Jaw-Muscle Activity Changes After the Induction of Osteoarthrosis in the Temporomandibular Joint by Mechanical Loading

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Aims: *To examine the effect of mechanical loading on the induction of temporomandibular joint osteoarthrosis (TMJ OA).* ***Methods:*** *Mechanical stress was applied to the rat TMJ by forced jaw opening of 3 hours a day for 5 days. The electromyographic (EMG) activity of the masseter and digastric muscles was continuously monitored by radio-telemetry. It was characterized by the total time each muscle was active (duty time), the number of bursts, and the average burst length. For histologic analysis, rats were sacrificed before, immediately after, and 3 weeks after the period of forced jaw opening.* ***Results:*** *The condylar cartilage revealed OA-like lesions with a decrease in the number of chondrocytes immediately after forced jaw opening. Three weeks later, the OA-like lesions were repaired to some extent. After the forced jaw opening, the duty time of the masseter increased, whereas the duty time of the digastric decreased significantly (*$P < .01$*) at the 5% activity level. Three weeks later, the masseter duty time had decreased and the digastric duty time had slightly increased, returning to the levels observed before forced jaw opening.* ***Conclusion:*** *These results suggest that mechanical overloading of the TMJ induced OA-like lesions with a simultaneous influence on jaw muscle activity, especially at the low activity level. This might imply that muscle activity adapted to reduce the effects of (forced) joint overloading.* J OROFAC PAIN 2008;22:153–162

Key words: electromyography, jaw muscle, mechanical stress, osteoarthrosis, temporomandibular joint

Temporomandibular joint osteoarthrosis (TMJ-OA) is characterized by deterioration and abrasion of the articular cartilage and local remodeling and thickening of the underlying bone.[1] Remodeling is a normal process essential to the maintenance of the structure of the bone and cartilage. Under excessive stress, such as overloading, this mechanism can be disturbed. Such disturbance can alter the TMJ morphology.[2] Among the various etiologic factors, mechanical overloading seems to be the most important in the cascade of events that leads to joint damage with TMJ-OA.[2–5]

The initial pathology of joints caused by TMJ-OA is difficult to characterize in humans because early TMJ-OA is often disregarded. Animal models of TMJ-OA can facilitate the understanding of early pathology of OA in relation to its effects on jaw muscle activity and jaw movements. Recently, animal models of induced OA have been established by a procedure involving repetitive forced jaw opening. Pathologically they resemble the OA that develops in humans.[4,5]

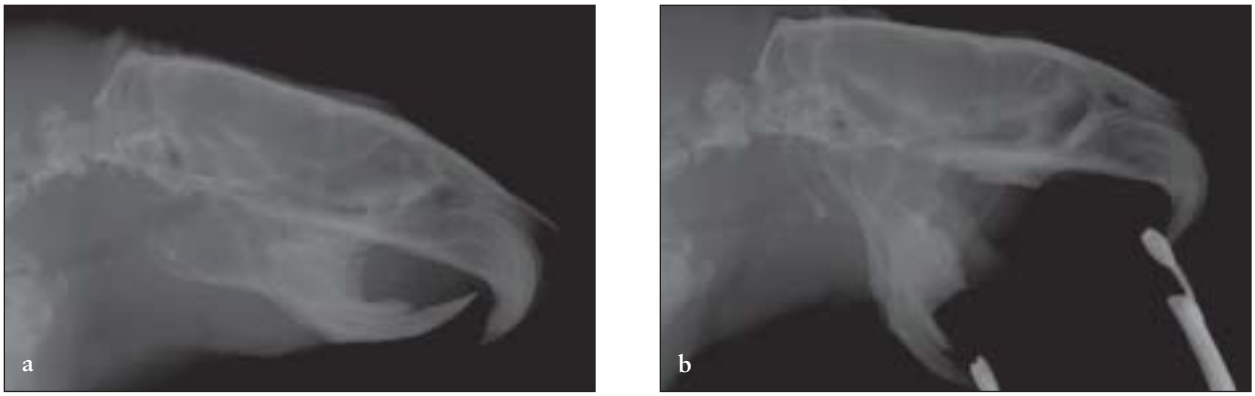

Fig 1 Lateral cephalograms of *(a)* control rats and *(b)* rats during forced jaw opening.

Recently, the relationship between TMJ-OA and muscle function has been reviewed.[3,6] In both clinical and community cases, most patients with TMJ-OA had abnormal muscle function.[6] However, the pathophysiology of jaw muscle disorder in relation to temporomandibular disorder (TMD) patients is still not fully understood.[7–11] To clarify motor control mechanisms and related nociceptive responses, several agents have been experimentally injected in the TMJ region.[12–14] For instance, Yu et al[12] reported increased jaw muscle activity in rats after injection of the algesic chemical mustard oil into the TMJ region.[15] These findings suggest that the intra-articular pathology of TMJ-OA might be associated with changes in motor function. Therefore, knowledge about daily muscle activity after experimentally induced TMJ-OA may contribute to insight into possible mechanisms leading to disordered jaw motor behavior.

The aim of the study was to examine the effect of mechanical loading on induction of TMJ-OA. Mechanical stress was applied to the rat TMJ by forced jaw opening of 3 hours a day for 5 days. The daily muscle activity in the masseter and the digastric muscle was recorded by radiotelemetry before and 3 weeks following the TMJ-OA induction. The authors hypothesized that this mechanical overloading would increase the daily jaw muscle activity.

Materials and Methods

Experimental Animals

Eighteen 14-week-old Wistar strain male rats weighing from 410 to 450 g were randomly divided into 3 groups (6 animals per group). In 2 experimental groups, the TMJ was repetitively overloaded during a period of 5 days. The first group was sacrificed immediately after this period and used for histologic assessment of the TMJ. The second group was sacrificed 3 weeks after cessation of overloading and used to examine the long-term effects of this overloading on jaw muscle activity and TMJ histology. The third group served as control group for histologic assessment. The protocol of the experiment was approved by the Animal Care and Use Committee at Hiroshima University.

Application of Mechanical Stress

Mechanical overloading was induced to the TMJ by forced jaw opening for 3 hours per day for 5 consecutive days. For this, a jaw-opening device was used, a custom-made bite block keeping the maxillary and mandibular incisors 20 mm apart (Fig 1). During this forced jaw opening, rats were anesthetized with intra-abdominal injections of sodium pentobarbital (Nembutal; Dinabott, Osaka, Japan) at a dose of 50 mg/kg body weight. In the control animals, no jaw opening was applied, although the same anesthesia schedule was maintained.

Histopathologic Study

After the experimental period, the animals were sacrificed with an overdose of anesthesia. Left and right TMJs were dissected, fixed in 10% buffered paraformaldehyde, and decalcified with 10% EDTA for 4 weeks at 4°C. Thereafter, they were embedded in paraffin, and serial sections (7 μm) were cut in the sagittal plane. The sections were stained with hematoxylin-eosin (H&E).

The masseter and digastric muscles of each animal were dissected, and serial transverse sections were made to examine the effect of the jaw-opening procedure on the fiber type composition.

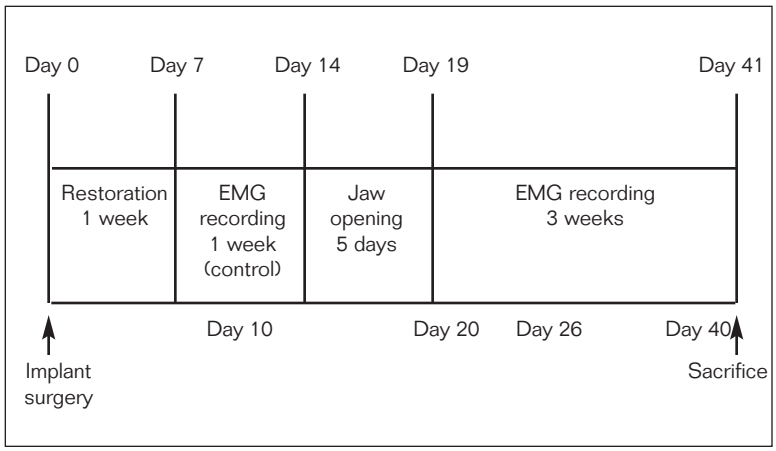

Fig 2 The schedule for this study. The forced jaw opening was applied for 5 days after muscle activities were continuously recorded during 1 week as a control, starting 7 days after surgery. After the forced jaw-opening procedure, muscle activities were recorded again for 3 weeks. After the recording period, the rats were sacrificed (day 41). Muscle activity was analyzed during the control week (day 10), directly after finishing the jaw-opening procedure (day 20), and 1 and 3 weeks after the forced jaw-opening procedure (days 26 and 40).

Telemetric System

Jaw muscle activity was recorded in freely moving animals by a telemetric recording system as applied in previous studies.[16,17] Briefly, bipolar electrodes (each consisting of a double helix, diameter: 0.45 mm) were connected to implantable transmitters for biopotential recording (F50-EEE, 45 mm × 17 mm × 10 mm, 14 g, Data Sciences International). The distance between the 2 tips of the electrodes was 1 to 2 mm, and the effective electrode tip length was 7 mm. The biopotentials were sampled (250 Hz) before transmission and collected by a receiver (RPC-1, DSI) placed under the cage. The signals were stored on a PC hard disk, using the Dataquest ART data acquisition system (Data Sciences International). Previously it has been shown that the electromyographic (EMG) activity recorded with this system is a reliable reflection of the actual biopotentials and can be used for estimation of muscle use.[16]

Each animal was anesthetized with intra-abdominal injections of sodium pentobarbital (Dinabott) at a dose of 50 mg/kg body weight. The transmitter was implanted in the shoulder area, and the bipolar electrodes were subcutaneously led to an incision in the right submandibular region. From there, they were inserted into the center of the superficial masseter and the anterior belly of the digastric muscles and sutured to the muscle surface to prevent them from dislodging. An antibiotic, phosphomycin disodium salt (Sigma-Aldrich) was administered for 3 days preceding and 2 days following surgery. An analgesic, buprenorphine (Lepetan; Otsuka Pharmaceutical), was provided immediately after surgery. From 1 week after surgery, muscle activity was continuously recorded. The first week of recording served as a control. Thereafter, jaw opening was applied to the experimental rats for 5 consecutive days. Muscle activity was recorded for another 3 weeks (Fig 2). After the recording period, the animals were sacrificed with an overdose of sodium pentobarbital for histopathologic study. After death, signals were recorded for another 5 minutes to determine the level of recording noise. The electrode locations were verified by dissection.

Each animal was kept in a cage (45 cm × 22 cm × 18 cm) and fed with pellets and water ad libitum. Day-night rhythm was ensured by automatic dimmed lighting (8 am to 8 pm). Twice a week the animals were weighed and checked for their physical condition. Except for the daily care and regular physical examination, they were left undisturbed to minimize any external influence.

Muscle Activity Analysis

The electrodes did not dislodge during the experiment. Therefore, 12 muscles were processed in the analysis. Recorded muscle activities were visualized using Spike2 software (Cambridge Electronic Design) and analyzed. An animal control group was not used for the EMG study; rather, the EMG recordings of the second week in each experimental animal served as a control. Analysis of 24-hour periods was performed during the control week (day 10), immediately after completion of the jaw-opening procedure (day 20), and 1 and 3 weeks thereafter (days 26 and 40). Motion artifacts caused by full-body actions, which resulted in small fluctuations in the telemetric data transfer, were suppressed (5 Hz high-pass filter), whereafter the signals were rectified and averaged (20 ms window, ie, 5 samples). To eliminate possible artifacts the 0.001% of the day's samples (ie, 43 samples) with the largest amplitudes was excluded. The peak in each of the EMG recordings was defined

Table 1 Body Weight and Food Consumption of the Experimental Animals

	Body weight (g)		Food consumption (g)	
Day	Mean	SD	Mean	SD
7	437.5	43.4	22.6	1.4
14	451.0	23.7	22.3	3.4
20	425.6	25.7	22.5	2.4
40	451.5	26.0	22.2	1.7

Day 7, EMG recording began; day 14: just prior to forced jaw opening; day 20; immediately after forced jaw opening; day 40: end of the experiment.

as the largest of the 99.999% remaining samples indicating the maximum activity for that day and was used for normalization. Activity levels were expressed as percentages of this peak EMG activity.[16–19] Daily muscle use was characterized by means of the total duration of muscle activity (duty time), the total number of bursts, and the average burst length. These parameters were determined for muscle activities exceeding 5% and 50% of the day's peak activity. A burst was defined as a series of consecutive samples exceeding the aforementioned activity levels.[18,19] Note that the duty time for activations exceeding a certain level includes also the duty times for activations exceeding higher levels. Five percent of the day's peak EMG level was well beyond the noise level attained after termination of the experiment. Duty time, number of bursts, and average length exceeding this 5% level were assumed to represent the overall daily muscle use, including all levels and types of muscle activities. Any muscle activity exceeding 50% of the peak EMG levels was considered representative of the most forceful muscle usage.

Analysis of variance (ANOVA) was used to monitor for significant differences in daily duty times, number of bursts, and average burst length exceeding 5% and 50% levels calculated for the 4 specified days (days 10, 20, 26, and 40). If the ANOVA was significant, the Bonferroni/Dunn procedure was used as a post-hoc test. In all tests, $P < .05$ was considered statistically significant.

Results

All animals showed normal feeding behavior and water intake except for the first 2 days after implant surgery, as indicated by the steady food consumption in the experimental groups (Table 1). Compared to their initial weight, the animals did not show any significant body weight change (Table 1). The physical condition and behavior of the experimental rats were normal just after the jaw-opening protocol, despite the stress of undergoing general anesthesia for 3 hours for 5 successive days.

Histopathology

Figure 3 shows H&E-stained sagittal sections of the rat TMJ. These sections were representative of control and experimental TMJs. The same histopathologic features were seen in both sides of TMJ, and no marked differences were found among the TMJs in each group.

In the control animals, the condyles showed smooth articular surfaces without pathologic signs. Four different layers of the cartilage could easily be distinguished (fibrous, proliferating, mature, and hypertrophic), and the cells were regularly arranged (Figs 3a and 3b). The disc contained many cells, and its collagen fibers were running regularly (Fig 3a).

Immediately after the forced jaw-opening procedure, marked OA-like lesions were observed in the condylar cartilage. Especially in the posterior region, a decrease in the thickness of the articular cartilage, irregularity of chondrocyte alignment, reduction of chondrocyte number, and hyalinization of the cartilage matrix were obvious in the proliferating, mature, and hypertrophic cell layers (Figs 3c and 3d). However, the disc showed no degenerative changes. Three weeks later, the OA-like lesion was repaired to some extent or at least exhibited an adaptive response, including an increase of the number of chondrocytes in the proliferating cell layer and the thickness of the articular cartilage. However, the chondrocytes remained irregularly arranged (Figs 3e and 3f).

No differences in the fiber type composition of the masseter or digastric muscles could be detected between the experimental and the control group (data not shown).

Muscle Activity

EMG recordings before and after the forced jaw opening showed large variations in both amplitude and number of activity bursts. An EMG recording of the masseter (300 seconds) is shown in Fig 4. Two 10-second periods are amplified to show the variation in activity patterns. The EMG recording shown is not representative for the daily muscle activity, as during large periods of time the muscle activity did not exceed the 5% of the peak activity.

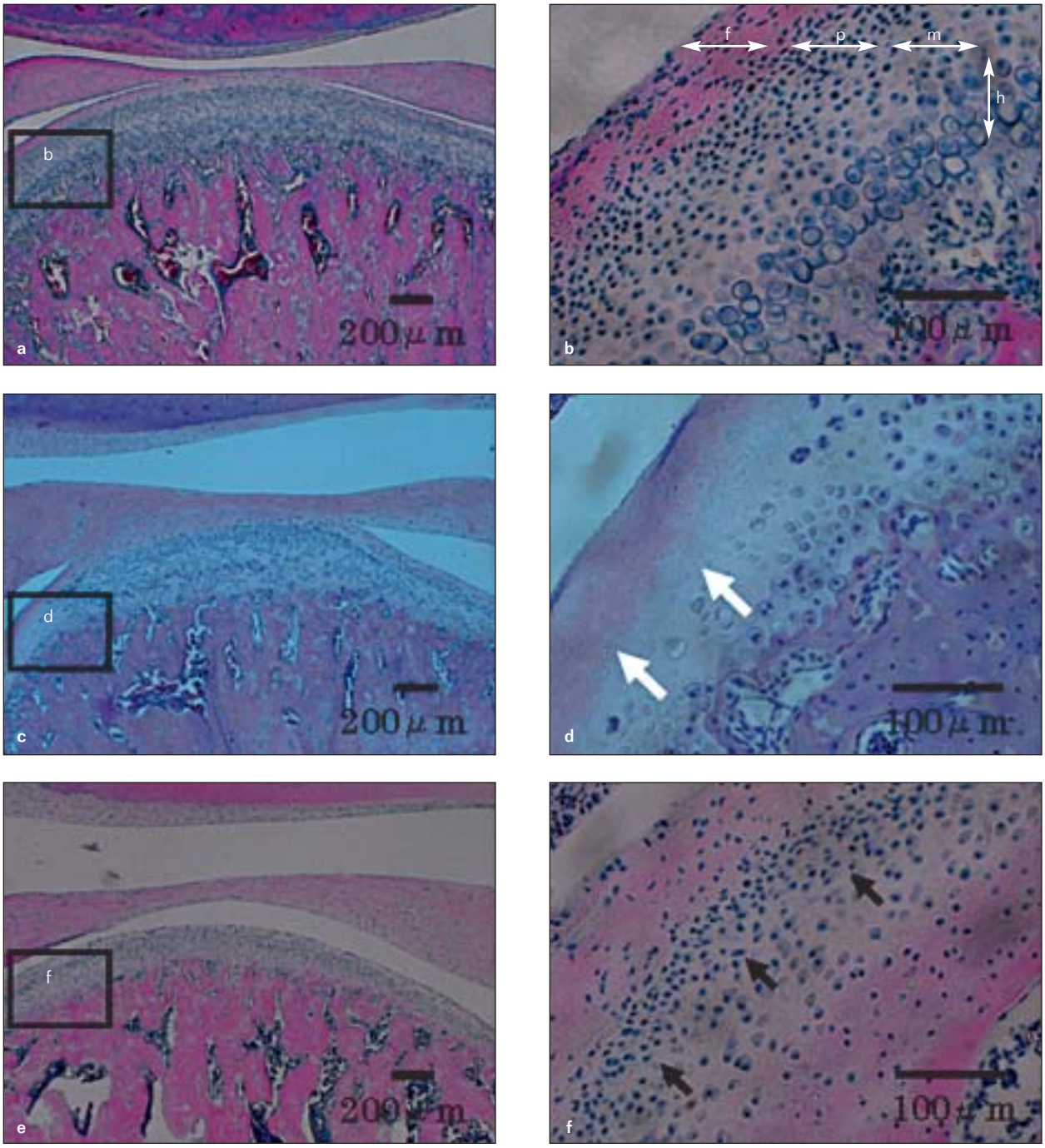

Fig 3 H&E-stained sections of the rat TMJ. *(a)* Control TMJ. *(b)* Higher magnification of the area within the rectangular frame placed in section a (f = fibrous cell layer, p = proliferating cell layer, m = mature cell layer, h = hypertrophic cell layer). *(c)* Experimental TMJ immediately after forced jaw-opening procedure. *(d)* Higher magnification of the area within the rectangular frame placed in section c. Osteoarthrosis-like lesions were observed in the condylar cartilage. The condylar cartilage showed hyalinization and a cell-free area *(white arrows)*. *(e)* Experimental TMJ 3 weeks after forced jaw-opening procedure. *(f)* Higher magnification of the area within the rectangular frame in section e. Osteoarthosis-like lesions were repaired to some extent. The number of chondrocytes increased in the proliferating cell layer *(black arrows)*.

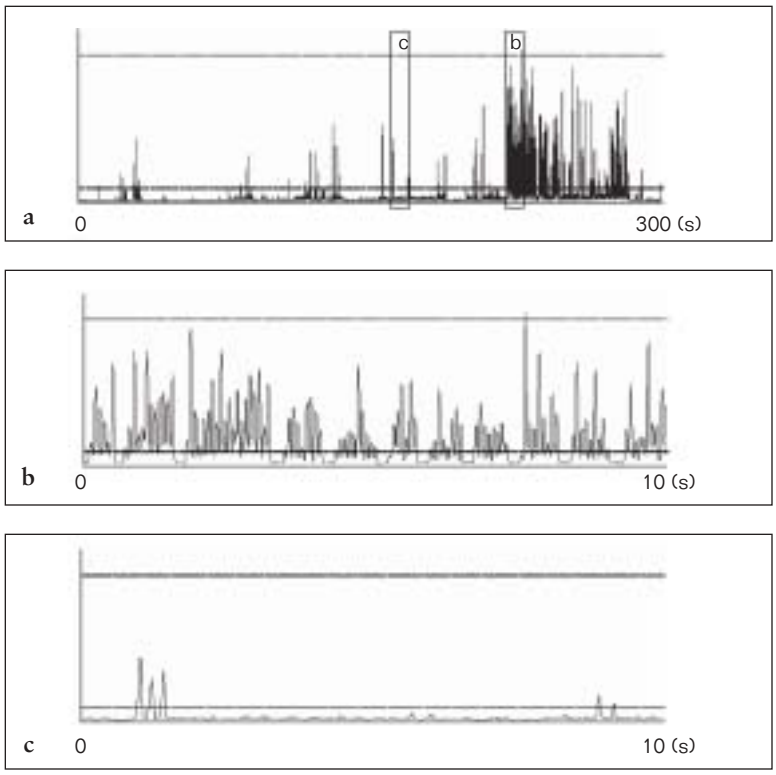

Fig 4 Rectified EMG recording of the masseter muscle. *(a)* Five minutes of recording showing the typical variations in muscle activity. The two 10-second periods that were amplified are indicated. *(b)* Rhythmic activity with many high-amplitude bursts (chewing). *(c)* Irregular muscle activity. Broken lines indicate 5% and 50% of the peak activity (100%). Note that the distribution of activity is not typical for the total daily muscle use.

Before the jaw-opening procedure (day 10), the duty times for activities exceeding 5% of the peak EMG levels of the masseter and the digastric (Fig 5a) were 4.64% ± 1.08% and 19.2% ± 9.18%, respectively. After the 5 days of the forced jaw-opening procedure (day 20), the masseter duty time increased (5.90% ± 1.36%, $P < .01$), whereas that of the digastric decreased (12.9% ± 7.71%, $P < .01$). At 1 week after the forced-opening procedure (day 26), the duty time of both muscles showed similar duty times as at day 20. However, 3 weeks after the procedure (day 40), the duty time of the masseter (4.86% ± 0.76%) showed a decrease ($P < .01$) to a value similar to the control measurement. Meanwhile, during the 3 weeks after the forced-jaw opening procedure, the duty time of the digastric increased only a little (NS) but remained below the preprotocol level (Fig 5a).

In the masseter, the changes in duty time were matched by similar variations in the daily number of bursts. Compared to the control value (day 10), burst numbers increased directly and at 1 week after the forced jaw-opening procedure ($P < .01$). After a recovery period of 3 weeks, the number of bursts returned to control values. The average burst length was constant (0.070 to 0.073 seconds) throughout the experiment. In contrast, the burst number of the digastric decreased (NS) and its average burst length decreased ($P < .01$) after the jaw-opening procedure and remained unchanged thereafter (Fig 5a).

Although a similar pattern of changes could be seen for activities exceeding the 50% of the peak EMG, most of them were not significant (Fig 5b). Only the burst number of the masseter increased significantly ($P < .01$) at 1 day after the jaw-opening procedure; it then remained significantly higher than the control measurement.

Discussion

Experimental Model

Various methods have been reported for the development of a model of experimentally induced OA.[4,5,20] These can be roughly divided into surgical, chemical, and biomechanical methods, all of which create damaged cartilage tissue on the articular surface. The surgical method creates a reproducible and progressive model of TMJ-OA. In the rat, however, this technique necessitates incision of the masseter to expose the TMJ. In the chemical approach, the injection of an inflammatory substance (collagenase,[21] complete Freund's adjuvant[22,23]) induces disease. However, unlike

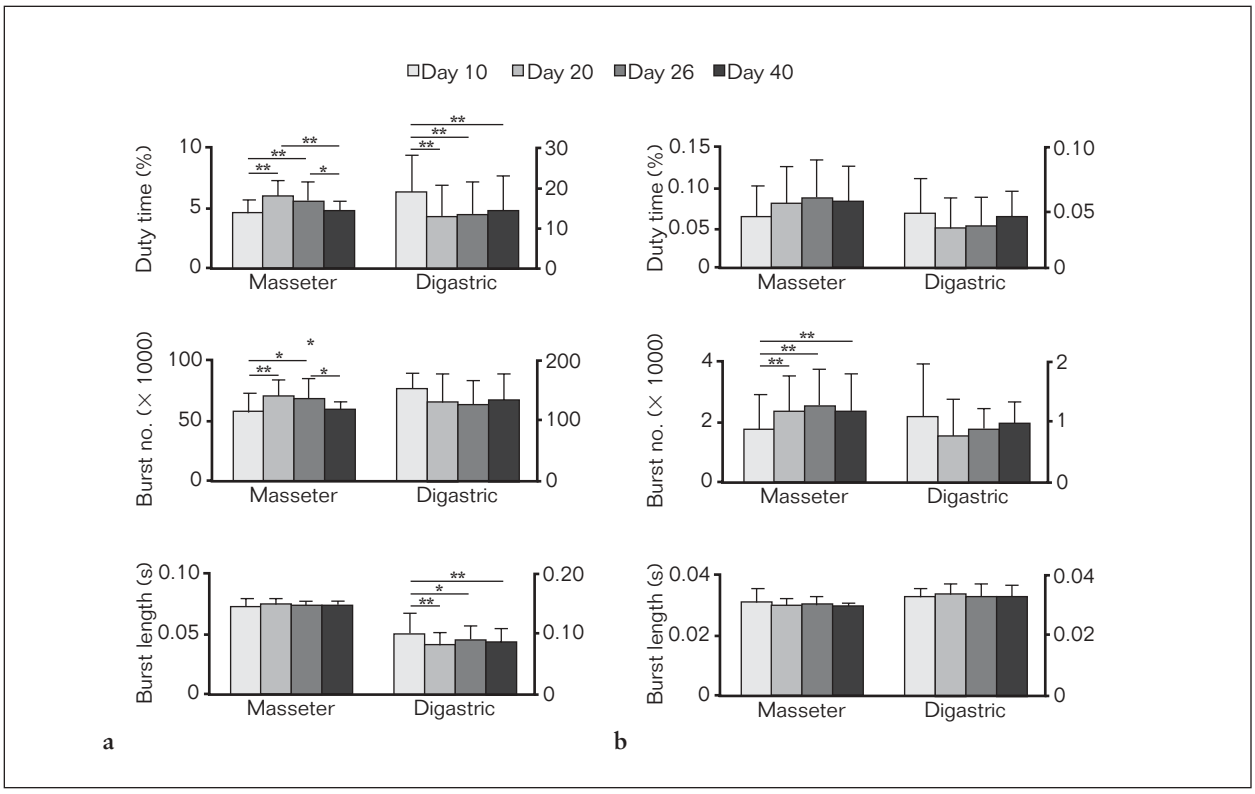

Fig 5 Activity characteristics of the masseter and digastric muscles during the control experiment (day 10) and after the forced jaw-opening procedure (days 20, 26, and 40). Duty time, burst number, and mean burst length for muscle activities exceeding *(a)* 5% and *(b)* 50% of the peak EMG. $*P < .05$; $**P < .01$. Means ± standard deviations are indicated.

rheumatoid arthritis or synovitis, TMJ-OA has primarily a noninflammatory origin.[1] Therefore, the chemically induced TMJ-OA cannot be considered a true model of OA. Pain models have been generated by the application of various agents, such as mustard oil,[12] formalin,[13] or glutamate,[14] to the TMJ region. Of these 3 substances, only glutamate is noninflammatory, but its capacity to provoke TMJ-OA-like lesions is unknown. In the present study, a biomechanical method used in previous publications[4,5] was applied. A forced jaw opening of 20 mm for 3 hours per day for 5 days resulted in marked OA-like lesions in the cartilage immediately after the protocol. In this procedure, the posterior region of the articular surface was continuously overloaded, provoking damage to the cells and matrix of the cartilage. Progressive cartilage breakdown eventually leads to perforation or disruption of the disc and denudation of the subchondral bone.[3] In this study, the lesion was localized in the cartilage, and 3 weeks later, the damaged tissues were mostly repaired. Therefore, the pathological change in this model can be categorized as an early stage of TMJ-OA. A progressive OA-like lesion with bone deformation might be caused in this rat model by increasing the number of days of mechanical overloading.

In an OA model, the effect of the forced jaw-opening procedure on the jaw muscles is a factor of concern. Skeletal muscles are able to adjust their phenotypic properties in response to altered functional demands.[24] It is known that extensive stretching of muscle fibers beyond their habitual range of lengthening results in a transition from fast to slow myosin types but does not result in a change in EMG activity.[25,26] It has been demonstrated that the activity of the jaw muscles and/or the growth of the cranium and mandible are influenced by changes in muscle length due to artificial repositioning of the mandible.[27–29] However, in this study the jaw was opened 20 mm (kept constant by a bite block under general anesthesia), well within the range of the natural mandibular motion in rats,[30] and jaw opening was limited to 3

hours a day for 5 days. Therefore, the impact of the muscle stretch in the current study was probably negligible. The procedure can be assumed not to affect the activity nor the fiber type composition of the jaw muscles as described for permanent muscle length changes. Muscle activity was not recorded during forced jaw opening; the modifications of muscle activity observed were assumed to be caused only by the OA-like lesion. No pathologic changes could be detected in the muscles.

Observed Change of Muscle Activity

Including all activities (> 5%), the duty time of the masseter increased and that of the digastric decreased at a low activity level (Fig 5a). At high activity levels (> 50%), fewer significant differences were found, although a similar pattern of changes could be seen (Fig 5b). For the masseter this duty-time increase was mainly the result of an increase in number of bursts. In the digastric, however, the decrease in duty time was caused by a significantly shorter average burst length. This differential change in duty time of both muscles might be the result of their having distinctly different functions. The affected area of the TMJ may have been irritated during jaw opening, when the digastric is active. The animal may have reduced the number of jaw-opening motions and/or the strength with which the jaw was opened to minimize the pain. The present results suggest that the latter is the case. The increased activity in the masseter could function as an additional stabilization of the system (thus the increase in bursts), keeping the TMJ loading clear of the irritated region. The recovery period suggests that the need for stabilization disappeared after 3 weeks, but the enduring decreased digastric activity suggests that the TMJ remained painful or at least sensitive to loading. It was reported that in a human study almost all muscle activity exceeding the 50% level appeared during meal time.[31] However, as a jaw-closing muscle, the masseter is not only recruited for high-power tasks such as chewing but also for low-power tasks, such as the maintenance of the mandibular rest position. Therefore, the significant increase at the low activity level can be thought as a behavior to protect against further damage of the TMJ by immobilization of the masticatory system. In contrast, feeding, although a high-power task, is necessary for maintaining life, and this may be why the activity of both muscles at the high activity level (50%) did not change significantly.

In a previous study, interindividual variation in the normal muscle activity was large, but the daily jaw-muscle activity of each of the rats was constant over the 4 weeks of recording.[17] These results indicate that the EMG recording method used is reproducible and that the change of muscle activity in this study was the effect of the forced jaw-opening procedure. Because of a large interindividual variation in muscle activity, no control animals were used. The muscle activity in the second week after surgery, before the forced jaw-opening procedure was applied, served as a control for the muscle activities recorded after the experimental procedure.

Influence of TMJ Damage on Jaw-Muscle Function

The human masticatory system is a complex musculoskeletal system where the jaw muscles, stretch and compression in the TMJ, and jaw movements interact.[32] If 1 of these factors changes, it will influence the others. This especially concerns the activation patterns of the jaw muscles, which more or less easily adapt to a change, eg, to relieve pain in a damaged joint. Therefore, the TMJ pain associated with collapse of cartilage tissue in TMJ-OA cannot be treated without taking jaw muscle behavior into account. In the present study, to investigate the relationship between joint pathology and muscle function, the daily muscle activity in the masseter and digastric muscles of the rats with experimentally induced TMJ-OA was recorded by a telemetry system. This is, to the authors' knowledge, the first attempt to examine changes of muscle activity due to intra-articular pathology. Although the jaw-closer muscle showed an increased amount of activity, the jaw-opener muscle demonstrated an opposite adaptation. This result shows that the masticatory system, including the TMJ and jaw muscle, was affected by the change of the orofacial condition. Yu et al[12] showed that injection of mustard oil into the TMJ region of rats caused a transient increase of the jaw-muscle activity. The trigeminal subnucleus caudalis has been shown to be an essential relay site of nociceptive inputs from deep craniofacial tissues, including the TMJ. It plays an important role in nociceptive reflexes evoked by injection of mustard oil into the TMJ region, although the central neural pathways underlying the mustard oil-evoked reflex EMG response in the jaw muscles are still unknown.[33] Although the underlying mechanism could be similar, the results of the current study suggest a much more adaptive and long-lasting response of the muscles, in contrast to the short change in muscle activities due to mustard oil injection.

It has been reported that the jaw-muscle activity of patients with orofacial pain increases at rest, but the relationship between muscle pain in the TMD patient and hyperactivity in the jaw muscles is still debated.[7–11] The present results suggest that the masticatory system is able to change differentially its motor behavior to minimize the effects of an induced disorder. Upon the onset of OA, the masseter muscle showed an increase of activity, while the digastric muscle decreased its total actions. This might be related to a protective mechanism requiring an increase in masseter actions to stabilize the joint position and a decrease in digastric activity to avoid the use of the damaged joint surface. The partial recovery of the cartilage tissue permitted a full return of the normal masseter function, while the digastric actions remained restricted to some extent. The present study did not clarify the mechanism of muscle pain, but the findings may be related to the muscle dysfunction in TMJ-OA patients and the presence of muscle splinting with muscle pain.

Conclusions

The results suggested that repetitive mechanical overloading to the TMJ components induced OA-like lesions in the condylar cartilage. This intra-articular pathologic status and the possible accompanying pain may influence jaw-muscle activity, especially at a low level. The changes in muscle activity observed in this study seemed to be an attempt to protect against further damage. These findings may be related to muscle splinting in TMJ-OA patients with muscle pain and suggest that TMJ-OA patients who suffer from a muscle disorder might be treated successfully by repairing the TMJ condition.

Acknowledgments

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