Pediatric obstructive sleep apnea and the critical role of oral-facial growth: evidences

Yu-Shu Huang1 and Christian Guilleminault2*

1 Department of Child Psychiatry and Sleep Center, Chang Gung Memorial Hospital and University, Taiwan, China
2 Sleep Medicine Division, Stanford University, Redwood City, CA, USA


Keywords: pediatric sleep-disordered-breathing, non-obese, oral-facial anatomy, hypotonia, oral-facial growth, oral-facial myofunctional dysfunction

INTRODUCTION
Since obstructive sleep apnea syndrome (OSAS) first was reported in children in Guilleminault et al. (1976), recognition of abnormal breathing during sleep has progressed. Prior to the introduction of the nasal cannula-pressure transducer (Serebrisky et al., 2002), thermistors were used to score abnormal breathing during sleep in association with esophageal manometry (Pes). The nasal cannula-pressure transducer is more accurate than its predecessor, and it allows for recognition of the “flow limitation” breathing pattern. This pattern is associated with an abnormal increase or decrease in respiratory effort associated with EEG changes that occur during sleep disturbances (Hosselet et al., 1998; Aittokallio et al., 2001; Lin and Guilleminault, 2011). These sleep EEG changes were also shown to be better recognized using the “cyclic alternating pattern” (CAP) scoring system, a visual scoring system commonly used in Europe and Latin America (Terzano et al., 2002). This visual scoring system recognizes sleep disturbances, particularly arousals indicative of sleep disruption, better than the most commonly used atlas, which requires disturbances to occur for at least 3 s to be scored. More accurate approaches have been used, such as computerized analyses of the sleep EEG based on specific algorithms (Chervin et al., 2004) or using well-known EEG analysis programs (e.g., fast-Fourier Transform, Wavelet, and Hiller–Huang Transform programs). Usage of these recording techniques has improved recognition of Sleep-Disordered-Breathing (SDB).

Poor tolerance of early cases of children treated with tracheostomy and home nasal CPAP (Sullivan et al., 1981) led to the advent of maxillomandibular advancement (MMA) surgery as a procedure designed to target more specifically the upper airway (Powell et al., 1983). Follow-up of one case for more than 25 years post-MMA demonstrated lasting and complete resolution of OSAS.

LESSONS FROM OSA TREATMENT WITH ADENOTONSILLECTOMY
Despite the widespread use of limited techniques to identify the complete cessation of abnormal breathing and its effects during sleep, many studies have demonstrated significant improvement in SDB without complete elimination of the phenomenon. Two studies showed that prepubertal adolescents initially considered to have been cured by adenotonsillectomy subsequently had recurrence of OSA as teenagers (Guilleminault et al., 1989; Tasker et al., 2002). In Guilleminault et al. (1989), subjects had narrowing behind the base of the tongue and oral-facial anatomic abnormalities that either did not exist initially or had not been identified previously. Tasker et al. (2002) also confirmed the presence of abnormal upper airway anatomy and SDB in subjects 12 years after adenotonsillectomy. This phenomenon was observed again in more recent larger studies. Guilleminault et al. (2004) demonstrated complete resolution of OSA following adenotonsillectomy in only 51% of non-obese prepubertal children that were studied with polysomnogram...
AASM 2007 scoring criteria (Iber et al., 2007). The prospective
narrow maxilla imparts on teeth positioning and facial growth
facilitated by orthodontia use.

Timms, 1974, 1984; Gray, 1975; Hershey et al., 1976; McNamara,
changes (Haas, 1961; Linder-Aronson, 1969, 1970; Wertz, 1970;
European orthodontists showed that abnormal nasal resistance
induced by enlarged adenoids and tonsils in children were asso-
ciated with mouth breathing and led to important craniofacial
abnormalities. The blockade of the nasal passage led to narrowing of
dental arches, increase in maxillary arch length, anterior cross bite,
maxillary overjet and increase in anterior facial height (Harvold
et al., 1981). Experimentally induced abnormal nasal resistance
led to systematic changes in the oral-facial muscles. The changes
were noted in the systematic recording of different muscles, in
particular the geniohyoid, the genioglossal muscles of the tongue,
the suprahyoid dorsal tongue fibers, the upper lip elevators, and
the digastric muscles. EMG testing showed abrupt induction of
rhythmic discharge patterns, a stark contradiction to the nearly
continuous and desynchronized discharges in most normal sub-
jects. Tonic EMG discharges changed back to the normal pattern
when nasal breathing was restored at the end of the 6-month
experiment (Vargervik et al., 1984 and Miller et al., 1984).

Increased nasal resistance has a dramatic effect on the maxil-
loapomandibular skeleton, halting growth (Harvold et al., 1981),
and bringing about adaptive changes in the soft tissues that are asso-
ciated with deviation in jaw posture and tongue activity (Miller
et al., 1984; Vargervik et al., 1984). Obstruction of nasal airflow
induces functional changes in the nasomaxillary complex and
on the mandible. In the subject group of newborn rhesus mon-
keys, there were several consequences: an absence of development,
which impacted the maxilla and restricted the nose and upper
jaw; displacement of the mandible leading to mouth breathing;
and oral breathing that developed in association with increased
nasal resistance, leading to mouth opening and mouth breathing
that occurred in the awake and sleep states. These changes
led to the narrowing of the cranial skeleton (Harvold et al., 1981;
Miller et al., 1984; Vargervik et al., 1984; Rubin, 1987; Vargervik
and Harvold, 1987). These changes were shown to be reversible if
the experimental nasal resistance was withdrawn while the infant
monkey was still in its developmental phase.

These experiments taught us that in growing animals in which
the nasal airway is gradually occluded, there is an adverse effect
on the morphology of the nasomaxillary complex, mandible, and
pharyngeal airway space. The morphometric changes are induced by
altered functioning of the muscles with changes in muscle fir-
ing that are triggered by abnormal nasal resistance. Unfortunately,
OSAS largely was unknown at the time of these investigations and
no sleep recordings were performed on the subject animals.

LESSONS FROM ORTHODONTIA AND THE EXPERIMENTAL
INFANT MONKEY MODEL

European orthodontists showed that abnormal nasal resistance
induced by enlarged adenoids and tonsils in children were asso-
ciated with mouth breathing and led to important craniofacial
changes (Haas, 1961; Linder-Aronson, 1969, 1970; Wertz, 1970;
Timms, 1974, 1984; Gray, 1975; Hershey et al., 1976; McNamara,
1981; Löfström-Tideström et al., 1999; Pirila-Parkkinen et al.,
2009). Adenotonsillar ablation led to cessation of mouth breathing
and progressive restoration of normal facial development facilitated by orthodontia use.

Other orthodontists, concerned by the negative impact that a
narrow maxilla imparts on teeth positioning and facial growth
during prepubertal development, performed “rapid maxillary
expansion” (RME) and reported that such treatment also had
made an impact on sleep-related complaints. In one study, children
treated with RME experienced elimination of nocturnal enuresis
(Timms, 1974).

However, the most important findings were obtained on infant
rhesus monkeys, when the important role of abnormal nasal
resistance during the developmental period was demonstrated.
Between 1970 and 1980, a number of very important experiments on
newborn rhesus monkeys were performed, whereby a small sil-
conic head was placed within the nostrils of infant monkeys and
held in place by a thin thread in order to induce nasal resistance
for the first 6 months of life (Harvold et al., 1981; Vargervik et al.,
1984). These experiments taught us that in growing animals in which
the nasal airway is gradually occluded, there is an adverse effect
on the morphology of the nasomaxillary complex, mandible, and
pharyngeal airway space. The morphometric changes are induced by
altered functioning of the muscles with changes in muscle fir-
ing that are triggered by abnormal nasal resistance. Unfortunately,
OSAS largely was unknown at the time of these investigations and
no sleep recordings were performed on the subject animals.

APPLICATION OF WORK IN ORTHODONTIA IN THE FIELD OF
SDB

More recent investigations demonstrating incomplete resolution of abnormal oropharyngeal growth by adenotonsillctomy
have led to the usage of orthodontic techniques to help treat pediatric SDB.

Based on prior research demonstrating the important role of the mesio-palatine suture in the nasomaxillary complex growth, much investigative effort has been invested in examining the complex’s ossification process. Cartilage is a connective tissue made of chondrocytes embedded in a collagen-rich matrix (particularly type II collagen), associated with proteoglycans in hyaline cartilage that strengthens it, as well as elastin (depending on the type of cartilage). Hyaline cartilage is the forerunner to skeletal bones in the fetus, and endochondral ossification is the process leading to formation of the nasomaxillary complex.

Rapid Maxillary Expansion (Pirelli et al., 2004) is a procedure applying orthopedic forces on the mid-palatal sutures using the first molars and permanent premolars as anchor teeth. While in deciduous dentition, the second primary molars are selected as long as they can provide the required firmness. The device is composed of a central expansion screw with four arms: two front arms and two back arms. The bone distraction (enlargement) at the suture level enables an effective enlargement of the maxillary skeletal base. Enlargement is visually appreciable with X-ray (as the gain appears as a radiotransparency corresponding to the visually seen space) as the bone distraction leads to an interincisive space (a diastema). The procedure usually takes 3–4 weeks with daily turning of a midline screw that allows distraction of the space at the level of midline suture. The transpalatal force, which exceeds the orthodontic one, produces an orthopedic force that opens the mid-palatal suture leading to maxillary movement without tipping teeth. Once the needed extension is obtained (end of the activation phase), the midline screw is locked and the device is kept in place for at least 4–6 months. This time period allows the newly formed bone to strengthen. However, this does not generate cartilage in the mandible. Nevertheless, manipulation and verticalization of teeth can stimulate mandibular growth and such bimaxillary distraction is often needed in OSA children. In addition, maxillary widening also seems to impact mandibular growth independently.

Contrary to its efficacy in lateral expansion, RME is limited in anteroposterior lengthening capabilities. In the past, appliances such as the Herbs appliance or its equivalent were thought to be capable of producing anterior-posterior growth in prepubertal children. However, while such appliances may protrude the lower jaw forward, there is no evidence currently that more growth than expected with age is attained. Distraction osteogenesis may be performed in these cases, but while such an approach is performed in children with clear malformations at birth, it has not been recommended in non-syndromic children with OSA until oral-facial growth is well advanced (Guilleminault and Li, 2004).

In normal individuals, 60% of facial growth is attained by 6 years and about 90% by 11–12 years of age. Thus, distraction osteogenesis is not usually performed before approximately 14 years of age in non-syndromic children with OSA. Even then, it must be determined whether the anteroposterior advancement will be sufficient on its own or the teenager will need both anteroposterior and lateral extension. If it is the latter scenario, as is most commonly the case, MMA (Holty and Guilleminault, 2010) is the best option. On the other hand, distraction osteogenesis may be useful in certain cases, such as in the elimination of residual OSA.

In summary, several studies have shown that RME or bimaxillary distraction have a clear impact on pediatric OSA and may resolve the residual symptomatology seen in post-adenotonsillectomy patients. The combination of adenotonsillectomy and RME leads to complete resolution of OSA symptoms in some cases, and a small prospective follow-up study demonstrated sustained results 36 months post treatment (Villa et al., 2011).

Two investigations have looked at the effects of RME versus adenotonsillectomy. In the first study, subjects presented with narrow jaws and both adenoid and tonsillar enlargement (3+ on the Friedman scale). Assignment to the initial treatment groups of RME and adenotonsillectomy was randomized. With the exception of one child who improved with orthodontic treatment alone, all subjects required both adenotonsillectomy and orthodontic treatment to see improvement (Guilleminault et al., 2011). In the second study, children with infectious tonsils were treated with adenotonsillectomy while the others were designated to the orthodontic treatment group, with the design to send the patients into the other treatment arm if initial therapy yielded incomplete results. In this study, more children were treated only with orthodontics, indicating that oral-facial factors may be dominant in at least a subgroup of OSA children (Pirelli et al., 2012). In both studies, several children were not completely cured with these approaches, indicating that more aggressive treatment may be needed. Persistent oral-facial problems were always identified as the prominent factor associated with failure to achieve a complete cure of OSA.

These investigations demonstrate that adenotonsillectomy in non-obese children does not cure OSA in many prepubertal children, and that oral-facial anatomical problems play a pivotal role in the development of OSA in children. Moreover, for some subjects these anatomical problems may be amenable to orthodontic treatment.

**INTERACTION BETWEEN ADENOTONSILS AND ORAL-FACIAL GROWTH AND EVIDENCES FROM PREMATURES INFANTS**

Swedish investigators suggested that children first become mouth breathers, and the subsequent subjectation to repetitive abnormal stimulations resulting from mouth breathing causes an inflammatory reaction in the tonsils (Zettergren et al., 2002). The resulting tonsillar enlargement involves inflammatory factors, such as leukotriene.

In Taipei (Taiwan), YS Huang has created a prospective cohort of 300 infants born between 25 and 37 weeks of gestational age. These infants are evaluated within 1 week following birth, then at 3, 6, 12, 18, 24, and 36 months of age. These children were evaluated for clinical development and neurologic function, including feeding behaviors, actigraphy, PSG, and systematic photographs of the face (frontal and lateral) and oral regions. Fiber optic illumination was used in the photographs of the oral regions to evaluate the size and presentation of the hard palate, and these photos were scored blindly by a specialist uninvolved in the clinical evaluations.

**PRELIMINARY RESULTS**

Three hundred children involved in the cohort have been followed until at least 24 months of age. At this time, infants who had nasal or mouth tube placed at birth were eliminated from evaluation. All infants born below 34 weeks of gestational age were found to
All of these children were in the 36 weeks and older gestational age group. None of them had ICU hospitalizations, but they did show positive “scarf” signs at 3 months follow-up evaluation. All of these children were bottle fed due to difficulties with breast feeding. At the 6-month follow-up, their tongues were flat and low lying as observed by examination and photography, a presentation similar to that of a hypotonic tongue. These children had normal breathing during sleep at birth evaluation, but developed SDB as documented by sleep recordings during the follow-up period.

INFANTS WITH NORMAL PALATE AT FOLLOW-UP

In this study only 9% of subjects (n = 22) had a completely normal hard palate, normal breathing during sleep, and normal development. With the exception of a pair of twins who were born at 34 weeks, all were in the 36 weeks and older age group and had normal breast feeding. The twins were followed by a special myofunctional reeducation team applying tongue reeducation techniques to strengthen the tongue and oral muscles in the early postnatal period (Page, 2003; Bahr, 2010). They were bottle fed with a special “hard” nipple, with the hardness and size adjusted overtime to elicit more effort from their tongue muscles when feeding.

ROLE OF ORAL-FACIAL MUSCLE HYPOTONIA AND USAGE OF MYOFUNCTIONAL REEDUCATION

The investigation of infant monkeys showing changes in EMG firing demonstrating that abnormal nasal resistance early in life leads to mouth breathing associated with abnormal muscle tone, oral-facial hypotonia, and secondary changes in maxillary-mandibular growth (Harvold et al., 1981; Miller et al., 1984; Vargervik et al., 1984; Vargervik and Harvold, 1987). In the 1970s, many researchers studied the many important functions oral-facial muscles played, including swallowing, breathing, phonation, mastication, facial mimicry, and overall head posture (Leech, 1958; Ricketts, 1958; Hawkins, 1965; Linder-Aronson, 1969, 1970; Solow et al., 1984; Rubin, 1987; Behlfeil et al., 1990).

Orthodontists across Europe concluded that myofunctional reeducation of the oral-facial region was an important part of treatment aimed at correcting abnormal maxillary and mandibular growth, as well as normalizing bite and teeth positioning. This was due to its effect in rehabilitating abnormal local muscle activity (Chauvois et al., 1991).

Creation of oral-facial muscle reeducation programs meant specialized re-educators had to be trained, which led to specific university training. Combined orthodontic and myofunctional reeducation was thereafter applied to children with narrow jaws. Looking at long-term outcomes, combination therapy was more successful than either treatment individually. More recently, after demonstrating the involvement of maxillary-mandibular growth problems in SDB, children were treated with both myofunctional reeducation and orthodontia (Chauvois et al., 1991; Guilleminault et al., 2012a,b; Guilleminault, 2012). In Brazil, these treatments were applied in children and adults, and a Brazilian team has published results of the combined treatment approach for adult OSA showing improvement of AHI in well established OSA patients (Guimaraes et al., 2009). Outcome reports for myofunctional reeducation in SDB children otherwise are rare.

However in the 1990s there has been evaluation of children with abnormal oral-facial development who received orthodontic treatment without sleep investigation (Chauvois et al., 1991), including results obtained from an appropriate reeducation regimen. Despite usage of combined approaches in specific geographic places for orthodontic problems, no prospective long-term study has been published in the treatment of SDB children. Studies recently have been initiated that compare outcome of adenotonsillectomy and orthodontic treatment without myofunctional treatment. We performed one study investigating the role of myofunctional therapy in association with orthodontia in children with SDB. While our own retrospective multi-center investigation was limited due to difficulty retrieving original data from the various locations, it produced evidence that the persistence...
of mouth breathing during sleep-related to myofacial hypotonia led to the reoccurrence of SDB (Guilleminault et al., 2012a). This recurrence in children treated appropriately with adenotonsillectomy and orthodontics was demonstrated, along with the presentation of clinical signs and symptoms and typical PSG findings. Myofunctional clinical evaluation revealed the presence of oral-facial hypotonia. These children also demonstrated mouth breathing during PSG.

This limited retrospective study (Guilleminault et al., 2012a) involved 24 early teenagers who previously had been diagnosed with SDB between ages 3/2 and 7 years and had been treated appropriately with adenotonsillectomy and orthodontia and also had been instructed to commence myofunctional reeducation. Recurrence of OSA at occurred in 13 subjects. Each of these presented with oral-facial hypotonia, mouth breathing during sleep, and reported not completing myofunctional reeducation. In contrast, the subjects with normal breathing at long-term follow-up had normal oral-facial tone, nasal breathing during sleep, and had completed myofunctional therapy. This study illustrates the potential importance of myofunctional treatment as an adjunctive treatment of SDB children, and that the presence of normal post-procedural PSG findings alone may not be sufficient to ensure long-term remission of abnormal nocturnal breathing.

Myofunctional reeducation is applied much less frequently in early infancy. The premature cohort investigation indicates that SDB is seen in very early life, and that abnormal anatomic features of structures limiting the upper airway are also present very early. In patients with these recognized abnormalities, application of myofunctional reeducation techniques may be helpful. Unfortunately, orthodontist exposure is rare in the pediatric arena, despite the pervasive knowledge of generalized hypotonia in premature infants.

Page (2003) speaks of the importance of dealing with oral-facial hypotonia and how to manage it in infancy, as it may be associated with negative facial anatomy problems later. There is data showing that the way an infant sucks on a nipple (breast or bottle) is important for the development of normal oral-facial muscle tone and the prevention of local hypotonia (Davis and Bell, 1991; Paunio et al., 1993; Ogaard et al., 1994). Breastfeeding is a complex reflex requiring considerable strength. During feeding premature infants may experience significant apnea associated with severe oxygen desaturation. Often they cannot breastfeed sufficiently at their mother’s breast, and therefore end up being bottle fed, since it requires less tongue strength and sucking effort.

In our premature infant prospective study, more than 90% of women with premature infants bottle fed their infants. Oral-facial hypotonia in premature infants has been the subject of much research. Page studied how to deal with this hypotonia. Bottle feeding may be performed with special nipples that require more effort from the oral-facial muscles, such as NUK-Gerber nipples (Ogaard et al., 1994), and oral reflexes may be triggered early in the postnatal period using finger stimulation of the lips and mouth. Progressive development of a normal palate can be attained using such approaches. (In one case, there was documentation of sustained results up to age 6, as reported by MJ Boileau, Department of Orthodontics, Bordeaux University Dental School, France.) We conducted a non-randomized small study with five infants. It showed that when mothers followed feeding recommendations to use these special bottle nipples and engaged in finger stimulation of oral reflexes, a progressive normalization of normal palatal anatomy associated with normal breathing during sleep was observed at 24-month follow-up. This was not observed in gestational age-matched infants using regular nipples.

This was also demonstrated in the premature twins referenced earlier, leading to secondary development of normal oral-facial features and absence of SDB. Feeding was associated with a special pacifier, but reeducation of muscle hypotonia involved more participation from mothers, including stimulation of the infant’s lips by placing a finger there and using FDA-approved chewing toys for ages 6 months and up, such as ARK’s Grabbers chewing toys (Bahr, 2010). These studies are very limited and are similar to case reports, but they complement observations in older children who had recurrence of SDB after appropriate treatment but did not have myofunctional therapy (Guilleminault et al., 2012a).

In summary, premature infants as well as some full-term infants present with abnormal oral-facial features, particularly a high and narrow hard palate. These findings are associated with oral-facial hypotonia. Systematic follow-up to 36 months of age indicates persistence of abnormal tongue position and abnormal breathing, with presence of mouth breathing demonstrated on PSG. Information from orthodontists indicates that performing special oral-facial exercises during feeding, and chewing in the first 2 years of life may lead to correction of abnormal anatomy, resulting in repositioning of the tongue and development of a normal nasomaxillary complex and mandible. A small non-randomized study indicates that premature infants may develop normal nasomaxillary complex and mandible when a strong effort is made to induce normal oral-facial musculature. Independent of sleep studies, years of experience in orthodontia also supports the important role of myofunctional reeducation in the presence of abnormal oral-facial anatomy (Chauvois et al., 1991). In our investigations, absence of SDB is associated with normal nasal breathing during sleep, but recurrence of OSA during the teenage years is associated with mouth breathing during sleep and documentation of oral-facial hypotonia.

CONCLUSION

The different data accumulated over time on SDB children and the experimental data obtained from infant monkeys years ago are indicative of a strong association between normal oral-facial muscle tone and the normal development of the nasomaxillary complex and mandible. Presence of abnormal muscle tone, either experimentally induced by creation of abnormal nasal resistance or due to premature birth, is associated with mouth breathing particularly during sleep, abnormal placement of the tongue, and either development or worsening of the oral-facial anatomy. In humans, SDB is noted in association with pathological hypotonia of the tongue muscles. In a small group of infants seen at birth with a normal hard palate, development of a high and narrow hard palate and SDB was documented in children with oral-facial hypotonia. When the high and narrow hard palate was noted at birth in these cases, hypotonia also was present, and SDB was noted. In rare cases efforts very early in life to counteract oral-muscle hypotonia and reverse the high and narrow hard palate.
A portion of the presented data (premature infant longitudinal study) is part of the PhD thesis of Yu-shu Huang. We thank H. Y. Chiu and Gerard Meskill for their help in the editing of the manuscript.

ACKNOWLEDGMENTS

REFERENCES


REFERENCES


of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. Lancet 1, 862–865.


Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received: 07 August 2012; accepted: 17 December 2012; published online: 22 January 2013.


This article was submitted to Frontiers in Sleep and Chronobiology, a specialty of Frontiers in Neurology.

Copyright © 2013 Huang and Guilleminault. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in other forums, provided the original authors and source are credited and subject to any copyright notices concerning any third-party graphics etc.