Effects of mandibular advancement on growth after condylectomy

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Short title: Mandibular Growth after Condylectomy

Key words: functional appliance, mandibular growth, condylectomy

Number of words in the abstract: 147

Number of words in the abstract and the text: 2493

Number of tables and figures: 4

Number of references cited: 24

ABSTRACT

Previous studies have indicated that an injured condyle during adolescence is a causative factor for reduced mandibular growth and resulting asymmetry of the mandible. The aim of this study was to examine the nature of mandibular growth after unilateral condylectomy and to elucidate the effects of mandibular advancement. Sixty growing mice were subjected to unilateral condylectomy and then one-half of them underwent treatment with a functional appliance. After 4 weeks, a unilateral condylectomy produced reduced growth of the mandible and a subsequent lateral shift to the affected side. However, reduced growth and a lateral shift of the mandible were eliminated by a functional appliance and prominent regeneration of the condyle was also demonstrated. It was shown that mandibular advancement provides for the ability to regenerate cartilaginous tissues on injured condyles and recovery of the reduced mandibular growth, leading to correction of the lateral shift of the mandible.

INTRODUCTION

There is a general belief that the mandibular condyle is a center of mandibular growth and has an essential ability to control cartilaginous growth of the mandible and the internal structures. As a result of the reduced growth and remodeling potential on the side of a fractured mandibular condyle, the mandibular growth becomes asymmetric in a progressive manner (Dimitroulis, 1997). Teixeira *et al.* (2006) concluded in their study that an experimental fracture of the mandibular condyle during the growth period in rats induced degenerative changes of the condyle, as well as an asymmetry of the mandible, affecting the height of the mandibular corpus. Therefore, it would be reasonably assumed that any injuries to the condyle in growing individuals surely disturb the growth and development of the mandible. Meanwhile, mandibular growth is controlled by membranous growth on the surface of the mandible, as well as cartilaginous growth in the condyle (Orliaguet *et al.* 1994). Furthermore, there have been a limited number of reports in the literature about growth of the mandible after injury of the condyle (Ito *et al.,* 1986; Tsolakis and Spyropoulos, 1997). It is thus unclear if such damage is a causative factor for less developed and asymmetric mandibles.

In previous studies, the effects of a condylectomy on the growth of a rat's mandible have been considered in a morphometric study (Spyropoulos and Tsolakis*,* 1997); however, the histologic change of the removed part or the variation of the internal structure of the mandible is not clear. Moreover, there is a report of mandibular growth during a growth period in rats equipped with a functional appliance (Tsolakis and Spyropoulos*,* 1997); however, no reports exist on mandibular growth with a functional appliance after a unilateral condylectomy by a morphometric or histological study.

In functional appliance treatment, additional growth may occur in response to a sliding movement of the mandibular condyle out of the fossa, mediated by reduced pressure on the condylar tissues or by altered muscle tension on the condyle (Proffit *et al.* 2007). The possibility of growth control of the mandible after an injury to the condyle by changing the intra-articular environment through the repositioning of the mandible with use of a therapeutic appliance was the basis of this study. The aim of this study was to examine the nature of mandibular growth after unilateral condylectomy, and to elucidate the consequent effects of a functional appliance on the structure and growth of the condyle and mandible in growing mice.

MATERIALS & METHODS

Experimental Animals

Ninety 3-week-old C57BL/6J mice (Jackson Laboratory, Bar Harbor, ME, USA) were divided equally into the following groups: 2 experimental groups (condylectomy and condylectomy + appliance groups) and the corresponding control group with a sham operation. In the condylectomy group mice, a unilateral condylectomy was performed on the right side, and the mandible was allowed to function. In the condylectomy + appliance group, the mandible was repositioned in the forward direction with a functional appliance after the unilateral condylectomy. The control mice underwent a sham operation in the condylar area on the right side without any use of the appliance.

The animals in all the groups were fed a granulated diet for the first four days and a solid one (CE-2: CLEA, Tokyo, Japan) thereafter. All the mice were sacrificed 4 weeks after the surgery with an overdose of sodium pentobarbital (nembutal: Dainippon Sumitomo Pharma, Osaka, Japan). The body weight was measured every 4 days during the experiment and used as an indicator of general growth. This study was approved by the Ethics Committee of Hiroshima University.

Unilateral Condylectomy

Under general anesthesia with pentobarbital, the condylectomy was performed. Through a prearticular approach, the condyle was totally exposed and the excision was performed carefully so as not to injure the surrounding structures. By means of a stereoscopic microscope (SZX9: Olympus Optical Co., Tokyo, Japan), a cut was made 0.5 mm below the condylar neck. The trauma from the external dermal incision was kept to a minimum and the incision area was sutured in a most cautious manner. An analgesic, buprenorphine (lepetan: Otsuka Pharmaceutical, Tokyo, Japan), was given immediately after surgery. These procedures were performed under sterile conditions.

Functional Appliance

The mandible was repositioned in the forward direction by use of a functional appliance consisting of a 0.016×0.022 inch Co-Cr wire (3M Unitek, Tokyo, Japan), as shown in Fig. 1. The appliance was fixed to the palate by tying the wire around the maxilla to reposition the mandible forward to the edge-to-edge occlusion when the mandible was closed. Then, lateral cephalograms were taken to examine if the anterior teeth of the mandible had been moved forward by about 0.5 mm by the functional appliance (Fig. 1a). During a series of experiments, we confirmed that the animals could eat while wearing the appliance for 24 hours a day.

Morphometric Analysis on Dorsoventral and Lateral Cephalograms

Four weeks after initiating the experiment, lateral and dorsoventral cephalograms were taken of all mice by use of a Rat & Mouse Cephalometer (RM-50: Asahi Roentgen Industry Co., Kyoto, Japan). The head of each animal was fixed firmly with a pair of ear rods oriented perpendicularly to the median sagittal plane. The cephalogram was taken with a dental occlusal film (DF-50: Eastman Kodak, Rochester, NY, USA) under electronic controls of 6 mA and 20 ~ 25 Kvp with an exposure time of 3.0 sec.

On both the dorsoventral and lateral cephalograms, landmarks and measurement items were established for the present study, as depicted in Figs. 1a and b. On the dorsoventral cephalographs, lateral shift of the mandible was defined as the distances between Mm and the median sagittal line (A-Fr; Fig. 1b). According to the modified method of Kiliaridis *et al.* (1985), morphometric analysis of the mandible was performed three times for each of the measurement items (Fig. 1c).

Histomorphometric Analysis

Four weeks after the beginning of the experiments, the mandibular condyles were removed under general anesthesia (nembutal). The specimens were fixed in 4 % formaldehyde, decalcified in citric-formic acid for 1 week, dehydrated in an ascending ethanol series (70, 80, 90, 95, 99, and 100%), embedded in paraffin, and cut into frontal sections of 5 μm thickness. The sections were stained with azocarmine-aniline blue (AZAN) (Sigma-Aldrich, St. Louis, Mo, USA) and subjected to histologic observation using an optical microscope (BH2-RFCA, Olympus Optical Co.).

Statistical Analysis

Analysis of variance (ANOVA) and pairwise comparisons (Fisher) were performed to examine the differences in measured values among the three groups at a confidence level > 95 %.

RESULTS

Body Weights

Body weights decreased in the experimental groups immediately after the surgery, but gradually increased approaching the same weight over 4 weeks in the sham-operated control mice. Thus, surgical intervention (condylectomy) and masticatory disturbance with the use of a functional appliance produced no substantial influence on general growth during the experiments (Fig. 2).

Morphometric Findings

As viewed on the dorsoventral cephalograms, in the mice in the condylectomy group, the mandible exhibited a significant lateral shift (0.31 ± 0.28 mm) to the affected side when compared to the controls (0.02 ± 0.16 mm). In the mice in the condylectomy + appliance group, no significant lateral shift was found (0.02 ± 0.05 mm; Fig. 3a).

On the lateral cephalograms, Pg-Go (mandibular corpus length) was significantly less on the right side of the condylectomy mice than on the left side and in the controls. No significant differences in the size of mandible were found between the right side of the condylectomy + appliance and control mice, and between the right and left sides of the condylectomy + appliance mice (Fig. 3b).

Histomorphometric Findings

Regeneration of the condyle and the disk was demonstrated in all the mice in the condylectomy and condylectomy + appliance groups. Although, the size of the condyle was twice as large when compared to the controls, its shape was irregular in the mice in the condylectomy group. Four layers of the condylar cartilage, observed in the controls, were not detected in the mice in the condylectomy group. Furthermore, various tissues, such as bone, muscles, and cartilage, were irregularly arranged in this group.

On the other hand, the size and shape of the condyle in all the mice in the condylectomy + appliance group were exactly equivalent to the controls. Four layers of the condylar cartilage were also clearly detected in the mice in the condylectomy + appliance group, although the proliferative layer was thinner and the hypertrophic layer was a little bit thicker than in the controls (Fig. 4).

DISCUSSION

In this experiment, unilateral condylectomy in growing mice generated a less developed mandible and a significant lateral shift to the affected side. With a unilateral condylectomy, the mandible loses the condyle, a center of mandibular growth (Berraquero *et al.*, 1992), and experiences the subsequent muscle imbalance and functional disturbances. Immediately after unilateral condylectomy, the mutual relationship between opening and closing jaw muscles was changed; when the temporalis and lateral pterygoid muscles are removed from the condyle, the masseter and medial pterygoid muscles pull the resected area in both the upward and forward directions and to the unaffected side (Bakker *et al.*, 1984; Alexandridis *et al.*, 1991). Thus, the resected area loses optimal joint space in the glenoid fossa with an intra-articular disorder. It may thus be a reason why less development of the mandible occurs.

On the other hand, mandibular repositioning with use of a functional appliance in this study produced significant growth of the mandible on the affected side, leading to the elimination of the lateral shift without any significant differences from the control group. Mandibular growth is achieved by a combination of cartilaginous and membranous growth (Orliaguet *et al.* 1994). Acquired environmental factors, such as occlusion, mastication, functional loading, and intra-articular pathology may change the inherent mandibular growth. The functional appliance used in the present study produced enough space between the surface of the glenoid fossa and the resected area, maintaining the mechanical stimuli on the temporomandibular joint structures at an optimal level. Furthermore, the appliance induces the mandible in to a forward position. If the mandible and condyle are intact, forward mandibular position increases mandibular growth (Tsolakis and Spyropoulos, 1997; Xiong *et al.*, 2005). Recent studies with animal experiments have reported that active mandibular protrusion produces adaptive remodeling of condylar cartilage, as evidenced by increased endochondral bone formation (Rabie *et al.*, 2003; Leung *et al.*, 2004; Shum *et al.*, 2004) and accelerates bone formation in the intact condyle (Shen *et al.*, 2006). It is thus confirmed from previous studies that functional loading, if optimal, is a key factor for the recovery of reduced condylar growth after condylar injury (Miyamoto *et al.*, 2002). From these findings, we have concluded that the acquired growth by the functional appliance to protrude the mandible can compensate for lesser development of the mandible, even after injury of the condyle.

Various studies have been conducted examining regeneration of the condyle after injury in various animal models (Strom *et al.*, 1988; Tomo *et al.*, 1995; Miyamoto *et al.*, 2001). Most joints showed poor regeneration of the condylar head, concluding that unilateral condylectomy in growing animal results in very poor regeneration of the condyle (Miyamoto *et al.*, 2001). From our histomorphometric findings, regeneration of the condyle after unilateral condylectomy was demonstrated to be poor in all sections and completely different from the controls. However, the condyle regenerated after the use of the functional appliance was exactly equivalent to the controls. The functional appliance makes a space between the glenoid fossa and the resected area, which is lost by condylectomy. Therefore, by protruding the mandible, space is created in the resected area allowing the condyle to regenerate and restructure itself. It is indicated that the functional appliance can induce adaptive remodeling of the condyle and the subsequent mandibular growth, leading to the prevention of mandibular asymmetry, despite the mandible having undergone substantial injury, such as condylectomy.

Since the entire condyle, including the bone 0.5 mm below the condylar cervix, was resected by unilateral condylectomy in the current study, it was thought that chondrocytes did not remain on the removed portion; however, regeneration of the chondrocyte was also observed in the removed portion. Condylar regeneration after the condylectomy was reported in rats (Ito *et al.,* 1986), sheep (Miyamoto *et al.,* 2001; 2002), dogs (Miyamoto *et al.,* 2004), and monkeys (Bakker 1984). They described the regenerated condyles in these animals after condylectomy exhibited an irregular shape similar to the results in the current study. Since the shape of the condyle is determined by the traction of a lateral shift and a habitual occlusion (Matsumoto, 1995), mandibular movement and the mechanical stimulus of muscles are disturbed after a unilateral condylectomy (Tsukamoto *et al.,* 1972); consequently the condyle might develop an irregular shape.

The duration for full regeneration of the condyle is about 3 months in the monkey and 1 month in the rat. This phenomenon can only be induced during the growth period. This restricted regenerative period was recognized after unilateral or bilateral condylectomy. The condyle, after unilateral or bilateral condylectomy of a juvenile and adult monkey, was observed for 18 months and as a result, the regeneration was not observed in the adult monkey, although the condyle covered with a cartilage was found in the juvenile monkey (Sarnat and Muchnic*,* 1971). Cartilage regeneration is a phenomenon which does not happen easily after the growth period. Since we used growing mice in this study, the regeneration of the condyle might be found.

In conclusion, it was shown that injury of the condyle reduces condylar and mandibular growth, leading to asymmetry of the mandible and the lateral shift. It was also emphasized that a functional appliance can regenerate the injured condyle and accelerate mandibular growth if used before and during adolescent growth, indicating an importance of condylar and mandibular repositioning to provide sufficient joint space between the injured condyle and the intact glenoid fossa, which may lead to the generation of the optimal loading onto to the temporomandibular joint components.

ACKNOWLEDGMENTS

This investigation was supported by Grants-in-Aid for Scientific Research of the Ministry of Education, Culture, Sports, Science and Technology in Japan

(20791577).

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Figure 1. a: X-ray films of rat mandibles. Upper: immediately after the condylectomy. Lower: after forward repositioning of the mandible in the edge-to-edge occlusion with a functional appliance depicted on the right.

b: Morphometric analysis of the mandible on the dorsoventral radiographs. Mm: Median point of the mandible, A: Most anterior point on the nasal bone, Fr: Intersection of the coronallis and frontal sutures, A-Fr: Median sagittal line on the maxilla of the mandible.

c: Morphometric analysis of the mandible on the lateral radiographs. Pg: Point on most inferior contour of the lower border of mandible, adjacent to the incisors, Go: Most posterior point of the angular process of the mandible, Mandibular body length: Pg-Go.

Figure 2. Changes in body weight between the experimental and control groups. Cd = Condylectomy, Appl = Appliance. Mean±SD. N = 30 on respective groups.

Figure 3. a: Lateral shift of the mandible on the dorsoventral cephalograms in the condylectomy, condylectomy + appliance, and control mice.

b: Size of the mandible in the condylectomy, condylectomy + appliance, and control mice. For controls, the values on both sides were averaged.

Cd = Condylectomy, Appl = Appliance. Mean ± SD. N = 30 on respective groups.

*$P < 0.05$

Figure 4. Photomicrographs of the condyles, stained with azocarmine-aniline blue (AZAN), in the condylectomy, condylectomy + appliance, and control mice (4 weeks after condylectomy or the corresponding sham operation). F: fibrous cell layer, P: proliferative cell layer, D: differentiative cell layer, H: hypertrophic cell layer, B: bone. Cd = Condylectomy, Appl = Appliance.

Figure 1

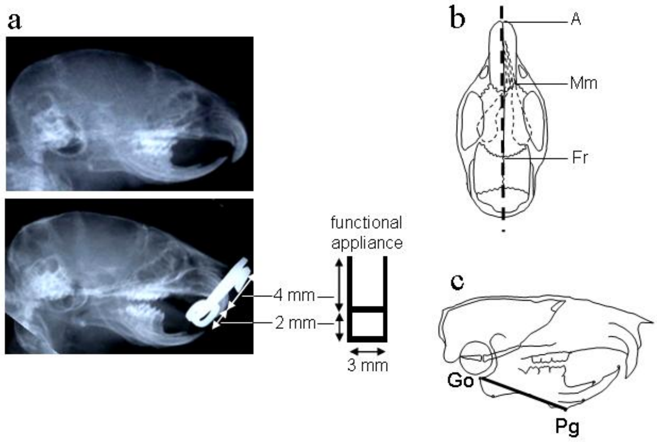

Figure 2

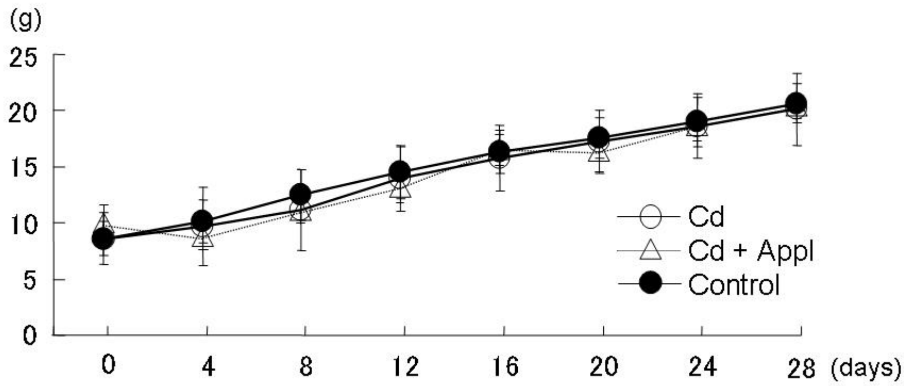

Figure 3

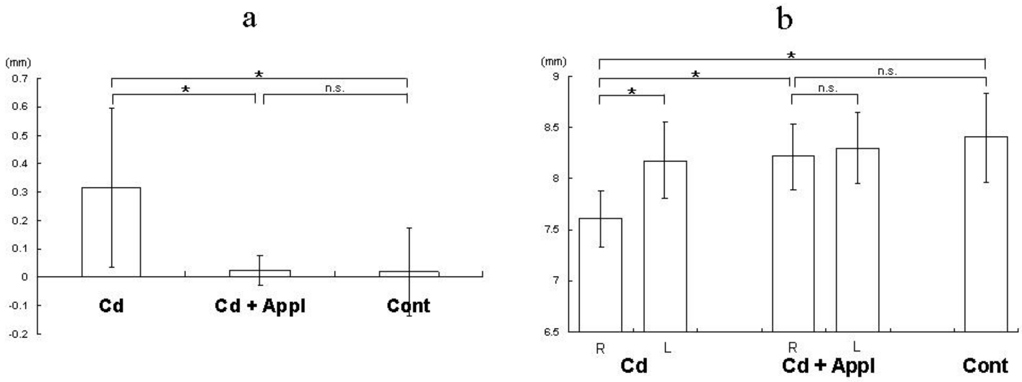

Figure 4