Dr. Miller

Experimentally induced neuromuscular changes during and after nasal airway obstruction

Arthur J. Miller, Ph.D., Karin Vargervik, D.D.S., and George Chierici, D.D.S.
San Francisco, Calif.

Neuromuscular changes were studied by electromyography in rhesus monkeys which adapted to nasal obstruction for 2 years and then in the succeeding year recovered to nasal respiration. Obstructing the nasal passage with silicone plugs induced specific behavioral responses which remained for the duration of nasal obstruction and were lost within 8 days after removal of the plugs. Animals demonstrated individual variations, but more than 80% consistently maintained a lower mandibular posture for the entire 2-year period. Rhythmic mandibular, tongue, and upper lip movements were evident in fewer than 60% of the animals. Certain craniofacial and tongue muscles (the genioglossus, dorsal tongue fibers, digastric, geniohyoid, dilator naris, and vertically oriented fibers of the superior orbicularis oris, that is, lip-elevator fibers) were recruited rhythmically and remained rhythmically active throughout the entire 2-year period of nasal obstruction. This rhythmic activity ceased within 1 week after removal of the nose plugs. A tonic or consistent discharge was also induced in the genioglossus, dorsal tongue fibers, the geniohyoid, superior orbicularis oris, and lip-elevator fibers over the entire 2 years of nasal obstruction. Not all muscles lost their tonic discharge after removal of the nasal plugs. The genioglossus, geniohyoid, inferior orbicularis oris, and lip-elevator fibers discharged tonically during the recovery period. These data suggest that nasal obstruction can induce neuromuscular changes which extend beyond the period of obstruction and remain after the original stimulus for neuromuscular change has been removed.

Key words: Neuromuscular activity, oral respiration, craniofacial muscles.

One of the most relevant and important concepts studied in the field of craniofacial research is the adaptability and plasticity of the craniofacial bone and the determination of those factors which can modify and remodel this structural complex. Most of these studies have emphasized the importance of the neuromuscular system. Removal of craniofacial muscles by surgery or detachment[1-7] or impairment of their function by a central motoneuron lesion[8-10] in an immature animal directly modifies the shape, bone density, and sutures of the cranioskeleton and mandible. While these studies suggest an effect of the muscular system on the skeleton, they do not differentiate among the various properties of the neuromuscular system which will affect the bone. In a few studies, muscle function has been altered. For example, McNamara and Carlson[11, 12] and Petrovic and his co-workers,[13, 14] have demonstrated that condylar growth and remodeling occur during treatment with an appliance designed to protrude the mandible of the monkey or rat.

From the Craniofacial Center, Department of Growth and Development, School of Dentistry, University of California, San Francisco.
This study was supported by Grant DE 05558 from the National Institute of Dental Research.

Research at our Center has used the rhesus monkey as an animal model to study the effect of almost complete nasal obstruction on craniofacial growth and adaptation. Previous reports have shown that specific skeletal and dental changes, including an increased gonial angle, lower face height, anterior downward tipping of the occlusal plane, and dual bites, crossbite, and open bites occur within 24 months after nasal obstruction in these monkeys.[15, 16] Soft-tissue changes, such as development of a triangular upper lip and a groove within the tongue, precede the skeletal and dental adaptation and are evident within the first 6 months of nasal obstruction.[17, 18] These animals also adapt their neuromuscular system in the level and type of EMG activity as documented within the first 6 months of nasal obstruction,[17, 19] and then with a separate experimental group, after 3 years of nasal obstruction.[20] These studies have emphasized that one of the neuromuscular properties modified is the active recruitment of the muscle, whether the muscle is phasically recruited in rhythmic discharge or tonically active with continually discharging motor units. This article extends these original electromyographic studies by following an experimental group beyond the 6-month pe-

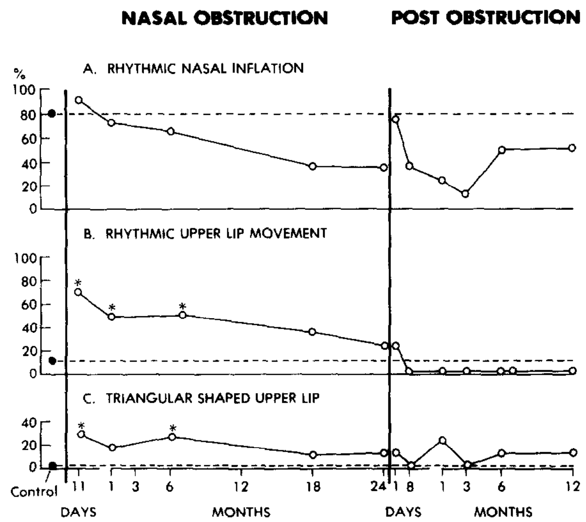

Fig. 1. The percentage of eight animals which demonstrated specific behavior responses prior to nasal obstruction, during 2 years of nasal obstruction, and for 1 year following removal of the nasal plugs. The control observations are from two recording sessions prior to the nasal obstruction. The dotted line indicates the mean of the control observations prior to the experimental period and is extended over the 3-year experimental period for reference. Asterisks refer to statistically significant results with a $p < 0.05$.

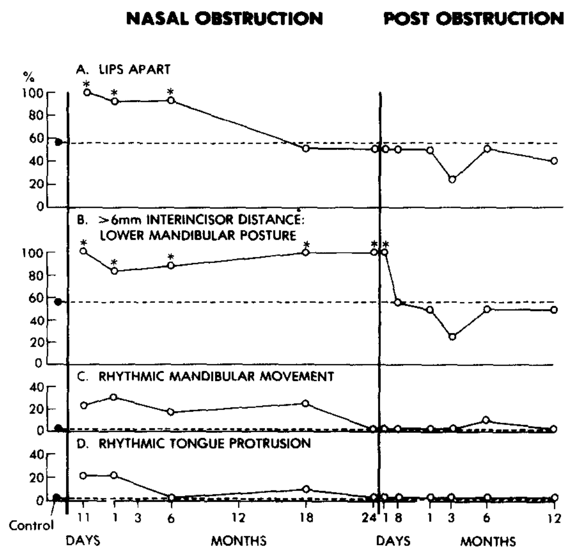

Fig. 2. Four additional behavioral responses exhibited by the eight rhesus monkeys prior to, during, and after nasal obstruction.

riod over the entire 2 years of nasal obstruction and then extending the study into the recovery period after the nasal plugs are removed. This is the first study which has systematically recorded the EMG response every 3 months throughout the period of nasal obstruction and after the plugs were removed.

One of our recently published articles[16] has compared each animal's morphologic adaptations on the basis of cephalometric analysis with the final EMG recording at the end of 2 years of nasal obstruction and 1 year after removal of the nasal plugs. That article emphasizes the individual variations.

METHODS

Eight rhesus monkeys (seven males and one female), ranging in age from 1 to 3 years, were used in the study. Changes in neuromuscular functions were determined by electromyographic intramuscular recordings from sixteen muscles. Behavioral responses were assessed simultaneously by observing the presence of rhythmic movements of the lips, tongue, and mandible. Soft silicone nose plugs were fitted to each nostril and attached with a ligature placed through the nasal septum.[16] At the completion of the 2-year study during nasal obstruction, the animals received one final recording session with EMG recordings before and after removal of the nose plugs. EMG activity was recorded during the succeeding 18-month recovery period.

Electromyography

Each monkey was examined in two control recording sessions prior to placement of the nasal plugs. Prior to each recording, the animal was initially anesthetized with ketamine (Ketalar, 10 mg/kg, intramuscularly) before it was removed from its cage to a recording chair. While the animal was under anesthesia, the fine wires were placed in pairs through a 23-gauge hypodermic needle into each muscle. Exact electrode placements have been described previously.[17-20] The recording session was then conducted over a 2-hour period after the animal recovered from the anesthesia.

The recorded EMG activity was analyzed for background activity levels in three 5-minute trials. The response of the muscles was also observed during mastication, and specific responses were evoked to recruit each muscle (lip compression to recruit the superior orbicularis oris, raising of the lateral upper lip by the levator labii superioris, etc.). Each pair of EMG electrodes was connected to a differential high-impedance amplifier (Tektronix 502 AM) and filtered between 10 and 10,000 KHz with a gain of 2,000×. The amplified, filtered signal was stored on FM tape with a frequency band width of 0 to 3000 KHz.

EMG activity was analyzed for two types of neuromuscular discharge patterns. Rhythmic discharge was compared to that of a primary respiratory muscle, the diaphragm or second intercostal muscle, and defined as a periodic discharge in synchrony with the EMG of the primary respiratory muscle. Consistent discharge was defined as a continuous discharge of motor units which could include low-amplitude motor

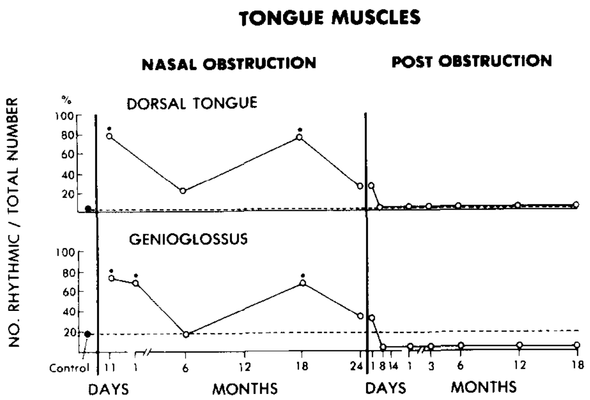

Fig. 3. The percentage of monkeys which rhythmically recruited two tongue muscles prior to, during, and after nasal obstruction.

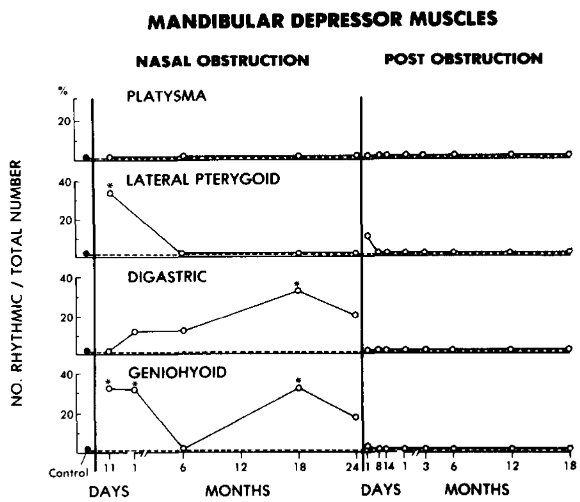

Fig. 4. The percentage of monkeys which rhythmically recruited four muscles active during jaw depressions prior to, during, and after nasal obstruction.

units as well as phasic activity which might recruit larger motor units. The original EMG signal was rectified, integrated (TEAC I-6 Autoreset integrator), and then the number of integrations over 5 minutes was displayed as a raster (WPI raster display).[17, 18, 21] The integration continued to a predetermined level and then reset so that the intervals between resettings of the integration could be displayed as a histogram with the mean interval per 100 integrations tabulated by a digital counter (Tektronix DC 505 digital counter). To determine a change in the use of the muscle, the activity of a given muscle was tabulated for all observations from all eight animals at a given recording time (3 months), and the percentage of total observations with rhythmic or tonic activity was determined.

In this article, the data have been pooled across all experimental animals to determine whether a trend occurred in the use of specific craniofacial muscles. The purpose of this approach was to determine whether nasal obstruction specifically altered and maintained an altered neuromuscular discharge through the entire period of nasal obstruction and whether this active control would modify with recovery.

The percentage of rhythmic or tonic activity during the control recordings was plotted across the 3½-year period for reference. Data were analyzed statistically by means of the nonparameter McNemar test or the binomial test with a $p < 0.05$.

RESULTS

Behavioral characteristics

In the normal resting rhesus monkey, systematic visual observations indicated that the nostrils will inflate with inspiration of air. Placement of the nose plugs did not increase the rhythmic inflation of the nostrils around the nares, but the nasal rhythmicity actually decreased over the 24-month period (Fig. 1). However, the nasal obstruction did markedly increase the rhythmic raising of the upper lip, which was most prominent within the first 2 weeks of nasal obstruction and then slowly declined over the 2-year period. The upper lip could also develop a soft-tissue change in the form of a triangular shape with a raised midline. This occurred in fewer than 40% of the observations during nasal obstruction and was evident as early as 11 days. Removal of the nasal plugs definitely stopped the rhythmic raising of the upper lip, while the rhythmic inflation of the nasal cavity and the triangular shape of the upper lip partially remained after removal.

Obstruction of the nasal cavity also caused the animals to separate their lips, with the most marked effect within the first 11 days, and this effect remained through the first 6 months (Fig. 2). The animals also maintained a lower resting posture of the mandible which remained throughout the entire 2-year period of nasal obstruction. The mandible was rhythmically lowered and the tongue rhythmically protruded, but in fewer than 40% of the animals. The rhythmic movements of the tongue and mandible were lost by the end of 18 months. Removal of the nasal plugs stopped the rhythmic recruitment of the tongue and mandible. The animals decreased the interincisor distance and returned to the normal resting posture for the mandible and lips.

Electromyographic characteristics: Rhythmicity

Tongue muscles. Nasal obstruction markedly increased the rhythmic recruitment of both tongue muscles studied—the dorsal tongue fibers and the genioglossus muscle (Fig. 3). The rhythmicity fluctuated within the 24-month period. On the day of removal of the plugs, the first postplug EMG recording indicated that rhythmicity remained in these tongue muscles. The

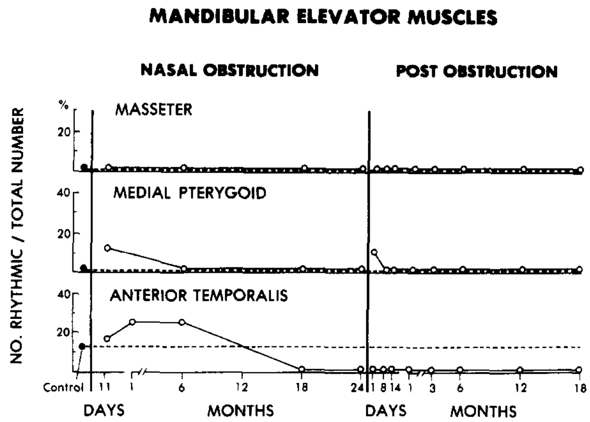

Fig. 5. The percentage of monkeys which rhythmically recruited the mandibular elevator muscles.

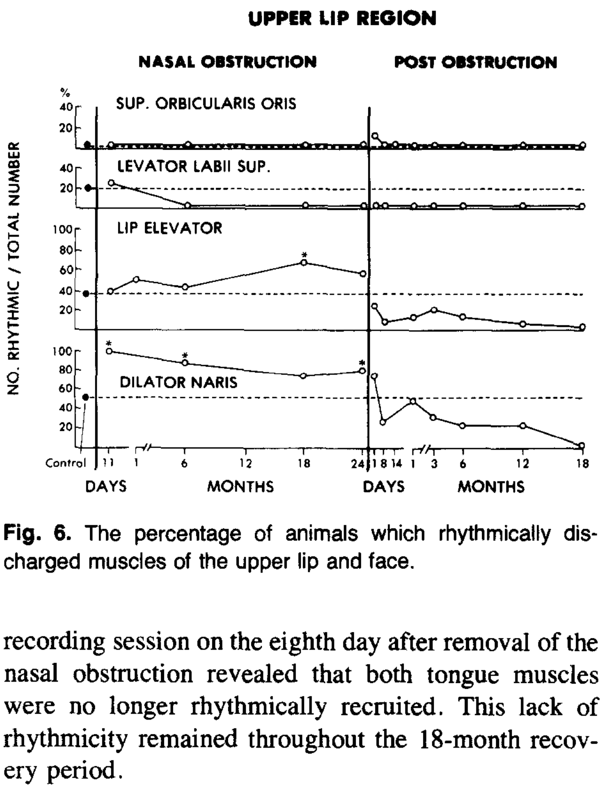

Fig. 6. The percentage of animals which rhythmically discharged muscles of the upper lip and face.

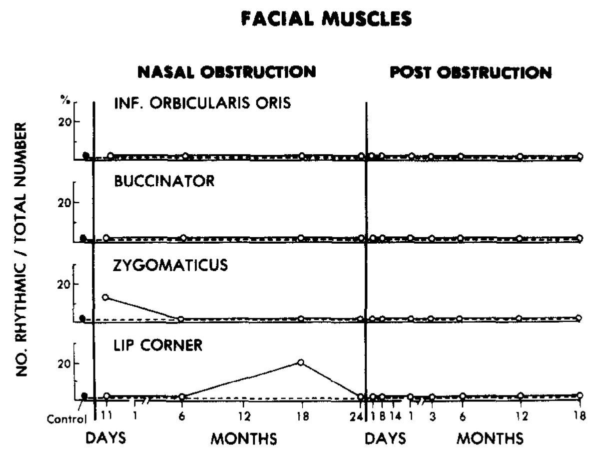

Fig. 7. The percentage of animals which rhythmically recruited four facial muscles.

recording session on the eighth day after removal of the nasal obstruction revealed that both tongue muscles were no longer rhythmically recruited. This lack of rhythmicity remained throughout the 18-month recovery period.

Mandibular depressors. Among those muscles that could potentially be involved in lowering the mandible, only the geniohyoid and digastric muscles demonstrated a consistent rhythmicity during the 2-year period, but in fewer than 40% of the animals (Fig. 4). In the initial adaptation to nasal obstruction (eleventh-day recording), the lateral pterygoid and geniohyoid were the only two of the four muscles rhythmically recruited. By the end of 1 month, the digastric had joined the geniohyoid and lateral pterygoid muscles in rhythmic recruitment. The geniohyoid, digastric, and inferior head of the lateral pterygoid were active during inspiration. By the end of 6 months, the rhythmic recruitment had ceased in the lateral pterygoid. Interestingly, of the two consistently rhythmic muscles, only the geniohyoid demonstrated the same loss of rhythmicity at the sixth-month recording period that was evident with the tongue muscles. The platysma was not rhythmic in this group of eight animals. Removal of the plugs eliminated the rhythmic discharge immediately, and these muscles maintained this lack of periodic discharge through the entire 18-month recovery period.

Mandibular elevators. Nasal obstruction induced a rhythmic discharge in only one of the three mandibular elevator muscles, the anterior temporalis (Fig. 5). Neither the masseter nor the pterygoid demonstrated much rhythmic activity. The anterior temporalis was rhythmically active immediately within the first 11 days following nasal obstruction, but in fewer than 30% of the animals, so that there was not a statistically significant difference ($p > 0.05$). The muscle discharged during expiration. After 6 months of nasal obstruction, no further rhythmic activity was evident in any of the three mandibular elevator muscles. Removal of the nasal plugs had no further effect.

Facial muscles. Of the eight facial muscles studied, only the dilator naris and the vertical fibers of the superior orbicularis oris (lip-elevator fibers) demonstrated rhythmicity in more than 50% of the animals throughout the entire 2-year period of nasal obstruction (Fig. 6). Nasal obstruction induced a rhythmic discharge in the dilator naris in all animals despite the fact that the nasal passage was significantly blocked, allowing a minimal airflow. Interestingly, none of the vertically oriented or laterally placed facial muscles, such as the levator labii superioris and zygomaticus, demonstrated consistent rhythmic recruitment over the 24 months

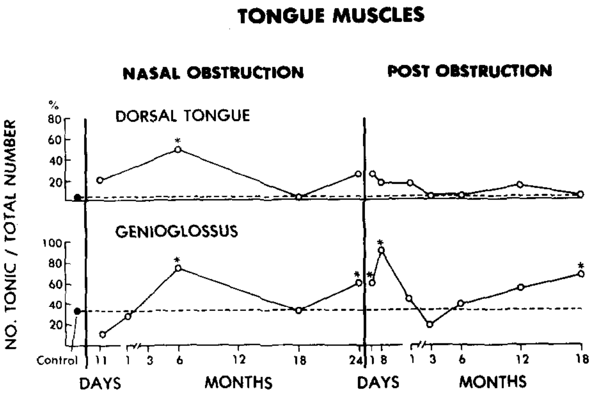

Fig. 8. The proportion of eight monkeys which consistently or tonically recruited two tongue muscles prior to, during, and after nasal obstruction.

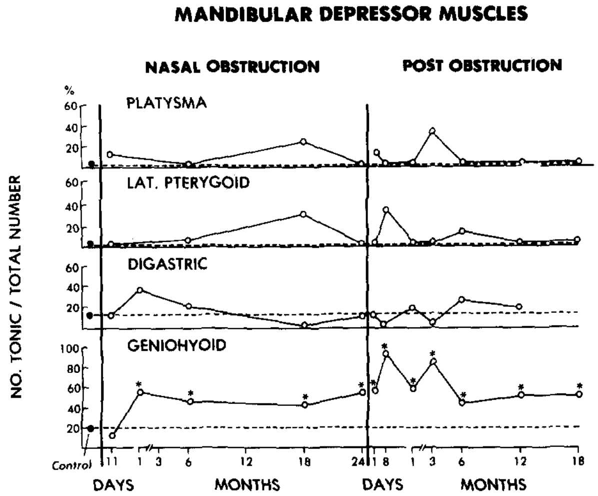

Fig. 9. The percentage of animals which tonically recruited muscles that potentially could be involved in depressing the mandible.

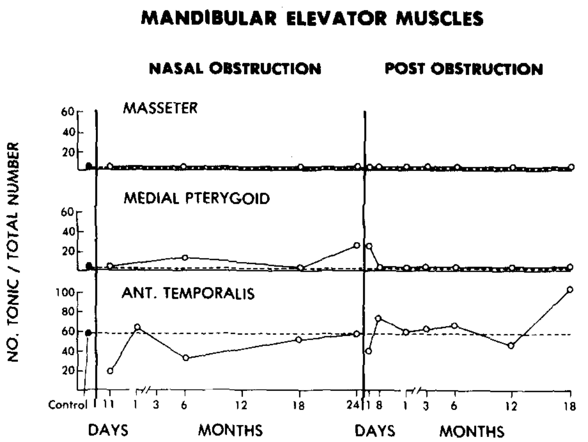

Fig. 10. The percentage of animals which tonically recruited the mandibular elevator muscles.

(Figs. 6 and 7). Removal of the nose plugs decreased the rhythmic recruitment of the lip-elevator fibers immediately, but the dilator naris remained rhythmic until the end of the first week of the post-obstruction period.

Electromyographic characteristics: Tonicity

Tongue muscles. Nasal obstruction altered the tonic activity (that is, consistent discharge) of the two tongue muscles (Fig. 8). Prior to placement of the nasal plugs, the genioglossus was consistently discharging in fewer than 40% of the animals, while the dorsal tongue demonstrated no tonic activity. Within 11 days after nasal obstruction, tonic activity was induced within the dorsal tongue fibers, while tonicity was depressed in the genioglossus muscle during the first month. The tonic activity flucutated over the 24-month period for both muscles. Removal of the nasal plugs decreased the tonic activity in the dorsal fibers, but the genioglossus demonstrated considerable fluctuation and remained tonic during the 18-month recovery period.

Mandibular depressions. Nasal obstruction appeared to induce tonicity in all four of the muscles often active during mandibular depression at some time during the 2-year period (Fig. 9). However, only the geniohyoid, which was more tonically active after 1 month of nasal obstruction, demonstrated a significant sustained tonicity through the entire 2-year period (in at least 40% of the animals). The digastric did not demonstrate a consistent tonic discharge pattern for a sustained period. Removal of the nose plugs terminated any sustained tonic activity in the platysma, lateral pterygoid, and digastric but not in the most tonically active muscle, the geniohyoid. The geniohyoid remained consistently tonic in more than 50% of the animals throughout the entire 18-month postplug recovery period.

Mandibular elevators. Nasal obstruction did not alter the tonic activity of the three mandibular elevator muscles—the masseter, medial pterygoid, or anterior temporalis (Fig. 10). Only the superficial region of the masseter was studied. The anterior temporalis was tonically active in 60% of the animals during the control period. Despite the lower mandibular position, tonic or consistent discharge was not enhanced throughout the 24 months of nasal obstruction and the response of these muscles was unaltered after removal of the plugs.

Facial muscles. Of the eight muscles studied, five were tonically active during the control period (Figs. 11 and 12). The zygomaticus (20%), inferior orbicularis oris (30%), and lip corner (40%) region (includes triangularis) were tonically active during the control period. Obstruction of the nasal cavity increased the tonic ac-

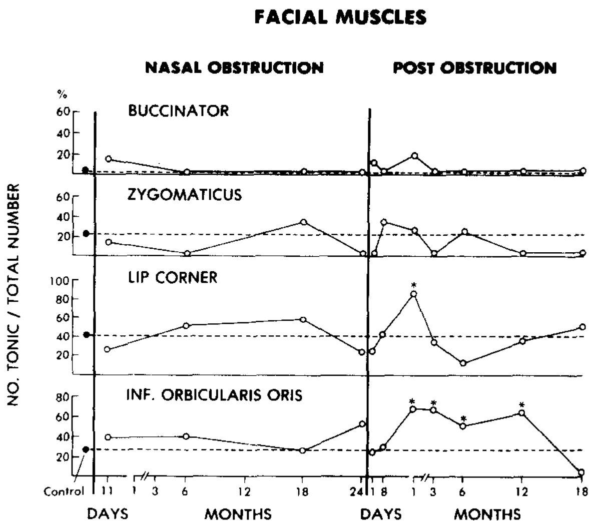

Fig. 11. The percentage of animals which tonically recruited four facial muscles.

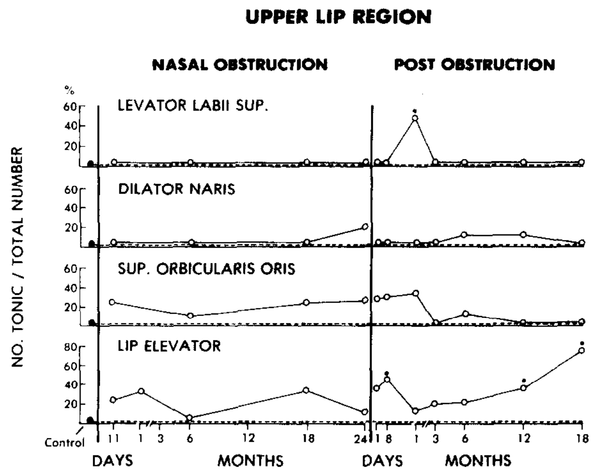

Fig. 12. The proportion of animals which tonically recruited muscles of the upper lip and face.

tivity in the two lip-constrictor muscles, the superior and inferior orbicularis oris muscles, and the vertical fibers of the superior orbicularis oris (lip-elevator fiber), but in fewer than 40% of the animals with the nasal obstruction. The lip corner, which was normally tonically recruited, was slightly more active between 6 and 18 months of adaptation to oral respiration. Removal of the nose plugs did not eliminate the tonic activity in two muscles—the inferior orbicularis oris and the lip-elevator fibers. This occurred despite most of the animals losing the triangular shape at the upper lip after removal of the nose plugs.

DISCUSSION

Nasal obstruction induces a change in respiratory function which involves the anterior portion of the upper respiratory tract. In this experimental model, the nasal cavity is almost completely obstructed, so that the oral cavity must assume an additional role as a functional airway, even during the resting condition. In exercise, the oral cavity often serves as a parallel pathway with the nasal cavity to handle the increased tidal volume. Nasal obstruction initiates a change in which the oral cavity must now serve as the major or perhaps the only pathway for periodic airflow during all respiratory demands.

In adapting the oral passage for chronic respiratory work, the anterior portal appears to be achieved by two mechanisms—raising the upper lip and lowering the mandible. The anterior seal created by the lips is broken by parting the lips. The mandible achieves a lower functional postural position. The posterior cavity can widen by a protrusive action of the tongue and/or the development of a groove within the tongue. The mandible can also rhythmically rise and fall in a periodic discharge correlated with the respiratory rhythm. Rhythmic movement of the mandible and tongue remains only during the nasal obstruction and is a mechanism used by fewer than 40% of the animals.

In the behavioral analysis of the functional responses, a new mandibular posture would presumably require active muscle control in rotating the mandible open. Our data indicate that the geniohyoid muscle is the primary suprahyoid muscle that becomes more tonically active and remains tonically active throughout the 2-year period of nasal obstruction. However, only 50% of the animals used this muscle, which means that an alternate physiologic mechanism is needed to account for more than 80% of the animals maintaining their mandible in a lowered posture. The rhythmic depression of the mandible was an alternate or complementary neuromuscular mechanism, but the geniohyoid and digastric muscles were recruited rhythmically in fewer than 40% of the animals.

The question arises as to what neuromuscular factors determine a lower mandibular posture. The data suggest that both active tonic recruitment of the geniohyoid muscle and rhythmic recruitment of the geniohyoid and digastric muscles may assist some monkeys through the entire period of nasal obstruction. However, soft-tissue changes with the upper lip and tongue may be sufficient to provide the patent airway at rest that is needed so that active suprahyoid muscle recruitment is not mandatory. Alternatively, a tonic stretch reflex of the jaw-elevator muscles might decrease so that the mandible may maintain a lower posture. This assumes that an active stretch reflex is an important contributing factor to determining the mandibular posture. Our data suggest a decrease in the active motor unit recruitment of the anterior temporalis, which may be dependent on a decrease in a tonic stretch reflex.

The behavioral responses in the rhythmic use of the upper lip, tongue, and mandible cease with loss of nasal obstruction, indicating a strong tie between nasal obstruction and rhythmic recruitment of these regions. It appears that the periodic discharge of the anterior temporalis ceases, whereas the rhythmic raising and lowering of the mandible continues through the period of nasal obstruction. However, the suprahyoid muscles maintain a rhythmic discharge during the entire period of rhythmic movement of the mandible and appear to be the key muscles involved with the rhythmic mandibular movements. It does not appear that the mandibular elevator muscles are critical to the rhythmic movements of the mandible.

It is evident that some muscles can change their discharge level and activity and yet not lead to an obvious change in the position or movement of the tongue or mandible. The genioglossus and dorsal fibers of the tongue can discharge rhythmically during the entire 2 years of nasal obstruction; yet the tongue ceased protruding rhythmically by the end of 6 months. The geniohyoid and digastric muscles can be rhythmically recruited (24-month recording) while there is no evidence of mandibular movement. In contrast, rhythmic raising of the upper lip is tied closely with the rhythmic discharge induced within the lip-elevator fibers of the superior orbicularis oris.

Nasal obstruction appears to have induced a neuromuscular change which can remain even after the nasal obstruction is removed. Some animals continued the tonic discharge of their most tonically active muscles, suggesting that some neuromuscular adaptation does not revert when the original stimulus is removed. This was particularly evident with the genioglossus muscle of the tongue, the geniohyoid muscle of the suprahyoid region, the inferior orbicularis oris muscle of the lower lip, and the lip-elevator fibers of the upper lip. This finding suggests that obstruction of the nasal cavity induces neuromuscular changes in specific muscles which will remain not only for the duration of the stimulus but after the stimulus is removed.

Two important concepts are evident from this study. First, almost complete nasal obstruction requires an active change in the synaptic motor control of craniofacial and oral muscles and has been documented by electromyography and soft-tissue deformation. However, removal of the original stimulus only partially disengages the central neural changes which have been dominated by the respiratory pathway; the rhythmic or periodic recruitment of specific craniofacial muscles ceases. However, nasal obstruction, as experimentally induced, appears to establish an altered neuromuscular drive of certain craniofacial muscles which becomes the normal mode. The original stimulus is supplanted by a learned central synaptic control of these specific muscles.[21]

In returning to the initial issue raised with this experimental model in the introduction, a question arises as to the significance of this altered neuromuscular activity to the morphologic adaptations that have been demonstrated. Despite individual variations in morphologic response of the rhesus monkey to almost complete nasal obstruction, there is a trend toward a longer vertical facial height. Such a response is associated with increased active discharge and use of the geniohyoid and digastric muscles, but not with the jaw-elevator muscles. The only other craniofacial muscles to alter their neuromuscular drive significantly are related to the upper lip and tongue. The issue as to whether the experimental model directly demonstrates that the muscular system affects the bone appears to involve more the secondary characteristics of growth that result because the mandible is held at a lower posture, allowing further alveolar growth and tooth eruption. This experimental model does not demonstrate an obvious and consistent change in bony attachment sites due to the increased use of a specific muscle. Despite the altered neuromuscular drive and the change in active recruitment of specific muscles, the altered morphologic changes occurred by repositioning the mandible. This means that the issue as to how muscle directly modifies bone still needs a direct answer which discerns among the neuromuscular characteristics.[22] At present, a new rhesus monkey model is being developed in which the mandibular elevator muscles will be programmed at specific levels of activity to determine if active motor unit recruitment can specifically alter the density of bone and remodel the mandible. It is only by careful and systematic programming of muscle activity that the question of which active properties of the neuromuscular system affect the bony morphology can be answered.

REFERENCES

1. Avis V: The significance of the angle of the mandible: an experimental and comparative study. Am J Phys Anthropol **19:** 55-61, 1961.
2. Boyd TG, Castelli WA, Huelke D: Removal of the temporalis muscle from its origin: effects on the size and shape of the coronoid process. J Dent Res **46:** 997-1001, 1967.
3. Horowitz SL, Shapiro HH: Modification of mandibular architecture following removal of the temporalis muscle in the rat. J Dent Res **30:** 276-280, 1951.

4. Horowitz SL, Shapiro HH: Modification of skull and jaw architecture following removal of the masseter muscle in the rat. Am J Phys Anthropol **13:** 301-308, 1955.
5. Rogers WM: The influence of asymmetry of the muscles of mastication upon the bones of the face. Anat Rec **131:** 617-629, 1958.
6. Soni NN, Malloy RB: Effect of removal of the temporalis muscle on the coronoid process in guinea pigs: quantitative triple fluorochrome study. J Dent Res **53:** 474, 1974.
7. Washburn SL: The relation of the temporal muscle to the form of the skull. Anat Rec **99:** 239-248, 1947.
8. Gardner DE, Luschei ES, Joondeph DR: Alterations in the facial skeleton of the guinea pig following a lesion of the trigeminal motor nucleus. AM J ORTHOD **78:** 66-80, 1980.
9. Phillips C, Shapiro PA, Luschei ES: Morphologic alterations in *Macaca mulatta* following destruction of the motor nucleus of the trigeminal nerve. AM J ORTHOD **81:** 292-298, 1982.
10. Shapiro PA: Morphological asymmetry in *Macaca mulatta* as a consequence of destruction of the motor nucleus of cranial nerve V. Am J Phys Anthropol **47:** 159-160, 1977.
11. McNamara JA Jr: Neuromuscular and skeletal adaptation to altered function in the orofacial region. AM J ORTHOD **64:** 578-606, 1973.
12. McNamara JA Jr, Carlson D: Quantitative analysis of the temporomandibular joint adaptations to protrusive function. AM J ORTHOD **76:** 593-611, 1979.
13. Charlier JP, Petrovic A, Herrman-Stutzman J: Effects of mandibular hyperpropulsion on the prechondroblastic zone of young rat condyle. AM J ORTHOD **55:** 71-74, 1969.
14. Petrovic AG, Stutzmann J, Oudet CL: Control processes in the postnatal growth of the condylar cartilage of the mandible. *In* McNamara JA Jr (editor): Determinants of mandibular form and growth, Ann Arbor, 1975, University of Michigan, pp. 101-153.
15. Harvold EP, Tomer B, Vargervik K, Chierici G: Primate experiments on oral respiration. AM J ORTHOD **79:** 359-367, 1981.
16. Vargervik K, Miller AJ, Chierici G, Harvold EP: Morphologic response to changes in neuromuscular patterns experimentally induced by altered modes of respiration. AM J ORTHOD **85:** 115-124, 1984.
17. Miller AJ, Vargervik K: Neuromuscular adaptation in experimentally induced oral respiration in the rhesus monkey *(Macaca mulatta)*. Arch Oral Biol **25:** 579-589, 1980.
18. Miller AJ, Vargervik K, Chierici G: Sequential neuromuscular changes in rhesus monkeys during the initial adaptation to oral respiration. AM J ORTHOD **81:** 99-107, 1982.
19. Miller AJ, Vargervik K: Neuromuscular changes during long-term adaptation of the rhesus monkey to oral respiration, *In* McNamara JA Jr (editor): Nasorespiratory function and craniofacial growth, craniofacial growth series, Monograph 9, Ann Arbor, 1979, University of Michigan Center for Human Growth and Development, pp. 1-26.
20. Miller AJ: Electromyography of craniofacial musculature during oral respiration in the rhesus monkey. Arch Oral Biol **23:** 145-152, 1978.
21. Miller AJ, Chierici G: Adaptation in the functions of the superior orbicularis oris muscle. Exp Neurol **76:** 594-605, 1982.
22. Miller AJ, Chierici G: Concepts related to adaptation of neuromuscular function and craniofacial morphology. Birth Defects **18:** 21-43, 1982.

Reprint requests to:
Dr. Arthur J. Miller
Department of Growth and Development
747-S
University of California
San Francisco CA 94143