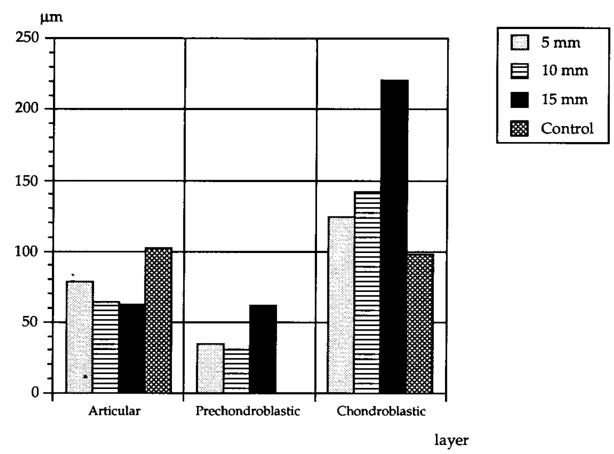

Figure 3
Mean thickness of the articular, prechondroblastic and chondroblastic layers at the posterosuperior aspect of the condyle. Notice the marked increase in the prechondroblastic layer in 15 mm group ($p < 0.01$) and the general correlation of splint size with layer thickness in the chondroblastic layer.

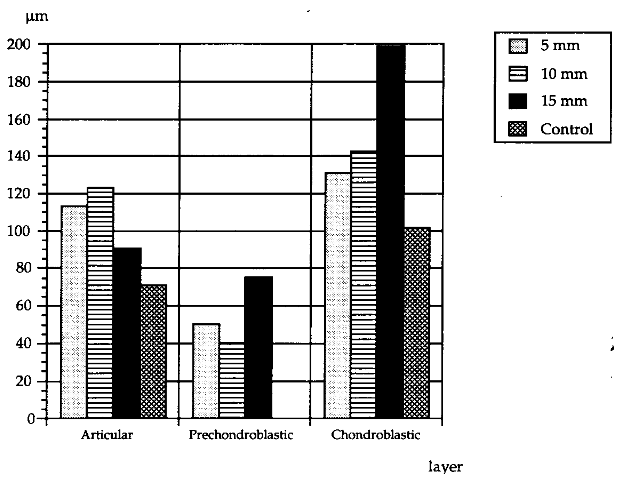

Figure 4
Mean thickness of the articular, prechondroblastic and chondroblastic layers at the superior aspect of the condyle. Notice the reduction of the articular layer in all experimental animals ($p < 0.05$) and the general correlation of splint size with layer thickness in the chondroblastic layer.

60% increase in thickness in experimental animals compared to the control group (**Figure 7**). Because of the limited number of animals, it was not possible to correlate bite-splint size with condylar adaptation; however, all experimental animals showed the same general response (**Table 1**).

Discussion

Introduction of maxillary occlusal bite-splints, 5 mm, 10 mm and 15 mm in height, forces the mandible to be rotated inferiorly and posteriorly, causing the condyle to become repositioned anteriorly.[7,10] A previous study indicated there was no significant change in the vertical posi-

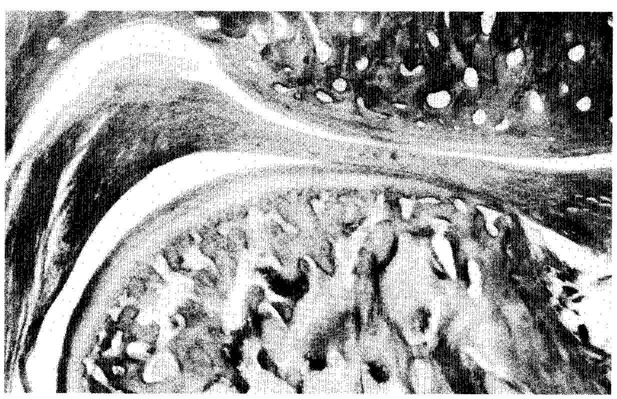

Figure 5
Left temporomandibular joint of monkey, the experimental group (5 mm) in 48 weeks. Note the very distinctive prechondroblastic layer as in dark band underneath fibrous articular layer. (Hemotoxylin & eosin; parasagittal section; x8)

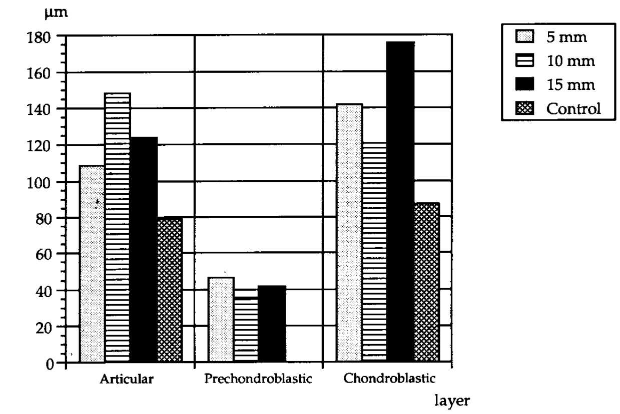

Figure 6
Mean thickness of the articular, prechondroblastic and chondroblastic layers at the posterior aspect of the condyle. Notice the marked increase in the articular layer in all experimental groups ($p < 0.05$) and the less noticeable increase in the prechondroblastic layer ($p < 0.01$).

tioning of the condyle.[10] The condyle was juxtaposed against the downsloping aspect of the articular eminence, which is slightly inferior to the roof of the fossa. However, this was not particularly restrictive with regard to anterior-condylar translation, because the articular eminence in the monkey does not protrude inferiorly as much as in man.[1]

The role of condylar cartilage in the growth of the TMJ was reviewed recently by Copray et al.,[18] who stressed the importance of considering the developmental status of the condyles when interpreting the results of altered functional loading experiments, because of the potential for condylar cartilage to vary with age. In a histological study, Takenoshita[19] found that histomorphologic pattern remained fundamentally unchanged throughout adulthood in the human condyle. A common feature was the

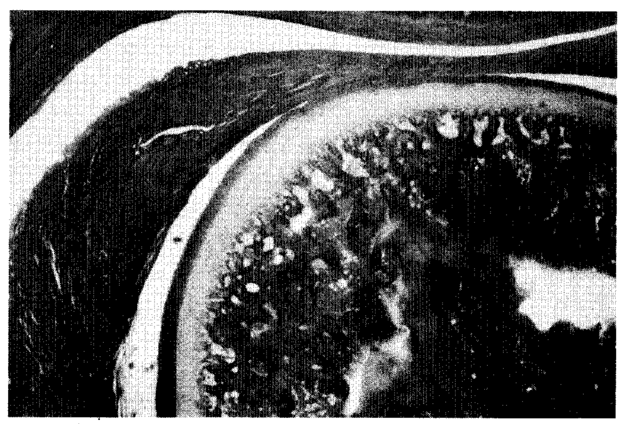

Figure 7
Left temporomandibular joint of monkey, the experimental group (15 mm) in 48 weeks. Note the marked increase in chondroblastic layer as in white band underneath prechondroblastic layer. (Hemotoxylin & eosin; parasagittal section; x8)

Table 1
Summary Statistics and Analysis of Variance (ANOVA) for Histomorphologic Measurements in μm According to Amount of Interincisal Vertical Opening (Bite-Splint Size) ANOVA Tests Significance of Differences in Controls and Experimentals (*p < 0.05, **p < 0.01 and NS: Not Significant).

Variable	Interincisal Vertical Opening 5 mm	10 mm	15 mm	Control
Superior Region				
Articular layer	78.7 (2.9)	63.8 (5.6)	62.6 (5.8)	101.9 (8.7)**
Prechondroblastic layer	34.9 (3.7)	30.2 (3.7)	61.7 (4.3)	0.0**
Chondroblastic layer	124.1 (13.7)	141.9 (13.7)	220.4 (16.4)	98.4 (16.0)NS
Post-Superior Region				
Articular layer	113.4 (14.7)	122.9 (4.3)	90.7 (3.9)	71.0 (7.6)*
Prechondroblastic layer	50.6 (2.6)	40.4 (3.0)	75.6 (6.1)	0.0**
Chondroblastic layer	131.3 (18.6)	142.4 (13.4)	199.0 (11.9)	101.4 (18.5)NS
Posterior Region				
Articular layer	108.4 (15.8)	148.0 (16.9)	123.9 (6.5)	101.9 (8.7)*
Prechondroblastic layer	46.3 (9.5)	35.2 (0.2)	41.4 (1.5)	0.0**
Chondroblastic layer	141.4 (16.3)	120.8 (19.1)	175.6 (18.3)	87.2 (21.1)NS
Condylar length (mm)	8.57 (0.2)	8.10 (0.2)	8.95 (0.5)	8.40 (0.4)

presence of chondrocytic remnants within the condyle.

Previous experimental studies clearly demonstrate that growth of the mandibular condyle in growing animals can be affected by its function and position.[3-6] The adaptive potential of the adult condyle with protrusive appliances was investigated by McNamara et al.,[20] who reported some, but indefinite results of, adaptive response. Another study by Carlson and Schneiderman[10,21] provided valuable information on adaptability of the mandible and its condyle of adult monkey. In their cephalometric studies, repositioning of the mandible using a similar bite-splint was associated with increased mandibular length due to biologically significant condylar growth.

In the present study, the microscopic changes of the mandibular condyle in 11 young adult monkeys were examined. Functional and structural loading was altered using bite-splints of different sizes for 48 weeks. Our histological analysis of the condylar response was supportive of general findings of previous cephalometric studies.[10,21]

All the experimental animals had similar responses in the defined condylar layers, especially in a marked increase in the thickness of the prechondroblastic layer. The prechondroblastic layer is composed of undifferentiated mesenchymal cells within a basophilic ground substance. Autoradiographic studies in the rat and in the monkey have demonstrated that the outer portion of the prechondroblastic layer is the main site of condylar growth activity.[2,16,22,23] This layer typically was absent in the control group but was distinctively increased in all experimental groups, indicating reactivation of quiescent cells. No abnormal cellular structure or response was noticed in any of the cartilage layers, and the articular layer was well intact in all experimental animals. The results from the histological examination in our study further suggested that the mandibular condyle of the young adult monkey is capable of adapting to alteration of chronic mandibular posture.

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References

1. Carlson DS, McNamara JA Jr, Graber LW, Hoffman DL: Experimental studies of growth and adaptation of TMJ. In Irby WB (ed), *Current Advances in Oral Surgery*, Vol III. St. Louis: Mosby, 1980
2. Petrovic A, Stutzmann J, Oudet C: Control processes in the postnatal growth of the mandibular condylar cartilage. In McNamara JA Jr (ed), *Determinants of Mandibular Form and Growth*, monograph 4, Craniofacial Growth Series, Center for Human Growth and Development, University of Michigan, Ann Arbor, 1975
3. Stockli PW, Willert HG: Tissue reactions in the temporomandibular joint resulting from anterior displacement of the mandible in the monkey. *Am J Orthod* 1971; 60:142-155
4. Petrovic A, Stutzmann J, Gasson N: The final length of the mandible: Is it genetically determined? In Carlson DS (ed), *Craniofacial Biology*, monograph 10, Craniofacial Growth Series, Center for Human Growth and Development, University of Michigan, Ann Arbor, 1981
5. McNamara JA Jr, Carlson DS: Quantitative analysis of temporomandibular joint adaptations to protrusive function. *Am J Orthod* 1979; 76:593-611
6. McNamara JA Jr: *Neuromuscular and Skeletal Adaptations to Altered Orofacial Function,* monograph 1, Craniofacial Growth Series, Center for Human Growth and Development, University of Michigan, Ann Arbor, 1972
7. Hiniker JJ, Ramfjord SP: Anterior displacement of the mandible in adult rhesus monkeys. *J Prosthet Dent* 1966; 16:503-512
8. Ramfjord SP, Enlow RD: Anterior displacement of the mandible in adult rhesus monkeys: Long-term observations. *J Prosthet Dent* 1971; 26:517-531
9. McNamara JA Jr: Neuromuscular and skeletal adaptation to altered function in the orofacial region. *Am J Orthod* 1973; 64:578-606
10. Schneiderman ED, Carlson DS: Cephalometric analysis of condylar adapta-

tions to altered mandibular position in adult rhesus monkeys, Macaca mulatta. *Archs Oral Biol* 1985; 30:49-54

11. Kantomaa T, Hall BK: On the importance of cAMP and Ca++ in mandibular condylar growth and adaptation. *Am J Orthod Dentofacial Orthop* 1991; 99:418-426
12. Carlson DS: Growth of the temporomandibular joint. In Zarb GA, Carlson DS, Mohl ND (eds), *The Temporomandibular Joint.* Copenhagen: Musksgaard, 1994
13. Hurme VO, Van Wagenen G: Basic data on the emergence of permanent teeth in the rhesus monkey. *Pro Am Phil Soc* 1961; 105:105-140
14. Gantt D: Patterns of dental wear and the role of the canine teeth in the Cercopithecinae. *Am J Phys Anthrop* 1979; 51:353-360
15. Carlson DS, Ellis E, Schneiderman ED, Ungerleider JC: Experimental models of surgical intervention in the growing face: cephalometric analysis of facial growth and relapse. In McNamara JA Jr, Carlson DS, Ribbens KA (eds), *The Effect of Surgical Intervention on Craniofacial Growth*, monograph 12, Craniofacial Growth Series, Center for Human Growth and Development, University of Michigan, Ann Arbor, 1982
16. Kanouse MC, Ramfjord SP, Nasjleti CE: Condylar growth on rhesus monkeys. *J Dent Res* 1969; 48:1,171-1,176
17. Carlson DS, McNamara JA Jr, Jaul DH: Histological analysis of the growth of the mandibular condyle in the rhesus monkey (Macaca mulatta). *Am J Phys Anthropol* 1977; 47:53-64
18. Copray GCVM, Dibbets JMH, Kantomaa T: The role of condylar cartilage in the development of the temporomandibular joint. *Angl Orthod* 1988; 369-380
19. Takenoshita Y: Development with age of the human mandibular condyle: Histological study. *J Craniomandib Pract* 1987; 5:317-323
20. McNamara JA Jr, Hinton RJ, Hoffman DL: Histological analysis of temporomandibular joint adaptation to protrusive function in young adult rhesus monkeys (macaca mulatta). *Am J Orthod* 1982; 82:288-298
21. Carlson DS, Schneiderman ED: Cephalometric analysis of adaptations after lengthening of the masseter muscle in adult rhesus monkeys, macaca mulatta. *Archs Oral Biol* 1983; 28:627-637
22. Blackwood HJ: Cellular remodeling in articular tissue. *J Dent Res* 1966; 45:480-489
23. Joondeph DR: An autoradiographic study of the temporomandibular articulation in the growing Saimiri sciureus monkey. *Am J Orthod* 1972; 62:272-286

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