TOP STUDIES:

Research that shows the efficacy of Myofunctional Therapy in the fields of sleep medicine, dentistry, and the physical body.

AOMT

ACADEMY *of* OROFACIAL MYOFUNCTIONAL THERAPY

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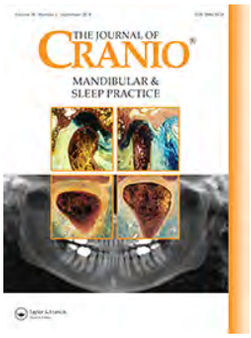

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The emerging area of orofacial myofunctional therapy: Efficacy of treatment in sleep disordered breathing bringing promise of a new field of medicine

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CONCEPTS

The emerging area of orofacial myofunctional therapy: Efficacy of treatment in sleep disordered breathing bringing promise of a new field of medicine

The term "orofacial myofunctional therapy" (OMT) was first introduced into the medical literature by orthodontic pioneer Alfred Paul Rogers 100 years ago as a means to describe what he thought was the critical nature of the position of the tongue on craniofacial morphology and the ensuing orthodontic and occlusal stability [1,2]. While OMT has remained at the margins of dentistry, speech-language pathology, and other disciplines touching the stomatognathic system (with some particularly bright exceptions in Brazil and regions of Spain and Portugal) gradually gaining interest, only in the last few years has it begun to emerge on the stage of international scientific medical meetings. This prominence is due to the many dozens of papers demonstrating efficacy in the treatment of sleep disordered breathing (SDB) published in just the last few years.

When my mother, Joy Lea Moeller (a pioneering leader in the development of OMT, particularly as it relates to SDB), was asked to write a Guest Editorial in this journal 6 years ago, "Orofacial Myofunctional Therapy, Why Now?" [3], we had a mere handful of papers on the efficacy of OMT as an adjunct treatment for SDB. Her bold claim that myofunctional therapy would come into greater prominence by its efficacy in treating OSA turned out a prescient call for action.

The key paper she spotlighted, Katia Guimares' [4] 2009 study from Geraldo Lorenzi Fihlo's stellar University of São Paulo Instituto do Coraçao team, showed in a randomized controlled trial that myofunctional therapy developed for the treatment of OSA patients significantly reduced severity and symptoms. That it was a well-designed study, published in the *American Thoracic Society's American Journal of Respiratory and Critical Care Medicine*, a very well-respected, high impact journal, led to this paper being in the top 10 of most referenced papers in sleep medicine for several years after its initial publication [5].

I have had the good fortune to be a witness and participant in this rising tide. To give a sense of the progression, the biennial 2013 World Sleep Congress in Valencia, Spain had five presentations that referred in some fashion to myofunctional therapy. The 2015 World Sleep Congress in Seoul, Korea had about 15 presentations making some reference. The 2017 World Sleep Congress saw over 40 presentations touch upon some reference to the field, including a formal satellite symposium of the recently founded (2012) world OMT scientific society, the Academy of Applied Myofunctional Sciences (AAMS) [6–8].

This momentum owes a great deal to visionary groundwork done at the Stanford University's School of Medicine's Division of Sleep Medicine, much of it led by Christian Guilleminault. Early, bold conviction with statements from 2012, suggesting that myofunctional therapy is critical for addressing pediatric OSA [9], were backed up with work done with Stanford [10] and further corroborated by important ongoing work done by teams led by Maria Pia Villa at Sapienza University of Rome [11].

A special center of growing importance in myofunctional therapy research has developed in Hong Kong, particularly at Kwong Wah Hospital in Kowloon, led by Daniel KK Ng. As a result of a comprehensive undertaking beginning 5 years ago, commencing with training a full spectrum of allied professionals (PTs, OTs, sleep physicians, ENTs, sleep techs, et al.), important work has been done that was the basis for the Asian Pediatric Pulmonology Society to formally update its pediatric OSA standard of care to include OMT [12].

The French Society of Research and Sleep Medicine has recently done the same [13], joining several other medical and dental societies around the world. Additional work had been done identifying orofacial myofunctional disorders (OMDs) as phenotypes for sleep apnea, such as an altered lingual frenulum [14].

Greater knowledge around phenotyping is making possible public health initiatives in which I have been privileged to have a direct role. The "Teste da Linguinha," or Frenulum Inspection Law we passed federally in Brazil in 2014 [15] requires all children to have their frenulums inspected at birth and then revised if indicated by the 1st validated tool for this purpose. Not only is this done to facilitate breastfeeding but also to avoid OMDs and their co-morbidities, like OSA, throughout the lifespan.

Furthermore, meta-analyses, such as those by Camacho [16,17] have created more consensus that there is a critical role for OMT in SDB treatment.

Even with this building momentum, for me, it is critically important to note that OMT is an emerging area of medicine, not formally yet checking the boxes to qualify as a "therapy" by a strict medical definition. We have no independent credentialing board/society, we have no licensure (except in Brazil) [18], we don't even have a textbook yet, but we are working on all of these things with a great sense of urgency.

What we do have is the beginning of a critical mass of literature that shows critical importance in the treatment of SDB, an epidemic affecting potentially upwards of 20% of the population, with 80–90% of those suffering undiagnosed. Recent literature has even begun to speculate that OMT could possibly prevent OSA [19].

Thus, clinicians around the world, from all professions who touch the stomatognathic system, are working with a sense of urgency to create care/therapy to bring to patients because we know enough now to realize it has an important impact on some SDB.

By forging ahead, with this patient centric focus and urgency to deliver care (upping and creating standards, validating protocols, and moving to establish actual multinational and randomized validation of therapeutic protocols), while building on a foundation of science, we are getting somewhere.

We must be on guard to resist the temptations found within all emerging areas of medicine that begin to gain traction, not cutting corners or succumbing to pressures to shorten treatment times, to resist the easy gimmickry of the "paper mill" certification entities that are popping up all over the world to sell a trademarked or weekend (or even 1-day) course, or appliances that promise to make someone an (unlicensed) professional, or cure all manner of ills.

Only by doing the heavy lifting required of all emerging areas of medicine that strive to move beyond being "emerging," fringe, or anecdotal will we, in OMT, become an actual field. We must follow the example of other fields and establish an objective, independent society to accredit curricula and curricular competency, as well as establish clinical competency accreditation that is independent of any teaching enterprise, membership society, or business entity. By acting responsibly as leaders in this emerging area, we will prepare ourselves so that when governments look to regulate us, we have solid standards in place that conform with other areas of medicine.

We can grow up and move forward at a quick pace, while maintaining ethics, rising to the standards required for fields of medicine and taking advantage of new ways of approaching disease, focused on breaking down silos and delivering care based on what the patients' phenotypes require, not what the specialty can gate-keep.

On the occasion of the publication of this editorial, we will hold the 3rd Academy of Applied Myofunctional Sciences Congress, representing 35 regional scientific societies already formed or in the process of formation, building growing scientific, academic, and clinical competency through which we can gain consensus and prominence. All of these collective societies together have been undertaking the steps to establish such standards; but we have much more work to do. We will rise to the profound opportunity bestowed upon us to help patients by prioritizing patient care on a foundation of science.

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Review Article

Model of oronasal rehabilitation in children with obstructive sleep apnea syndrome undergoing rapid maxillary expansion: Research review

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ABSTRACT

Rapid maxillary expansion (RME) is a widely used practice in orthodontics. Scientific evidence shows that RME can be helpful in modifying the breathing pattern in mouth-breathing patients. In order to promote the restoration of physiological breathing we have developed a rehabilitation program associated with RME in children. The aim of the study was a literature review and a model of orofacial rehabilitation in children with obstructive sleep apnea undergoing treatment with rapid maxillary expansion. Muscular training (local exercises and general ones) is the key factor of the program. It also includes hygienic and behavior instructions as well as other therapeutic procedures such as rhinosinusal washes, a postural re-education (Alexander technique) and, if necessary, a pharmacological treatment aimed to improve nasal obstruction. The program should be customized for each patient. If RME is supported by an adequate functional rehabilitation, the possibility to change the breathing pattern is considerably amplified. Awareness, motivation and collaboration of the child and their parents, as well as the cooperation among specialists, such as orthodontist, speech therapist, pediatrician and otolaryngologist, are necessary conditions to achieve the goal.

1. Introduction

Rapid maxillary expansion (RME) is a widely used practice in orthodontics. The purpose of RME is to correct transverse maxillary deficiency, a rather common skeletal anomaly of the maxillofacial area. It is often found in children with impaired respiratory function [1–5]. Scientific evidence shows that RME can be helpful in modifying the breathing pattern in these patients. This modification involves nasal cavities [6–11] and, indirectly, the jaw. The jaw is thus repositioned

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and this causes the root of the tongue to move forward [12] and it changes the pharyngeal structures [13]. Early studies related to the effect of RME on the nasal cavity and on breathing patterns date back to 1886 [14]. Several studies on the same topic were published later. Postero-anterior cephalometry [7,8,15,16], latero-lateral cephalometry [17,18] and tomography [11,19–22] have been used to estimate the changes in shape and size of the nose. Acoustic rhinometry [7,8,23–25] and rhinomanometry [7,8,26,27] have been used to adequately assess the airflow. The former provides anatomical information about the nasal airways (minimal cross-sectional area—MCA, minimal cross-section volume—MCV), while the latter measures the nasal resistance to airflow (nasal air resistance—NAR), an essential parameter for a functional assessment. In addition, in some studies, patients were asked to respond to special questionnaires in order to determine their perceptions on changing their breathing [28–30]. Hershey et al. [28] performed a comprehensive evaluation of the nose-breathing parameters mentioned above and it reported positive changes in the amplitude of the nasal cavities and a reduction in the values of NAR after RME to levels comparable to those of physiological nasal breathing. Those values would remain almost unchanged in the post-expansion contention months mentioned in the study. Additionally these Authors did not find any significant variations between the values of NAR in subjects who reported a subjective improvement in breathing and those reported no improvement. In later decades, other Authors analyzed changes in one or more of the parameters described above, which in most cases, caused dimensional and volumetric expansions of the nasal cavity, in particular of its lower part, and a decrease of the NAR. The stability effect achieved by RME and its role in actually changing breathing patterns remains a subject of debate. This debate is still ongoing despite evidence of anatomical and functional changes in the nasal complex after RME, as reported in the orthodontic literature, and notwithstanding the enthusiasm among some Authors who support the hypothesis that it is a means to eliminate or reduce the problem of mouth breathing. Clinical practice presents many cases in which, in spite of orthodontic treatment recovery of all the dental and skeletal conditions for a restoration of physiological nasal breathing, oral breathing persists. Cases of children who underwent tonsillectomy or adenectomy, did not experience an adequate functional recovery despite a clear airway are also common. Hershey et al. [28] confirmed the thesis of Watson et al. (1968—cited in Hershey et al. [28]) pointing out that the reduction of the NAR does not necessarily coincide with a disappearing of mouth breathing in a child. He concluded that RME, although it could potentially result in the recovery of the respiratory function also in the case of nasal stenosis, does not guarantee a resolution of all cases of oral breathing. According to Warren et al. [31] the enlargement of the nasal cavity is not sufficient to modify breathing patterns, in particular in cases of nasal obstruction. An analysis of recent reviews of the literature [9,10,32] has shown that a change in breathing after RME does not represent a predictable result to the point that mouth breathing does not seem to be a primary reason for an expansion procedure. Compradetti et al. [8] also report that a certain percentage of children, in spite of having structurally adequate nasal airways, do not change their breathing pattern from oral to nasal, which would lead to the need to 'learn' how to breathe properly. In order to promote the restoration of physiological breathing, it might be helpful to associate the expansion of the palate to myofunctional rehabilitation practices. Several articles in orthodontic literature highlight the need to combine orthodontic treatment with myofunctional therapeutic procedures [33–36]. Several procedures are meant to correct the position and the abnormal function of the tongue [34,37], while less emphasis is put on specific breathing exercises included in an orthodontic treatment plan [1,2,3,38–42]. Cozza et al. [40] describe a myofunctional rehabilitation program supporting the traditional orthodontic therapy in patients affected by breathing problems. The program involves exercises for the proprioception of the primary breathing apparatus, a costo-diaphragmatic training and respiratory exercises. The Authors underline that this rehabilitation program is advised to patients diagnosed with chronic mouth breathing, i.e. without any mechanical obstruction of the upper respiratory tract. Villa et al. [39] treated a group of children with nasal chronic obstruction with a myofunctional therapy aimed to re-establish a physiological nasal breathing and lip seal as well as to modify an abnormal swallowing pattern. Their protocol includes nasal exercises for the mobility of alar cartilages, labial exercises to straighten orbicularis oris muscles, tongue exercises to improve swallowing and breathing body exercises. Nasal irrigations using a hypertonic saline solution was added to the myofunctional therapy. The results showed that both myofunctional rehabilitation and nasal irrigation improve significantly nasal obstruction, oral breathing and chronic snoring in 5–10 years old children. A physical therapy program for mouth breathing children was adopted by Correa and Bérzin [41]: muscular stretching and strengthening exercises using a Swiss ball were combined to naso-diaphragmatic re-education. However, the study focuses on the effectiveness of this therapeutic program on cervical muscle activity and body posture which would have seemed to be impaired in the patients in question. No evaluations were made with regards to changes that occur in the respiratory pattern. Guimarães et al. [42] use a myofunctional approach consisting of oro-pharyngeal exercises derived from the traditional speech therapy techniques; it involves the soft palate, the tongue and mandibular and facial muscles. These exercises, combined with insufflation ones, would eventually lead to an improvement in adult patients affected by obstructive sleep apnea (OSA) as an outcome of the upper airway remodeling and its subsequent increase of patency. In a randomized placebo-controlled study Diaféria [43] evaluates the effects of speech therapy on clinical and polysomnographic parameters in obstructive sleep apnea syndrome (OSAS) patients and concludes that speech therapy could reduce OSAS symptoms and increase the adherence to the treatment with continuous positive airway pressure (CPAP). The speech therapy consists of muscular endurance exercises aimed at toning the oropharynx muscle groups, optimizing muscle tension mobility and adjusting the position of the soft tissues and the suitability of the chewing, sucking, swallowing and breathing orofacial functions, according to previously

standardized protocols [44–50]. In a later study Diaféria et al. [51] confirm that speech therapy, alone as well as in association with CPAP, leads to an improvement of quality of life in patients with OSAS. Dantas et al. [52] focuses on the genesis of the upper airway collapsibility in adult patients with OSAS. The Authors suggest that an increased collagen type I in the pharyngeal muscular wall in patients with OSAS could delay the contractile-relaxant responses of the pharyngeal muscles during the transition from inspiration to expiration, increasing pharyngeal collapsibility. Exercises that target the oropharynx region increase the strength of the oropharynx muscles, thus repositioning the tongue under anteroposterior stress, could help to reduce the collapse of the pharynx. The increased strength of the tongue and the soft palate related to the speech therapy could explain the improvement of the Modified Mallampati Index (MMI) and the other objective sleep parameters in patients affected by OSAS [43]. Scientific evidences for speech therapy in children affected by OSAS are rare. Schievano et al. [53] reported an enhanced respiratory function experienced by habitual mouth breathing population who underwent a therapeutic program based on facial massages and myofunctional exercises involving mental, labial and lingual area, feeding re-education included. The Authors argue that the muscular and functional alterations were not completely recovered due to the lack of morphological and structural correction during the therapeutic period; thus they underline the need for a multidisciplinary approach to solve the problem From these considerations, this study aims to present a literature review and a model of orofacial rehabilitation in children with obstructive sleep apnea undergoing treatment with rapid maxillary expansion. Once, speech therapy presents a promising future in the treatment of patients with obstructive sleep apnea and the lack of standardization of rehabilitation exercises of oronasal in different studies, were the main reasons that encouraged the making of this article.

2. Respiratory rehabilitation program

Muscular training is the key factor of the respiratory rehabilitation program described in this paper. The exercises are grouped according to the body area of interest into local exercises (involving nose, lips, antigravity muscles of mastication), see Table 1, and general ones (physical therapy), Table 2. These exercises are taught with the cooperation of a speech therapist and they are performed by the patient in a work at home program. Muscular training must be performed for the whole period of active expansion by the maxillary expander and for at least one month during the post-expansion retention period. The patient and their parents must really commit and cooperate to keep the therapy effective. The results achieved would allow to assess whether to continue the therapy for an additional variable period. With regards to the number of the exercises, we suggest to choose two kinds of general exercises and two kinds of local ones for each body area, alternating their prescription in the sessions. The patients are requested to carry out the whole series of the prescribed exercises (local exercises and general ones) twice a day at least; three times a day would be the ideal frequency. Whenever the child successfully completes the whole series he will note it on a chart marking the current date. This would make the child more aware and the operator will be able to monitor patient's compliance with the therapy. In order to promote the restoration of physiological breathing it would be useful to add to the muscular training hygienic and behavior instructions as well as other therapeutic procedures such as rhinosinusal washes. We also suggest a postural re-education (Alexander technique) and, if necessary, a pharmacological treatment aimed to improve nasal obstruction. An otolaryngologist consultancy before the orthodontic-myofunctional therapy is advisable in order to prevent and treat nasal obstruction. The therapeutic program

Table 1 – Local rehabilitation—work at home program.

Body area	Therapy	Type of exercise	Number of repetition/ timing for each exercise	Daily frequency
Nasal area	Blow the nose	–	–	At least 3 times per day
	Nasal washes	–	–	At least 2 times per day
	Muscular training	n.2 amongthe following exercises: wet gauze,siren, foot of the nose,alternate ventilation, piglet,bunny	n.10 or n.5 per nostril	2–3 times per day
	Massages	n.2 among the following exercises: slow circular movements, tap the nose, pinch the nose	–	2–3 times per day
Lips	Muscular training	n.2 amongthe following exercises: kiss,pencil,button, inflated cheeks,patch, button-bottle, lip massages or upper lip stretching in patients with only upper lip hypotonia	n.10/10 min	2–3 times per day
Jaw elevator muscles	Muscular training	n.2 among the following exercises: count to10,TIII,CIUUU, peg	n.10	2–3 times per day

Table 2 – General rehabilitation—work at home program.

Therapy	Type of exercise	Number of repititions for each exercise	Daily frequency
Body training	n.3 among the following exercises: breathing awareness, diaphragm mobilization, perception of breathing sensations, sniff-test, diaphragmatic-abdominal mobilization, supine position and extended legs, supine position and flexed legs	n.10	2–3 times per day

is described below, organized following a topographical criteria. It must be customized for each patient, considering their needs and level of collaboration.

3. Local rehabilitation of the nose

3.1. *Instructions to blow the nose*

The breathing re-education concerning the nose district consists of a first phase in which the operator explains to the patient the importance of blowing the nose and teaches them how to do it properly. Blow the nose one nostril at a time keeping the head down and the mouth closed. It is helpful to include nasal hygiene in their daily routine in order to establish a habit in the child. This is why we suggest the patient to blow the nose always after brushing teeth: the patient will do this two-three times a day at least, more if necessary. It is really important to use paper towels and replace them frequently. The patient and his parents should be aware about how harmful is to sniff up the nose because of the increased infection risk.

3.2. *Nasal washes*

Nasal irrigations are considered by literature to be an additional or the only treatment for several sinonasal conditions associated with oral breathing [54–58].

In our program we recommend to wash the nostrils twice a day, before performing breathing exercises. There are several nasal irrigation systems available. Among them there is Fluirespira® nasal douche device (Zambon, Italy) which is a certified medical device able to spray aqueous solutions. It comes with a button to activate the spray, a suction valve for minimizing the noise level and two adjacent chambers, one designed to atomize the solution, the other one to recover the solution. It is easy to handle and, once charged it can be used wireless. Fluirespira comes with nasal adapters in three different sizes. As an alternative we suggest to use a nasal cup, also known as 'neti pot'. The technique described by Rabago and Zgierska [57] and proposed herein consists of the following passages: lean over a sink looking into the basin with the head down; gently insert the spout of the nasal irrigation pot into a nostril, without pressing the spout against the nose; rotate the head slightly so that the spout is placed into the upper nostril. Breathe through the mouth and lift the container to let the solution into the nostril where the spout is placed; the solution will drain soon through the lower nostril. At the end of the wash, exhale through both nostrils to clear them removing the mucus and the reminder solution; then blow the nose. Repeat this procedure for the other nostril.

A variety of sterile solutions are commercially available. However, another option could be preparing the saline solution at home using non-iodized salt. The literature does not provide consistent data inherent the adequate temperature and concentration that should be used. We suggest a warm saline solution to obtain an additional antimicrobial effect. The first times the irrigation is done it is better to use a lukewarm solution; afterwards the temperature could be increased, compatibly with patient's tolerance. Obviously really high temperatures should be avoided because they might cause nasal irritation and burns. As per solution's concentration, we would prefer a hypertonic one on the assumption that, despite its greater irritation potential, the hyper-tonicity enhances the mucociliary function proven by the increase of the ciliary beat frequency (Marchisio et al.) [58]. In case of mucosal irritation, the sodium chloride concentration should be adjusted. As already stated by other Authors, nasal irrigations can be performed with safety on children of any age and they are compatible with all pharmaceutical therapy.

3.3. *Nasal exercises*

The nasal respiratory rehabilitation involves the following nasal exercises which will be explained and shown by the operator. Each exercise is described by its name followed by its description in the paragraph below. Alternate these exercises and exhort the patient to perform the series two-three times per day.

3.3.1. *Wet gauze*

Wet a folded gauze with cold water, squeeze it and inhale several times through the gauze keeping the mouth closed. Not only there will be a muscular benefit derived from the forced inspiration but also a positive effect on the mucosal membrane. The benefits are linked to the airway humidification caused by the cold water particles in the gauze. Ten repetitions.

3.3.2. *Siren*

Breathe through both nostrils, close one of them with a finger, then exhale forcefully through the previous nostril to produce a sound comparable to a ship's siren. Perform five repetitions per nostril and then other five repetitions emitting a louder sound.

3.3.3. *Foot of the nose*

Put the thumb under one of the nostril, like it is its foot. Exhale forcefully through the previous nostril, then move the thumb under the other nostril and inhale. During the exercise the child must check they are performing a thoracic-abdominal breathing by placing a hand on the abdomen. Because of inhalation

and exhalation are always performed through the same nostril, carry out five repetitions, then invert the role of the nostrils during the further five repetitions.

3.3.4. *Alternate ventilation*
Put the thumb of the left hand on the left nostril being careful not to bend the cartilage of the nose and inhale through the right nostril; put the left index finger on the right nostril and exhale through the left nostril. Five repetitions per nostril.

3.3.5. *Piglet*
While keeping the mouth half-opened, inhale wrinkling the nose, dilating the nostrils to emit a noise like a grunt; then relax the involving muscles and exhale. This exercise allows the elevator muscle of the nose and the dilator muscle of the nostrils to train and it also has an effect on pharyngeal muscles. Ten repetitions.

3.3.6. *Bunny*
Keeping the mouth closed, inhale imitating a rabbit sniffing, then relax the muscles and exhale causing the nostrils opening. Ten repetitions.

Nasal massages

- Assuming that rubbing the region of the nasal wings improves ventilation, we suggest to perform the following exercises. Each kind of nasal massages is described by its name followed by its description in the paragraph below.
- *Slow circular movements:* Massage the wings of the nose using the tip of the index finger in slow circular movements, then inhale.
- *Tap the nose:* Gently tap the wing of the nose from the top downwards with the index.
- *Pinch the nose:* Pinch the nose with two fingers for a second and inhale.
- Choose a type of massage to be performed two-three times per day, then switch.

4. Local rehabilitation of the lips

The myofunctional local therapy of our program is also aimed at improving lips function and tone, often found deficient in mouth breathing children [1,2]. For children showing hypotonia of both lips and not affected by hypertonia of the mental muscle a considerable improvement can be achieved by performing the following exercises. Each exercise is described by its name followed by the description of the exercise in the paragraph below. Perform the chosen exercises two-three times a day.

Kiss: Strongly push the lips forward like kissing, then bring them upwards trying to almost touch the nose; afterwards, pull them to the right before then to the left. Five repetitions.
Pencil: Hold a pencil between nose and upper lip, so that it does not fall down, even tilting the head down.
Button: Hold a button between upper lip and lower lip.
Inflated cheeks: Keep the mouth closed and inflate the cheeks, then try to push all the air in the mouth against the lips. Five repetitions.
Patch: Put a paper patch that can be easily removed on the lips, then try to remove it just using the lips, no hands or tongue. Five repetitions.
Button–bottle: With the head downwards-facing, hold, between lips and teeth, a button fixed to a string which is tied to a plastic bottle (500 mL) filled with water. The exercise must be 10 min long; the amount of water will be gradually increased up to fill the entire bottle.
Lip massages: Lift the lower lip to the point that it covers the upper lip, then massage it with thoroughly.
In oral-breathing children the functional failure is often limited to the upper lip [59]; in these patients the only practice to perform is the stretching of the upper lip.
Upper lip stretching: Stretch the upper lip downward using one hand and pull down the lower lip with the other hand to avoid the contraction of the mental muscle, if it has an increased tone.

5. Local rehabilitation of the tongue

When the child becomes able to breathe with the nose and achieve the lip seal, he becomes able to activate a physiological deglutition scheme too. However, in the treatment of some patients affected by oral-breathing and visceral swallowing, it may be helpful following a specific re-education therapy for the tongue, aimed at normalizing its altered perception and posture.

The purpose of the tongue exercises is to maximize the mobility of the muscles styloglussus, genioglossus, hyoglossus, palatoglossal muscle superior longitudinal and transverse. The patient is requested to move the tongue tip in clockwise and counter clockwise directions within the vestibule of oral cavity for 20 times in each direction, three times a day, in the morning, afternoon and night, every weekday [60].

6. Exercises of the muscles velopharyngeal sphincter

Exercises of the muscles velopharyngeal sphincter: executed to maximize the mobility (isothonic exercise) and to increase the tension (isometric excercise) of the muscles *uvula*, *palatopharingeo*, *tensor and levator soft palate*. The patient was oriented to emit a /ra/ syllable extending the /r/ consonant, with change of head position to facilitate the muscles mobility, that is, the patient could hold his head straight up or bend it down or up as he wished to facilitate the proper movement of the cited muscles, while producing the syllable. Three series of 10 repetitions were executed, three times a day, in the morning, afternoon and night every day of the week [49].

7. Exercises of the muscle suprahioideos and tongue

Exercises for muscles suprahioideos and tongue: were executed with the purpose to increase mobility (isothonic exercise) and

tension (isometric exercise) of muscles suprahióideos (mylohioid, genyohioid, digastric tyroid) and the tongue genioglossus, hyoglossus, palatoglossus, styloglossus superior longitudinal and transverse. Description: the patient position the tip of the tongue at *papilla incisive*, and then open and close his oral cavity forcing the tongue, but not projecting the jaw forward, while maintaining his head bent backwards. Repetition: 30 times interleaving with swallows keeping the head at the same position, three times a day, in the morning, afternoon and night, every day in the week [61].

8. Exercises of the soft palate

Exercises for soft palate has the purpose to work mobility (isotonic exercise), tenstion (isometric exercise) and resistance (isokinetic exercise) of the muscles *palatopharingeo*, uvula, tensor and the levator *soft palate*. The patient was oriented to: a) open wide his oral cavity, position the tongue against mouth floor and produce abrupt sounds of open vowel /a/, generating the elevation of the soft *palate* (isotonic exercise), in a rate of 3 series of 10 repetitions; and b) emit a sustained /a/ vowel, to keep the velum raised and contracted, while keeping the tongue in the mouth floor, making 10 repetitions, three times a day, in the morning, afternoon and night, every day in the week [60,42].

9. Local rehabilitation of the jaw elevator muscles

This training task targets jaw elevator muscles which appear to be hypotonic in mouth-breathers [62]. Changes in tone and strength of the muscles in question are the outcomes of these exercises. Each exercise is described by its name followed by its description in the paragraph below. Alternate the listed exercises according to the prescription and carry out the whole series of the chosen exercises two-three times a day.

Count to ten: Tighten the teeth with the lips in a half-closed way and keep this position counting to ten; at the same time place the index and middle finger on the posterior area of both of the cheeks in order to feel the muscular contraction, then relax. Ten repetitions, each one for 10 s.
Tiii: With tightened teeth and half-closed lips, pronounce strongly the sound TIII, exhaling across the teeth. Ten repetitions.
Ciuuu: With tightened teeth and half-closed lips pronounce the sound 'CIUUUU' and move, by blowing out air, a piece of paper placed on the palm of the hand. Ten repetitions.
Peg: Open and close a wooden peg by tightening and relaxing the teeth. Ten repetitions.

With the same purpose of the previous exercises we would suggest to use chewing gums as an effective means for the voluntary development of the muscular strength. It could be useful to stick the gum on the palate roof, then pinch it with the back of the tongue. This exercise is meant to improve self-perception of tongue's peristalsis, as well as to tone up its muscles.

10. General rehabilitation

The ventilation model of the lower airway appears to be often impaired in mouth-breathers [1,2,39]. The procedure to restore the respiratory function via body training exercises has been known for many years; the purpose is to ease the cost-diaphragmatic breathing by finding out the right balance of the muscles involved. The program presented consists of the following exercises a speech therapist would have to teach to the patient. Perform two-three series a day of the chosen exercises, then switch them.

10.1. *Breathing awareness*

Place the hand on the abdomen, just below the chest, and slide it upwards during inhalation, downward in exhalation. Ten repetitions.

10.2. *Diaphragm mobilization*

Supine position, lay one hand on the upper chest and the other one on the abdomen; slowly breathe through the nostrils imagining that the hands are placed on the plates of a scale and are alternatively raised and lowered during breathing. Ten repetitions.

10.3. *Perception of breathing sensations*

While sitting, slowly inhale, then stop breathing for two-three seconds and slowly exhale, perceiving the warm air flow incoming and the cold one outgoing. Ten repetitions.

10.4. *Sniff-test*

Exhale three times quickly and as many times slowly paying attention to the movement of the diaphragm. Ten repetitions.

10.5. *Diaphragmatic-abdominal mobilization*

While sitting with crossed legs, perform a total exhalation, then expand the chest in apnea contracting the muscles of the rib cage; voluntarily contract the belly, slowly let the air through the lips, then slowly relax. Ten repetitions.

10.6. *Supine position and extended legs*

Supine position with extended legs and the arms along the body, exhale by blowing and retracting the abdomen or, in other words, by pressing the lower back against the floor, then relax the muscles, inhale and inflate the abdomen, making sure to detach the back from the floor. Ten repetitions.

10.7. *Supine position and flexed legs*

Supine position with flexed apart legs, the soles well flat on the floor and the feet in contact with each other, exhale

closing the knees and pressing the back against the floor. Then let the air in, dropping the knees toward the outside and slightly lifting the pelvis off the floor, meanwhile the abdomen and the chest are inflating. Ten repetitions.

Since we treat young patients we think that using pictures to explain the correct movement of the chest is useful. The lower chest that expands due to the movement of the rib is comparable to lift a bucket handle, while the upper chest movement, i.e. the sternum that lifts, can be pictured as the lever of a pump [63].

In order to learn the perception of respiratory muscles and to set a correct breathing dynamic, our therapeutic program involves breathing exercises which derive from the ancient yoga technique of pranayama, where this term means the control of life energy through breathing [64].

The 'square breath' is the basic exercise we refer to. The four phases of breathing, namely inhalation, retention of breath, exhalation and retention of emptiness, are bonded in a rhythmic form. This breathing scheme can be viewed as a square: the patient ideally follows the left vertical side of the square from the bottom upwards (inhalation), the upper horizontal side from the left to the right (retention of breath), the right vertical side from the top downwards (exhalation), the lower horizontal one from the right to the left (retention of emptiness). One must start the exercise emptying the lungs completely, then go ideally along each side of the square with the right rhythm, keeping open the vocal cords for the whole exercise timing. It is important to underline that the break between inspiration and expiration phases are different from the state of apnea, during which the glottis is involuntarily closed. Progressively it will be possible to add some variants within the same exercise such as the contraction of the abdominal wall during the breathing retention. The deep and slow breath of pranayama seems to modify the autonomic control of breathing by increasing the vagal tone and reducing the sympathetic activity [65].

Scientific literature shows the decrease of the breathing dead space and the increase of the vital capacity of the lungs when pranayama exercises are performed by young adults in good health conditions [66]. The same exercises are practiced, particularly in India, as a non-pharmacological treatment of respiratory diseases, such as the bronchial asthma, with proven positive effects on the patient's symptoms [67,68].

In our program we suggest to integrate the mentioned breathing exercises with the so-called 'Alexander technique'. This technique, introduced by Alexander more than a hundred years ago, is a form of physical therapy aimed at the correction of posture by keeping head, neck and trunk in their natural alignment. It does not involve exercises, rather these are lessons of musculoskeletal proprioceptive education during which an adequately trained instructor teaches the learner, via explanations and hand contact, to adjust their posture; the instructor modifies patient's movement habits and their body response to external stimuli [69].

Early evidence in literature state that the Alexander Technique may positively influence the lung function [69,70]. Austin [71] assumes that the subjective breathing improvement experimented by healthy young adults involved in his study is linked to the following steps: reduction of cervical lordosis, increase of the muscular strength of the abdominal wall, decreased muscular tension of the chest wall with greater expansion of the rib cage, reduction of musculoskeletal interferences in the respiratory movement coordination. These effects would justify the use of the Alexander technique in mouth-breathing children, who often present postural alterations as well [72–74].

11. Conclusion

If RME is supported by an adequate functional rehabilitation, the possibility to change the breathing pattern is considerably amplified. The physical exercises (local and general ones) and the nasal washes represent the crucial points of our program that should be customized for each patient. Awareness, motivation and collaboration of the child and their parents, as well as the cooperation among specialists, such as orthodontist, speech therapist, pediatrician and otolaryngologist, are necessary conditions to achieve the goal.

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Original Article

The effect of orofacial myofunctional treatment in children with anterior open bite and tongue dysfunction: a pilot study

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Summary

Objectives: Insufficient attention is given in the literature to the early treatment of anterior open bite (AOB) subjects receiving orofacial myofunctional therapy (OMT), which aims to harmonize the orofacial functions. This prospective pilot study investigates the effects of OMT on tongue behaviour in children with AOB and a visceral swallowing pattern.

Materials and methods: The study comprised of 22 children (11 boys, 11 girls; age range: 7.1–10.6 years). They were randomly assigned into OMT and non-OMT subjects. The randomization was stratified on the presence of a transversal crossbite. At baseline (T0), at the end of treatment (T1) and at 6 months after T1 (T2) maximum tongue elevation strength was measured with the IOPI system (IOPI MEDICAL LLC, Redmond, Washington, USA). Functional characteristics such as tongue posture at rest, swallowing pattern and articulation and the presence of an AOB were observed.

Results: OMT did significantly change tongue elevation strength, tongue posture at rest, and tongue position during swallowing of solid food. At T2 more OMT subjects had contact between the lower central incisors and their antagonists or palate ($P = 0.036$). More OMT subjects performed a physiological pattern of water swallowing than non-OMT children at T1 and T2, although the differences were not significant. Articulation of /s,l,n,d,t/ was not improved by OMT. No interaction between OMT and expansion was found for any of the parameters.

Conclusion: OMT can positively influence tongue behaviour. However, further research is recommended to clarify the success of OMT as an adjunct to orthodontic treatment and to identify possible factors influencing the outcome.

Introduction

Malocclusions such as anterior open bite (AOB) are often associated with orofacial dysfunctions (1). It has a multifactorial etiology comprising inherited skeletal pattern and environmental causes, such as thumb or dummy sucking, mouth breathing, lip or tongue thrusting and posture, tooth ankylosis, and eruption disturbances. Some researchers have focused on the tongue as the primary factor in the etiology of AOB. Proffit (2) and Proffit *et al.* (3, 4) measured force levels of the tongue against the maxillary incisors and palate during rest and normal swallowing. They concluded that the resting

position of the tongue was a more contributing factor than the swallowing position in determining dental arch form. The inadequate tongue position during swallowing must then be regarded as a result of a pre-existing morphological alteration, thus as a consequence and not as a cause of the AOB. Other investigators however have shown that functional tongue movements during deglutition are significantly correlated with certain features of maxillofacial morphology such as AOB (5–7). Individuals with partial AOB and incorrect tongue position exhibit impaired gnostic sensibility of the tongue (8, 9), which is a symptom of disturbed sensorimotor coordination and is connected with the incorrect position of the tongue. This results in imprecise action and reduced vertical movement of the tongue. Cayley *et al.* (10) reported that children who swallow incorrectly very rarely touch the anterior part of the palate with the tip of the tongue. They perform predominantly horizontal tongue movements and place the tongue between their anterior teeth while speaking and swallowing (11). Although studies have demonstrated that tongue thrust plays an important role in the etiology of AOB as well as in the relapse of treated AOB patients, the exact etiological connection between malocclusion and malfunction during swallowing remains controversial (12). This applies in particular to the extent to which orofacial dysfunctions foster the development of malocclusions and how a dysfunction can be positively influenced by a change in structure (13).

From the standpoint of developmental physiology, a distinction is drawn between visceral, somatic, and inconstant swallowing (12, 14). Visceral swallowing exists at birth and is also termed 'infantile swallowing'. It is characterized by a forward movement of the tongue tip and pressure against the lingual surfaces of the anterior teeth. A visceral type of swallowing can persist well after the fourth year of life and is then considered as a dysfunction or abnormality because of its association with certain malocclusions (12, 14). Normally, the visceral swallowing pattern changes gradually into a mature or somatic swallowing pattern. The latter is characterized by a cranial movement of the tongue and pressure on the incisive papilla (12). Inconstant swallowing is characterized as a pattern of swallowing during the transitional period between infantile and somatic swallowing. According to Christensen and Hanson, a visceral swallowing pattern is seen in 50% of 5-year olds and in 33% of 8-year olds (15).

In the age range between 6 and 8 years, AOB is a predominant type of malocclusion (16). A prevalence of 1–17.7% of AOB (defined as the lack of overlap between the upper and lower incisors) in the mixed dentition is reported in the literature (1, 16–19). In the mixed dentition AOB is registered more often in girls (1, 19). Keski-Nisula *et al.* (17) reported in their study that at the onset of the early mixed dentition, 39.1% of the children had no contact either between the mandibular incisors and maxillary incisors or palatal gingiva. In 4.6% no incisal overlap was present. Some authors mention that the prevalence of AOB is not significantly variable with age (20), however, other state that the frequency of AOB undergoes a significant decline from the deciduous to the mixed dentition (1, 18, 21–22). Almost 70% of the AOB cases is self-corrective during the transition from the primary to the early mixed dentition (18). The main factor underlying the self-corrective tendency is the early interception of infantile habits (18, 23). According to Klocke *et al.* (21) the frequency of AOB also declines from the early to late mixed dentition. AOB associated with orofacial dysfunctions however declines only gradually with increasing age and therefore children whose open bite is associated with substantial dysfunctions are to be regarded as high-risk children for the further development of the dentition (1).

Several treatment approaches with regard to early treatment of AOB can be found in the literature. Many authors agree that clinicians should be able to distinguish an AOB of dental and dentoalveolar origin from a skeletal open bite so that treatment is directed towards the cause of the problem. Unfortunately, in most cases this distinction is not so clear and both dental and skeletal characteristics are present. The treatment modalities for early correction of AOB include functional, fixed, and removable appliances, with the goals of impeding mechanical factors that maintain the open bite (like thumb sucking or tongue thrust) and limiting excessive vertical growth of the craniofacial skeleton (24–31). However, few publications exist on early interceptive treatment in AOB patients with a persistent aberrant swallowing pattern using orofacial myofunctional therapy (OMT) (32–35). Some authors question the clinical use of OMT (22). Others support the reestablishment of a normal oral function after OMT in patients with myofunctional disorders such as tongue thrusting (36, 37).

The aim of a myofunctional program is to establish a new neuromuscular pattern and to correct abnormal functional and resting postures. Cayley *et al.* (38) demonstrated that normal swallowing function resumes after OMT in subjects with AOB. Also the improvement of the resting position of the tongue has been described (35). It has been suggested that an OMT therapist should train the patient to lift the body of the tongue in order to learn a normal resting position of the tongue. Other treatment objectives are strengthening of the orofacial muscles to pave the way for mouth closure, establish nasal breathing, and learn a physiological swallowing pattern (39). However, Smithpeter and Covell (40) cited the following reasons for the lack of enthusiasm for OMT: 1. limited office space for providing therapy, 2. absence of OMT providers, 3. difficulty and amount of time required, 4. inadequate training, 5. hope that a change in function will be induced by a change in form, 6. belief that there is insufficient scientific evidence to support OMT and 7. observation that not all OMT providers have the same expertise, so successful results are unpredictable.

The aim of the present pilot study is to investigate the effects of OMT on tongue behaviour in children with AOB and a visceral swallowing pattern.

Subjects and methods

Twenty-two children (11 males, 11 females; age range: 7.1–10.6 years) were included in this prospective pilot randomized study. The inclusion period started in February 2012 and ended in February 2013. The inclusion and exclusion criteria are described in Table 1. All children were seen at the orthodontic department of the University Hospitals Leuven and informed consent was obtained. The research project was approved by the Ethics Committee of the University Hospitals Leuven (B322201316750).

The subjects were randomly assigned into two groups: OMT-patients and non-OMT-patients (Figure 1). The randomisation was stratified on the presence of a transversal crossbite (uni- or bilateral); so each randomized group consisted of two subgroups, patients with and without expansion, respectively. If no crossbite was present, the subjects were randomly assigned in the MYO subgroup (n = 6, mean age 8.3, age range 7.1; 9.3) or CON subgroup (n = 6, mean age 9.1, age range 7.7; 10.6). The MYO subgroup underwent 10 hours of OMT, during 10–20 sessions of 30–60 minutes. The children were furthermore instructed to perform exercises at home. The CON subgroup was observed after 6 months without treatment. However, if a crossbite was present, the subjects were randomly assigned

Table 1. Inclusion and exclusion criteria.

Inclusion criteria
Lack of contact between the lower central incisors and the upper central incisors or palate
Early or intermediate mixed dentition
Visceral swallowing pattern
Exclusion criteria
Age less than 6 or more than 10 years old
Sucking habits not ceased for at least 6 months prior to intake
History of myofunctional therapy
Mental retardation
Orofacial congenital deformities or orofacial syndromes
Muscular or connective tissue disorders
Macroglossia or ankyloglossia
Obstructed nasal airway

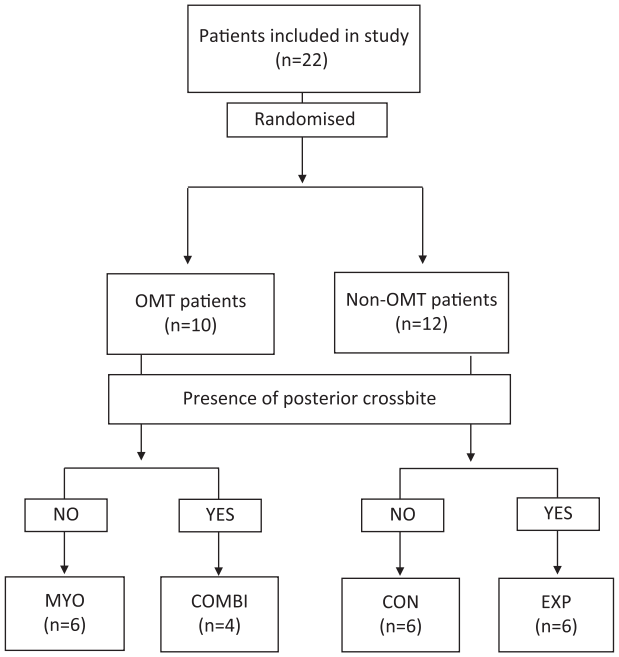

Figure 1. Flow chart of patient allocation.

in the EXP subgroup (n = 6, mean age 8.7, age range 7.5; 9.8) or COMBI subgroup (n = 4, mean age 8.4, age range 8.1; 8.7). The EXP subgroup was treated with a removable expansion device and the COMBI subgroup first underwent 10 hours of OMT, followed by a treatment with a removable expansion device.

An overview of the different stages of the myofunctional training program is listed in Table 2. The OMT phase of intervention lasted 4–6 months. The sessions were given weekly (30 minutes) or every 2 weeks (60 minutes) and were individually held with each patient. The removable expansion device consisted of an acrylic resin plate with coverage of the occlusal surfaces of the posterior teeth and a jack-screw which was activated 1–2 times a week by the patient. At baseline (T0), at the end of treatment or after 6 months in the CON subgroup (T1) and after 6 months of follow-up (T2) maximum tongue elevation strength was measured. Functional characteristics as tongue posture at rest, swallowing pattern and articulation, were examined by means of a clinical evaluation performed by a speech pathologist.

The maximum tongue elevation pressure was measured using the IOPI system (IOPI MEDICAL LLC, Redmond, Washington, USA).

Table 2. Overview of the different sessions during the myofunctional training program.

1	Explanation of treatment process and motivation
2–3	Strengthen tongue and lip musculature
4–5	Basis of the swallowing process
6	Strengthen the anterior part of the tongue
7–9	Strengthen the mid part of the tongue
10–11	Strengthen the posterior part of the tongue
13–14	Coordination of the total swallow movement
15–16	Practice on conscious habit formation
17–18	Practice on unconscious habit formation
19	Control of physiological swallowing act
20	Control of physiological swallowing act and follow-up

Table 3. Overview of the categories scored during clinical examination.

Tongue posture at rest	
1. Physiological	Resting position of the tongue in contact with the palate extending to the palatal aspect of the alveolar ridge
2. Inter- or addental	Resting position of the tongue between the anterior and/or posterior teeth
3. Caudal	Resting position of the tongue directed towards the lower anterior teeth
Swallowing pattern	
1. Physiological	Characterized by tongue contact with the hard palate and the simultaneous absence of tongue contact with the anterior and canine teeth when swallowing, while the lip and mentalis muscles are inactive
2. Anterior interdental	Tip of the tongue presses between the anterior incisors
3. Anterior addental	Tip of the tongue presses against the lower incisors
4. Lateral interdental	The tongue presses against or between the posterior teeth
Articulation	
/l,n,d,t/	
1. Physiological	Tip of the tongue touches the incisive papilla while speaking
2. Inter- or addental	Tip of the tongue presses between or against the anterior teeth while speaking
/s/	
1. Physiological	Tip of the tongue is behind the lower anterior teeth while speaking
2. Addental	Tip of the tongue touches the upper anterior teeth while speaking
3. Interdental	Tip of the tongue is between the anterior teeth while speaking
4. Lateral	Tongue edges are between the posterior teeth while speaking

The IOPI measures the amount of pressure exerted on a small air-filled bulb. Pressures obtained are digitally displayed (expressed in kiloPascal) on the LCD panel on the instrument. To measure maximal tongue elevation strength, the same procedure as described by Vanderwegen *et al.* was applied (41).

The tongue posture at rest was clinically visualized and evaluated by asking the child where their tongue was located and the answer was converted in one of the categories represented in Table 3, similar to the protocol used by Stahl *et al.* (42). To determine the swallowing pattern the child was asked to swallow water and solid food three

times (in the form of a cookie). Swallowing patterns were assigned in one of the categories represented in Table 3. During swallowing the lips were gently separated to visualize tongue position. Tongue position during the production of the sounds */l,n,d,t,s/* was recorded as the child spoke Dutch test sentences and words. Articulation findings during speech were categorized as described in Table 3.

The lack of contact between the lower central incisors and their antagonists or the palate was evaluated at T0, T1, and T2.

Statistical analysis

An analysis of covariance (ANCOVA) was performed separately on the tongue pressure measurements at T1 and T2, using the baseline pressure level as a covariate. OMT (no/yes) and expansion (no/yes) are considered factors in the ANCOVA model. An estimate of the difference between OMT and non-OMT patients is given for the patients with and without expansion separately, followed by the effect estimate for both groups of patients combined. Furthermore, it has been verified if the effect of OMT depends on expansion (by evaluating the interaction between expansion and OMT in the ANCOVA).

Since the randomization was stratified on expansion, the comparison of proportions between patients with and without OMT was done based on a common odds ratio (OR) in a stratified 2×2 table. The two-sided *P*-value from an exact test for the common OR is reported and an exact two-sided 95% confidence interval (CI) has been constructed. The homogeneity of the ORs in the two strata is verified with Zelen's test.

The alpha-level was set at 0.05 in this pilot study. A single significant *P*-value needs to be interpreted with caution since due to the exploratory character of the study no corrections for multiple testing are considered. All analyses were performed using SAS software for Windows (SAS Institute Inc., Cary, NC, USA).

Results

At baseline, 31.8% of the children did not have vertical overlap between their lower and upper central incisors. The other individuals (68.2%) did have an anterior non-occlusion. All children showed a non-physiological swallowing pattern (water and/or solid swallow) and 95.5% also had a non-physiological (addental, interdental, or caudal) tongue position at rest.

Age distribution and the mean maximum tongue elevation pressure at T0, T1, and T2 are represented in Table 4. At T1, the difference in maximum tongue pressure between all OMT and non-OMT subjects, aggregated over both strata and using the baseline pressure as a covariate, was significant (estimate difference 5.6 kPa; $P = 0.015$). The interaction between OMT and expansion was non-significant ($P = 0.379$), hence reporting the combined effect is meaningful. Note however that whereas in the stratum of patients without expansion the effect was significant (MYO compared with CON, $P = 0.016$), evidence was lacking in the stratum of patients with expansion (COMBI compared with EXP, $P = 0.28$). Also at T2, there was a significant higher pressure for OMT subjects compared to non-OMT subjects (estimate difference 7.6 kPa; $P = 0.004$). Again, no interaction between OMT and expansion was found ($P = 0.94$). At this timepoint, tongue pressure was found to be significantly increased in MYO and COMBI subgroups, respectively compared with CON and EXP subgroups ($P = 0.029$ and $P = 0.040$).

At the end of treatment 10.0% and 8.3% of the respectively OMT and non-OMT subjects had contact between the lower central incisors and their antagonists or palate. This difference was not significant. However, at T2 there was a significant difference between both groups (OR = 12.200, $P = 0.036$; 60.0% in the OMT group and 8.3% in the non-OMT group). There was no evidence that the ORs were different in both subgroups with or without expansion (T1, $P = 1.000$; T2, $P = 0.471$, Table 5).

Tongue posture at rest was physiological in 10.0% of the OMT subjects and in 0.0% of the non-OMT subjects. At T1, respectively 60.0% and 0.0% demonstrated a normal rest posture and the difference was found to be significant ($P = 0.006$). At six months follow-up, the difference was also significant ($P = 0.036$, 60.0% and 8.3%) and no evidence was found that the ORs were different in both subgroups with or without expansion ($P = 0.471$). The common ORs and 95% CIs are shown in Table 5.

No difference was found between the amount of OMT subjects and non-OMT subjects showing a physiological pattern of water swallowing at T1. At 6 months follow-up, the percentages were respectively 50.0% and 8.3% but were not found to be statistically significant ($P = 0.059$). The common ORs and 95% CIs are shown in Table 5. During the swallowing assessment on solid food, a significant difference between both groups was observed at T1 and T2 ($P = 0.036$ and $P = 0.015$, respectively). There was no evidence that the ORs were different in both subgroups with or without expansion (Table 5).

At baseline, 21 of all subjects showed a non-physiological articulation of */s/*. At T1 and T2 no significant difference between the OMT and non-OMT subjects was observed ($P = 0.338$ and $P = 0.758$, respectively). Also, the */l,n,d,t/* articulation had not significantly improved in the OMT children at the end of treatment and after short-term follow-up ($P = 0.400$ and $P = 1.000$). The common ORs and 95% CIs are represented in Table 5.

Discussion

This pilot study has a strict exploratory character and aims to stimulate further research in the field of OMT. Randomization

Table 4. Age distribution and maximum tongue elevation pressure (expressed in kiloPascal).

	No expansion		Expansion	
	OMT (MYO)	Non-OMT (CON)	OMT (COMBI)	Non-OMT (EXP)
N	6	4	6	6
Mean age (SD)	8.3 (0.8)	9.1 (1.2)	8.4 (0.3)	8.7 (0.9)
Mean (SD) pressure at T0	36.3 (9.9)	43.9 (15.0)	48.2 (7.5)	38.3 (12.1)
Mean (SD) pressure at T1	45.4 (7.4)	44.7 (16.3)	51.8 (9.3)	39.6 (11.2)
Mean (SD) pressure at T2	46.1 (7.4)	44.2 (14.5)	52.3 (8.2)	37.5 (7.6)

SD, standard deviation.

Table 5. Observed frequencies (%) of positive outcome in OMT and non-OMT patients aggregated over both strata (expansion–no expansion).

	Timepoint	OMT (*N* = 10)	Non-OMT (*N* = 12)	OR (CI)	*P*-value OR	*P*-value Zelen
AOB	T1	1 (10%)	1 (8.3%)	1.00 (0.011; 94.0)	1.00	>0.99
	T2	6 (60%)	1 (8.3%)	12.2 (1.1; 669)	0.036	0.47
Tong posture at rest	T1	6 (60%)	0 (0%)	ND (2.8; ND)	0.006	—
	T2	6 (60%)	1 (8.3%)	12.2 (1.1; 669)	0.036	0.47
Swallowing pattern (water)	T1	4 (40%)	1 (8.3%)	6.67 (0.49; 334)	0.23	0.47
	T2	5 (50%)	1 (8.3%)	25.0 (0.93; 1035)	0.059	>0.99
Swallowing pattern (solid)	T1	6 (60%)	1 (8.3%)	15.0 (1.12; 669)	0.036	>0.99
	T2	5 (50%)	0 (0%)	ND (2.19; ND)	0.015	—
Articulation */l,n,d,t/*	T1	2 (20%)	0 (0%)	ND (0.35; ND)	0.40	—
	T2	1 (10%)	1 (8.3%)	1.25 (0.02; 98)	>0.99	>0.99
Articulation */s/*	T1	6 (50%)	4 (33.3%)	3.9 (0.44; 45)	0.34	>0.99
	T2	1 (10%)	3 (25%)	0.34 (0.01; 5.36)	0.76	>0.99

OR, odds ratios for the effect of OMT with exact 95% confidence intervals (CI) and *P* value. *P*-value Zelen, test for the interaction between OMT and expansion (homogeneity of the ORs between both strata). ND, not defined due to the presence of cells with zero observations.

had been stratified on the presence of a transversal crossbite. If a crossbite was present, expansion of the upper arch was intended to correct the transversal discrepancy and to provide more space for the tongue. The interrelation between maxillary constriction and orofacial dysfunctions is highlighted in the literature (43, 44) and the correction of maxillary constriction has been regarded as an additional target for early treatment in AOB patients (30, 45). Since no interaction between OMT and expansion was found, all OMT subjects with and without expansion might be combined into one major group to investigate the effect of OMT. Although it was assumed that the resin of the expansion plate on the palate may interfere with the tongue position, this was not confirmed by the results. A lack of evidence exists whether OMT should start prior to orthodontic treatment or not. Speech pathologists and orthodontists seem to have different opinions on this subject (46). Mason and Role (47) argue that if a posterior crossbite exists the treatment should be accomplished prior to the initiation of OMT. However in our study, the COMBI first group underwent 10 hours of OMT prior to maxillary expansion due to practical reasons. In this study, all OMT subjects underwent the same standardized protocol of myofunctional training. In typical clinical settings however, OMT exercise regimens and duration of therapy are often tailored to the needs and responses of each individual patient. No consensus can be found in the literature regarding the ideal protocol to treat orofacial dysfunction. More research concerning different treatment protocols would be of value. This study included subjects in the early or intermediate mixed dentition, to correct the aberrant tongue function at an early age. Different opinions are expressed in the literature regarding the ideal age to start OMT (48). Some dentists recommend treatment or have successfully treated pediatric patients under the age of 10 years with the aid of OMT (33, 40, 44). On the other hand, others authors suggest waiting until patients are 10 years of age or older, because of the possibility of spontaneous closure of the AOB (49). OMT aims to harmonize the orofacial functions and to exclude factors interfering with the normal development of the dental arches. In this study, the children were assumed to be old enough to understand the aim and exercises of OMT and the authors do believe in the adaptability of young tissues. A comparable control group, matched for age and gender, was also followed-up to eliminate changes due to growth and maturation. However, at this young age, a tongue thrust can be the result of a 'gap-filling' tendency which may impede treatment and the available oral space might not be developed enough in all subjects. It is obvious that there is a lack of evidence defining the ideal age to start OMT and more research is needed.

Patients with oral phase swallowing problems are assumed to have a tongue strength that is significantly lower than in normal subjects (50). Several methods have been used to measure tongue strength as pressure within the oral cavity, including strain-gauge manometry, force sensitive resistors and bulb pressure sensors, like the IOPI system (3, 4, 51–58). The IOPI has been utilized in many published experiments, mainly in speech and language pathology, and has established high inter- and intrajudge reliability (59–62). Potter and Short (56) concluded that maximum tongue strength can reliably be evaluated in pediatric patients using the IOPI. In this study, a significant increase in maximal tongue pressure was found in subjects who received OMT compared to those without at T1. This finding presumes that the tongue musculature was effectively strengthened by the daily exercises of the myofunctional program. The increase was maintained at short-term follow-up. Although there was an increase in strength in the OMT subjects at T1 and T2, the maximum pressure values were not necessarily higher in subjects with OMT compared to subjects without. In cross-sectional studies no differences in maximum tongue pressure are found between children with and without tongue interposition during swallowing (32, 51, 63). This finding can be explained by a large inter-participant variation in tongue strength (3, 64, 65). The authors believe that it would be difficult to control the inter-participant variation because of the varied functional responses among subjects and similarities in occlusion and facial morphology do not account for similarities in functional pattern. This has been described by Di Fazio *et al.* (64) as well.

Observation of the tongue movements during swallowing with lips apart is a simple and fast method for diagnosing the swallowing pattern. However, since the lips are involved in the act of swallowing, some authors argue that a forced opening of the lips might disturb an individual swallowing pattern (12, 66). Effort has been made in the literature to evaluate the swallowing type in a more objective way, by using techniques like radiocinematography, electropalatography, and electromagnetic articulography (5, 6, 10, 38). However, due to many reasons, especially the risk of irradiation, these techniques did not prove to be appropriate for observation in small growing children (12, 66). Also the use of ultrasonography to assess swallowing type has been described (12, 66). Yet, the reliability of this method has not been extensively verified. The fact that a clinical diagnosis is subjective in nature and inter-individual variability of tongue position and

motility might influence the swallowing type assessment, must be taken into account (67). Another method to overcome this problem is the Payne technique advocated by Garliner, whereby fluorescent orabase paste is applied on the tongue (68). However, for practical reasons it was not used in this study.

As part of OMT the tongue can be re-trained, meaning that optimal motility of the tongue can be created (67). At T1 and T2, OMT did increase the proportion of subjects performing a correct swallow pattern, both during swallowing of water and solid food. This increase might be caused by the fact that some of the OMT children effectively achieved the habit correction, but it might be biased by the fact that some of these children just perform a correct swallow during the clinical trials or by the fact that the evaluation was not performed blindly. However, the transition from conscious to unconscious habit correction can not be assessed during a clinical examination. An intra-oral device sensitive for detecting tongue position and movements during daily activities can elucidate this problem. Cayley *et al.* (38) have reported that normal swallowing function resumes after OMT in subjects with AOB. However, in this study not all OMT children performed a correct swallow at T1. This might indicate that some children needed more training or more time to achieve a correct conscious swallow or that in some children OMT could not correct the aberrant swallowing pattern. The myofunctional protocol has to be adapted to the needs of every individual. As an active exercise concept, the success of OMT is also crucially dependent on motivation and compliance of both child and parents. An evaluation of patient's cooperation would be of value for further research. During the OMT the children's oral awareness increases. Since individuals with AOB and incorrect tongue position exhibit impaired gnostic sensibility of the tongue (8, 9), it has to be determined whether oral sensory perception can improve with training.

Various types of therapy for tongue dysfunction or faulty tongue posture have been reported in the literature like spurs, tongue cribs, vestibular shields, trainer appliances, and functional appliances; resulting in an increase of overbite at the end of treatment (25–27, 29, 31, 68–72). However, little is known about the adaptation of the soft tissues after the discontinuation of treatment, which can influence the stability of the obtained result. When a habit appliance is removed and the cause of the tongue pattern is not addressed, the forward tongue posture and functions are expected to return (73). Sayin *et al.* demonstrated that during deglutition in subjects with a tongue crib, adaptive changes occurred in selective regions of the tongue's dorsum, to compensate for the posterior position of the tongue's tip (71). However, it is not clear if these functional adaptations persist after discontinuation of the crib appliance. Meyer-Marcotty *et al.* hypothesized that spurs exert continuous control by means of a biofeedback mechanism in which they 'inform' the patient of the faulty tongue position (68). The neuro-physiological basis for their clinically observed correction of the dysfunction is a neuromuscular adaptation based on a somato-sensitive feedback. It is unclear if the functional adaptations remain after discontinuation of the spurs, since they did not mention post-treatment data. Knösel *et al.* mentioned that the instruction to position the tongue at the palate during deglutition or to perform tongue reposition manoeuvres appears to be a valid aid in training tongue-palate contact (70). They stated that the additional use of an oral screen did not produce a significant effect on the duration of the favourable cranial tongue rest position and so it can be dispensed. However, other authors found Face Former therapy (oral screen with lip piece) to be more successful than conventional OMT in establishing nasal breathing and a physiological swallowing pattern within a six months period. More research is needed to explore the benefits of this kind of treatment modality (39).

OMT aims to make the patient conscious of the false static and dynamic tongue position and to learn a physiological myofunctional behaviour. Although some authors assumed the tongue's position at rest unconsciously except during exercises (68), our study demonstrated a significant increase of subjects with a physiological tongue posture at rest and during swallowing after completion of OMT. At T2 the children with a normal tongue posture at rest did had contact between the lower central incisors and their antagonists or the palate. This finding hypothesized that OMT effectively changed the rest posture of the tongue in some individuals. Since the tongue was positioned at the palatal aspect of the alveolar ridge in these subjects, the further eruption of the lower incisors was no longer impeded by the tongue. This high percentage of subjects with contact is influenced by the fact that at baseline most of the subjects had an anterior non-occlusion. The authors do not presume that OMT *per se* cause morphological alterations in subjects with more severe or skeletal open bites. OMT is not a substitute for orthodontic treatment and inducing morphological changes is even not a primary purpose of OMT. However, our findings demonstrate that OMT can be a helpful adjunct to orthodontic treatment in patients with aberrant tongue behaviour. Other authors emphasized the potential of myofunctional treatment as well (32,33,35,40). Nevertheless, further research is needed to elucidate factors influencing the outcome of OMT, in order to select the appropriate patients.

Children with articulatory speech disorders are reported to have systematically more inaccurate tongue movements and poor movement coordination than children without speech defects (74). The most common misarticulations associated with orofacial myofunctional disorders are inter- or addental production of apico-alveolar consonants like */s,z,n,l,d,t/*. Eslamian and Leilazpour (74) demonstrated in their study that during the pronunciation of these consonants the tongue made contact more anteriorly on the palate in individuals with tongue malfunction than in those without. However during pronunciation of whole words, the contact points were located similarly on the palate in both groups. This study demonstrated a non-significant difference in both groups on the physiological production of */s/* and */l,n,d,t/* during Dutch test sentences at T1 and T2. Korbmacher *et al.* (39) didn't find an improvement of the articulation of /s/ after OMT as well. Although the OMT protocol in our study includes some articulation exercises and strengthening of the anterior and mid part of the tongue musculature is intended, no significant improvement was found.

Further research is recommended by means of larger, blindly performed and long-term follow-up studies, to confirm our results, to clarify the success of OMT as an adjunct to orthodontic treatment and to identify possible factors influencing the outcome.

Conclusion

OMT can positively influence tongue behaviour. However, further research is recommended to confirm our results, to clarify the success of OMT as an adjunct to orthodontic treatment and to identify possible factors influencing the outcome.

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Myofunctional
THERAPY

Posture

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Lingual Frenectomy: functional evaluation and new therapeutical approach

ABSTRACT

Aim *When ankyloglossia is relatively severe and generates mechanical limitations and functional challenges, surgical reduction of the frenum is indicated.*
Materials and methods *Laser technique is an innovative, safe and effective therapy for frenectomy in both children and adolescents. Erbium:YAG laser (2940nm) can be useful for paediatric dentist: 1.5W at 20pps is a commonly used average power to easily, safely and quickly cut the frenum.*
Results *Usually after laser frenectomy, the postoperative symptoms and relapse are absent.*
Conclusion *Early intervention is advisable to reduce the onset of alterations correlated to the ankyloglossia. A multidisciplinary approach to the problem is advisable, in collaboration with orthodontist, physiotherapist and speech therapist, to better resolve the problem.*

Keywords *Ankyloglossia; Erbium laser; Laser frenectomy; Lingual frenectomy.*

Introduction

The lingual frenum is a mucosal fold that connects the bottom of the body of the tongue to the floor of the mouth and to the mandibular bone. When the frenum is thick and very tight and/or its place of insertion limits the mobility of the tongue, it can result in ankyloglossia (from the Greek "ankylos" which means tied and "glossa" which means tongue) [Various authors, 1975].

Ankyloglossia is an embryological anatomical malformation that usually affects males more than females in a 3:1 ratio. It occurs in newborns with an incidence of about 5%, more frequently as an isolated event and sometimes associated to malformative syndromes (Simpson-Golabi-Behemel Syndrome, Optiz Syndrome, Beckwitz-Wiedemann Syndrome, Oro-facial-digital Syndrome; cleft palate) [Kloars, 2007].

If the anomaly is relatively severe and generates mechanical limitations and functional challenges, surgical reduction of the frenum is indicated, followed by speech therapy for an immediate rehabilitation of the lingual muscle [Campan, 1996].

Furthermore, it should be also emphasised that a short frenum is not always tight or fibrotic; in fact, despite the reduced length of the lingual frenum, the elasticity of the floor of the mouth may still allow a normal mobility of the tongue thus making the frenectomy unnecessary.

Functional problems of ankyloglossia

- Breastfeeding difficulty is caused by the lingual hypomobility and the resulting inability of the nursing infant to squeeze the nipple against the upper arch and hard palate during suction; furthermore, the lateral margins of the tongue raise to form a U-shaped channel that wraps around the nipple to avoid the milk leaking into the vestibule of the mouth. During suction, the lips are also involved as they maintain the nipple in place while providing a seal to prevent loss of milk.
  The complexity or, in more severe cases, the inability to correctly perform suction causes weight problems to the infant as well as a decrease in the production of maternal milk during the early stage thus encouraging bottle-feeding [Dollberget al, 2006; Wallace and Clarke, 2006; Srinivasan et al, 2006; Kotlow, 2004; Margolis, 2008].
- Tongue is a fundamental organ for deglutition and a short lingual frenum can become a mechanical impediment to its proper function. Swallowing, a natural function which involves very complex neuromuscular activity, occurs with a progressive push of the tongue apex onto the retroincisal-palatal spot followed by the posterior and medium area of the tongue pressing on the hard palate first and soft palate after, thus ending on the wall of the pharynx. Anyone with ankyloglossia will have difficulty in swallowing, as it will be impossible to perform the movements described above [Garliner, 1996].
- A short and fibrotic lingual frenum can cause functional problems starting at neonatal age with breastfeeding difficulty or early childhood with speech impediment for the correct pronunciation of dento-lingual-labial phonemes due to the reduced lingual mobility. A study on 1402 patients reported that more frequent speech disorders were: omission and substitution of /r/, and consonant clusters with

/r/, and of /s/ and /z/. Frontal and lateral lisps also occurred. The relation between altered frenum and speech disorders was considered statistically significant with p< .001 [Queiroz Marchesan, 2004].

Orthodontic evaluations

Bearing in mind the close relationship and interdependence between function and form (the "functional matrix" theory of Melvin Moss) [Moss, 1985], we can understand why various orthodontic problems can be correlated with the low position of the tongue and the consequent atypical swallowing [Genovese and Olivi, 2010; García Pola et al, 2002; Defabianis, 2000].

Some of the most frequent problems are:

- possibility of an anterior and/or posterior cross-bite due to a disproportionate growth of the lower jaw in relation to the upper maxilla. An anomalous and not physiological low lingual posture promotes an excessive growth of the mandible, while the growth of the upper arch is not stimulated in its anterior aspect (premaxilla) and transversal planes by the tongue, during each swallowing process (approximately 1500/2000 times every 24hrs);
- possibility of an open bite caused by the placement of the tongue in between the two arches during the deglutition and speech;
- inadequate labial seal and tendency to mouth breathing;
- possible opening of diastema between the lower incisors resulting from an anomalous lingual thrust.

Postural evaluation

Altered postures are present in individuals with ankyloglossia due to:

- tongue anatomically attached to the bone and fascial structures of the head and torsum;
- muscle synergisms existing between the lingual muscle and muscles of the anteromedian chain [Scoppa, 2005];
- neurophysiological connections between the exteroceptors of the palatine spot (emergency zone of the naso-palatine spot, maxillary nerve ramus which is a branch of the trigeminal nerve), trigeminal nuclei of the encephalic trunk, reticular substance, locus coeruleus, cerebral and cerebellar cortex [Halata and Baumann, 1999; Martin et al, 2004].

Ankyloglossia is normally associated with a higher and more advanced position of the hyoid bone; this condition is the result of the hypertone of the extrinsic and suprahyoid lingual muscles (attached to the jaw and skull) and the consequent stretch of the subhyoid muscles (connected with sternum, clavicle, scapula, larynx, pericardium and mediastinum through the cervical mid-fascia).

Observing the patient from a lateral view:

1) The subject may appear with a body posture leaning anteriorly with head and shoulders projected forward and body's center of mass shifted forward. (Fig. 1).
   In an attempt to compensate and maintain the body's center of mass over its base of support, and depending on the muscle support, a cervical hyperlordosis (increased cervical lordosis) with high dorsal kyphosis (dorsal kyphosis) (Fig. 2) or a lumbar hyperlordosis (increased dorsal lordosis) with predisposition to abdominal ptosis and inguinal hernia may occur (Fig. 3).
2) The subject may appear with a scapular plane in line with the glutei plane (normal scapulum) but with the head propelled forward and straightening of the cervical area; in these subjects, during the dysfunctional deglutition, the head typically performs a "chicken-like" movement [Scoppa, 2005] (Fig. 4, 5).

Tongue assessment

The frenectomy or frenotomy is a surgical procedure

FIG. 1 Postural examination in lateral view: body posture leaning anteriorly with head and shoulders projected forward in relation to the buttocks (front scapulum) and body barycenter moved forward.

FIG. 2 Postural examination in lateral view: cervical hyperlordosis (increased cervical lordosis) with high dorsal kyphosis (dorsal kyphosis).

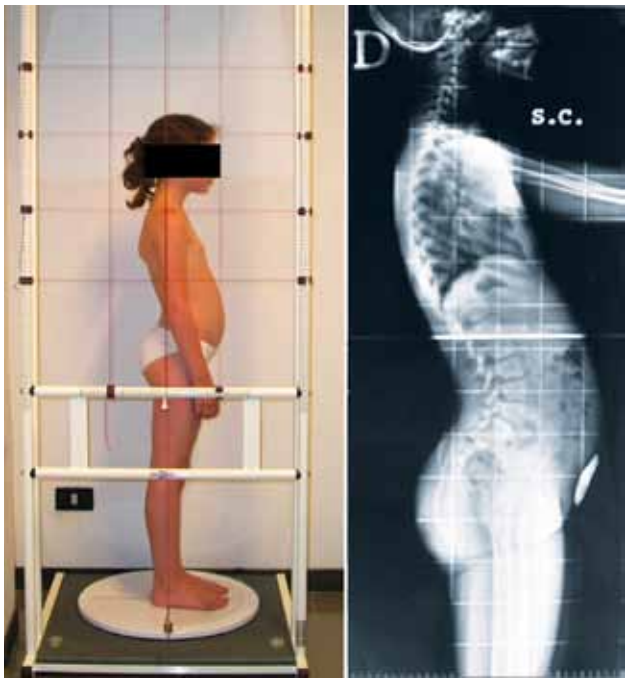

FIG. 3 Postural examination in lateral view: lumbar hyperlordosis (increased dorsal lordosis) with a predisposition to abdominal ptosis and inguinal hernia may increase.

FIG. 4 Postural examination in lateral view: scapular plane in line with the gluteal plane (normal scapulum) but with the head propelled forward and straightening of the cervical area.

FIG. 5 Postural examination in lateral view: correction of the head and neck postion 4 months after lingual frenectomy.

indicated for cases of ankyloglossia with functional impediment.

Surgical intervention must be planned early to avoid functional, anatomical and postural consequences, depending on the severity of the case.

Morphological and functional criteria and tables are available to assist the operator in confirming the indication for surgery:

- the morpho-functional assessment proposed by Hazelbaker [1993], endorsed by the American Academy of Pediatrics, evaluates the degree of anklyoglossia through a score and the ankyloglossia status is diagnosed with a morphological score less than 8 and functional score less than 11;)
- also a morphological classification, based on the distance from the tip of the tongue to the attachment of the frenum, has been suggested by Kotlow [1999] (Table 1).

Kotlow recommends revising the frenum in case of Class IV and Class III ankyloglossia; Class II and Class I ankyloglossia are the most difficult to evaluate and functional criteria of normal range of motion of the tongue can be utilised for surgical indication. Hence, upon completion of the diagnosis, a clinical-functional evaluation for possible surgical indication has been suggested by Olivi et al. [2011] (Table 2).

It should be stated that a short frenum is not always inelastic or fibrotic and, despite the reduced length, it may allow a normal lingual mobility thus not necessitating a reduction intervention; also,

CLINICALLY ACCEPTABLE NORMAL RANGE OF FREE TONGUE: GREATER THAN 16 MM	
Class I	Mild ankyloglossia: 12 to 16 mm and is mild.
Class II	Moderate ankyloglossia: 8 to 11 mm and is moderate.
Class III	Severe ankyloglossia: 3 to 7 mm and is severe.
Class IV	Complete ankyloglossia: less than 3 mm

TABLE 1 Morphologial classification of ankyloglossia (Kotlow L., 1999).

the elasticity of the floor of the mouth can mitigate the effects of the ankyloglossia and help the lingual mobility.

Surgical technique

Traditional frenectomy technique is performed using local anaesthesia, scalpels for incisions according to the technique and sutures. All this requires surgical dexterity as well as the capacity to work with small

Breasthfeeding difficulty
Speech impediment
Atypical swallowing
Impossibility to sweep upper and /or lower lips
Limitation of the tongue to reach the palatal retroincisal spot when the mouth is wide open.
Shape of the tongue distorted and/or Invagination at the tongue tip during the protrusion outside the mouth

TABLE 2 Clinical and Functional criteria for surgical indication (Genovese and Olivi, 2011.

patients: often paediatric dentists or oral surgeons do not have both these capabilities.

Laser technique is an excellent alternative to traditional surgery. It is simple and rapid to perform, well accepted and tolerated by patients [Boj et al., 2005; Haytac and Ozcelik, 2006; Genovese and Olivi, 2008; Kara, 2008], requires a minimal anaesthesia, with an asymptomatic postoperative period, without relapse.

Different wavelengths can be utilised for this procedure and the principal concept to remember for all wavelengths is that the minimum effective energy must be used because the lower the energy applied, the less the damage on the targeted tissue and the faster the healing process.

All the wavelengths in the electromagnetic spectrum are useful tools for mucogingival surgery; the visible and non-visible near infrared lasers work in a non-specific mode on the vascular component of the frenum that are not directly responsible for the process of ankylosis, while the medium and far infrared lasers targeting the aqueous component (Hydroxyl radical) of the collagen fibrotic tissue of the frenum are more specific for this procedure.

The KTP (532 nm) laser, the diode laser (810 - 980 nm) and the Nd:YAG laser [Fornaini et al., 2007] can be safely used, allowing for a good and clean cut while also better controlling the bleeding; it is important not to exceed with the frenectomy incision, as this will avoid overtreatment and subsequent fibrotic scars. Special attention should be paid to the parameters used and the exposure time, keeping in mind the different penetration depth of these wavelengths.

The medium and far infrared lasers are the best choice for targeting the fibrotic tissue of the frenum, as they in fact work, superficially, on the aqueous component of collagen fibers.

The CO_2 laser has a distinct affinity for water as well as for collagen (peak of absorption in the 7000 nm) [Bullock, 1995; Fiorotti et al., 2004]. In our clinical practice, according to Kotlow [2004] and Margolis [2008], for this surgical procedure we prefer the Erbium-family laser (2780 nm and 2940 nm).

Materials and methods

Laser surgical intervention may be performed with topical anaesthesia, but we recommend that inexperienced operators use a minimal amount of anaesthetic injected directly and gently in the frenum; 1/3 of vial (about 0.6 ml), using a 30 G needle, is enough to carry out the procedure with minimum stress for both patient and operator.

The use of magnification loupes is advisable; lingual anatomy, the veins and ducts of the salivary glands must be investigated first, with a close-up picture: after this, it will be much easier to select the area of incision and selectively act on the fibrotic component thus avoiding vascular trauma. With this approach, a profuse bleeding will be avoided and the subsequent scar (which is to be avoided) will also be minimised. The tongue is held upwards with a gauze or, better, with a special tongue retractor (W. Lorenz instruments; Miltex GmbH Germany). In this study an Erbium:YAG laser of 2940 nm was used (LightWalker AT-Fotona; Ljubljana Slovenia). Usually, conical tips of different lengths are used: these tips have a smaller terminal diameter which allows for a higher power density (up to 600 micron) (Fig. 6). The incision of the frenum is performed with low-energy (50-60 mJ) and low-frequency pulse (10-15 pps) for a better and easier control in the selective vaporisation of the collagen fibers; pulse frequency can be increased up to 30 pps with power never greater than 1.5-1.8 W, in order to increase the coagulating effect. In the presence of a very fibrotic frenum the energy can be increased up to 75mJ (at 20pps), while maintaining the power at 1.5W.

If the laser pulse duration is adjustable, it is possible to use from 300 microsecond or longer pulse duration (600 microseconds) in order to achieve a better thermal interaction with the tissue. The tissue shows a linear

FIG. 6 Erbium laser handpieces with 600 micron conical tips of different length.

temperature rise with increasing duration of irradiation and the effects of laser irradiation vary depending on the level of temperature rise within the target tissue; accordingly surgical intervention is performed with a little air-water spray to cool the tissue as well as keep the targeted area clean and more visible, so that the minimal increase of heat will not produce carbonisation and will allow a healing process with less connective tissue. In order to reduce scar tissue on the frenum, the tongue must be mobilised immediately after the laser session by explaining and instructing the patient to perform simple mobilisation and stretching exercises several times a day; a speech therapy session will start the day after the laser treatment and possible osteopathic care will complete the functional rehabilitation of the lingual fascia [Ferrante, 2004].

Discussion

Early diagnosis and intervention in ankyloglossia are fundamental for the subsequent morpho-functional development of the child and of the adolescent. In the newborn period, the presence of ankyloglossia, with or without a concomitant short upper labial frenum, can already create breastfeeding difficulties. The permanence of atypical swallowing may then be responsible for functional alterations with speech impediment, as well as morphological dentoskeletal alterations with orthodontic problems. The persistence of these morpho-functional alterations can cause suprahyoid and subhyoid muscular-facial alterations, alterations of the neck muscles and spinal column with a tendency toward altered posture initially and later with postural alteration.

Collaboration with the speech therapist, the physiotherapist/osteopath is fundamental to complete the therapeutic approach.

Laser technology allows early intervention by the paediatric dentist, with a simple and effective laser therapy, eliminating the need to refer the patient to a specialised surgeon for a conventional procedure, thus offering the patient a complete tratment, from diagnosis to minimally invasive therapy. Laser treatment, widely known and documented today, is extremely effective for this type of surgical interventions: it is simple and rapid to perform for the clinician and is safe and minimally invasive for the patient. Laser therapy is always better accepted than traditional therapy; the post-operative period is usually asymptomatic; relapse is minimal or absent (fig. 7).

The use of the Erbium:YAG laser is particularly effective. It is selective for hydroxyl radical fibrotic tissue; if utilised with water spray, there is no thermal damage, minimizing scar tissue and post-operative pain. The laser procedure does not require sutures, eliminating a technical step that is often difficult in the child and decreasing operating time; a second intention healing allows the tissue to heal with an increase in tissue formation.

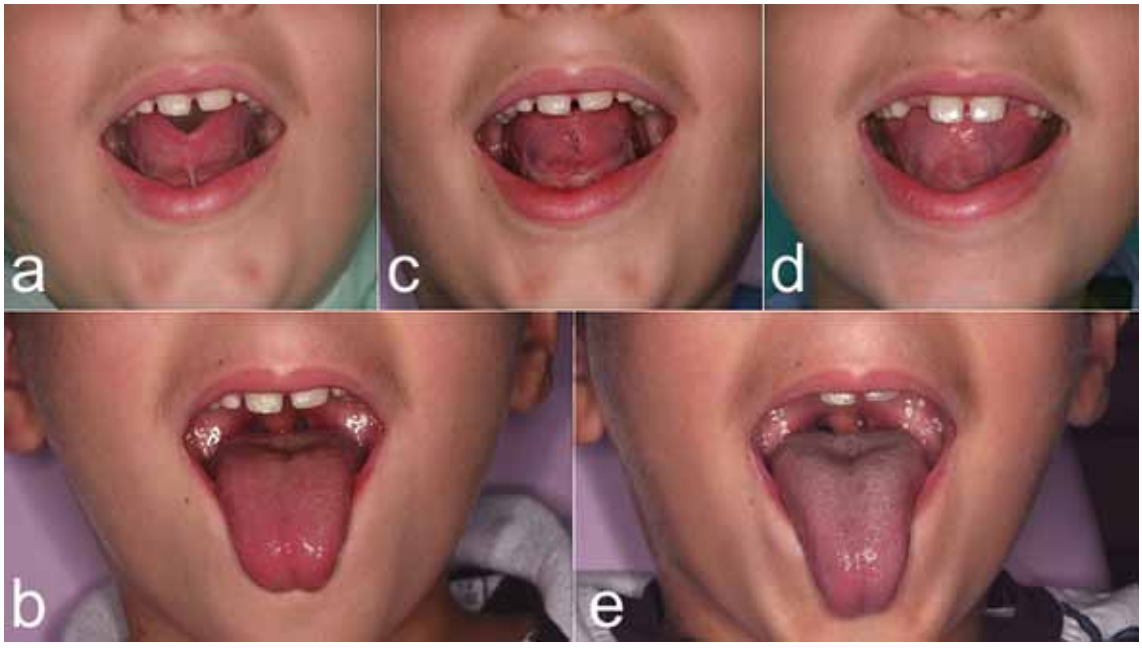

FIG. 7 Short lingual frenum: a) shape of the tongue distorted (cleft); short distance from the tip of the tongue to the attachment of the frenum; b) functional reduction of lingual movement: limitation of the tongue to reach the palatal retroincisal spot when the mouth is wide open; c) Erbium laser frenectomy at 1,4W, 20pps and 70mJ. Water 3-Air 2. Selective and minimally invasive incision of the lingual frenum with no bleeding; d,e) healing and improved lingual function after 3 weeks.

Moreover the laser is seen by the patient and parents as a less invasive and magical instrument and, for this reason, better tolerated and accepted.

Conclusion

Early diagnosis of ankyloglossia is important for correct morpho-functional growth in the child. The use of laser therapy is always more diffused as a valid and effective instrument in infantile orthodontics. The lingual frenectomy procedure with the Erbium:YAG laser has been demonstrated to be simple and safe. A multidisciplinary approach completes the therapy and improves the results. It is important to underline that a period of education in laser physics and training is highly recommended before applying this technology on paediatric patients. However, correct information and motivation of both parents and children as well as an adequante psychological approach to the patient are important elements for the full success of the therapy.

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Myofunctional THERAPY

Sleep

ORIGINAL ARTICLE
SLEEP

A frequent phenotype for paediatric sleep apnoea: short lingual frenulum

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ABSTRACT A short lingual frenulum has been associated with difficulties in sucking, swallowing and speech. The oral dysfunction induced by a short lingual frenulum can lead to oral-facial dysmorphosis, which decreases the size of upper airway support. Such progressive change increases the risk of upper airway collapsibility during sleep.

Clinical investigation of the oral cavity was conducted as a part of a clinical evaluation of children suspected of having sleep disordered breathing (SDB) based on complaints, symptoms and signs. Systematic polysomnographic evaluation followed the clinical examination. A retrospective analysis of 150 successively seen children suspected of having SDB was performed, in addition to a comparison of the findings between children with and without short lingual frenula.

Among the children, two groups of obstructive sleep apnoea syndrome (OSAS) were found: 1) absence of adenotonsils enlargement and short frenula (n=63); and 2) normal frenula and enlarged adenotonsils (n=87). Children in the first group had significantly more abnormal oral anatomy findings, and a positive family of short frenulum and SDB was documented in at least one direct family member in 60 cases.

A short lingual frenulum left untreated at birth is associated with OSAS at later age, and a systematic screening for the syndrome should be conducted when this anatomical abnormality is recognised.

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A short lingual frenulum left untreated at birth is associated with obstructive sleep apnoea syndrome at a later age http://ow.ly/6kMQ30163nG

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Introduction

Obstructive sleep apnoea syndrome (OSAS) is related to the abnormal collapse of the upper airway during sleep. This abnormal collapsibility in both children and adults has been related to sleep, which causes fundamental modifications to the pharyngeal muscle tone and reflex responses; position, given that sleep usually occurs in a recumbent position; and intrinsic and extrinsic factors: the upper airway has an intrinsic collapsibility that is studied by evaluation of the "critical pressure", and extrinsic factors may lead to increased collapsibility. Three external factors impacting the retropalatal and retroglossal space of the upper airway have been firmly established: upper airway fat deposits; non-fat-related hypertrophy of upper airway tissues in which chronic inflammation is a factor; and craniofacial features impacting the upper airway size, possibly related to genetic and environmental factors. Genetic mutations present at birth may not impact the upper airway until later in life. Environmental factors have a variable effect: the speed of their impact on upper airway collapsibility may be slow, and these factors may be present for a long time before the onset of clinically observed sleep disordered breathing (SDB), which may result in clinical symptoms only recognised during adulthood despite the presence of anatomical and/or functional anomalies during childhood. In addition, environmental factors interact with the genetic constitution of the individual, impacting the expression of a genetic trait [1].

We have already reported several factors that impact normal growth of the oral-facial structures leading to the development of OSAS in both children and adults [2–4]. Our study addresses one of these risk factors, which has not yet been linked to the development of OSAS. It investigates the association between a short lingual frenulum and OSAS.

Normally at birth, the tongue is placed high in the palate, and its continuous activity related to sucking, swallowing and masticating induces stimulation of the intermaxillary synchondrosis [1], which is active until 13–15 years of age, leading to normal oral-facial growth. Normal nasal breathing is associated with this tongue position.

A short lingual frenulum has been associated with sucking and swallowing difficulties early in life, leading to "clipping" of the frenulum in the newborn [5–8]. In older children speech difficulties have been related to an untreated short frenulum [8–10]; it was also shown to lead to mouth breathing with modification of the position of the tongue and secondary orthodontic impacts resulting in an anterior and posterior crossbite, a disproportionate growth of the mandible and an abnormal growth of the maxilla [8, 10, 11]. All these anatomical changes impact the size of the upper airway and increase the risk of its collapse during sleep.

Recognition of the negative role of a short lingual frenulum led myofunctional specialists to develop sophisticated protocols to investigate infants and children with short lingual frenulua [12, 13], but the association between a short lingual frenulum and OSAS is currently unrecognised.

"Clipping" of the short lingual frenulum is still proposed when difficulties are recognised during very early infancy, but if a simple clipping is performed after the first few months of life, the long-term results are reported as unpredictable [14], with persistence of an abnormal short lingual frenulum.

This retrospective study on anonymised data was approved by the Stanford University institutional review board. It investigates the association between a short lingual frenulum and OSAS in children.

Method

The investigation is a retrospective study of children aged 3–12 years who were referred to our clinic between January 1, 2014 and August 1, 2015 for "sleep disorders". Syndromic children, children with neuropsychiatric syndromes, chronic medical conditions and obesity were not included in this survey. The presented children may have initially been referred for diagnosis of OSAS, for other sleep-related complaints, or for a post-treatment follow-up after a diagnosis of OSAS (adenotonsillectomy in most cases).

Definition and measurement of a short lingual frenulum

The lingual frenulum is a vestigial embryological element that is mostly fibrous in its consistency, a result of adhesion between the tongue and the floor of the mouth during embryogenesis. Apoptosis controlled by genes separates the tongue from the primitive pharynx during embryogenesis [12, 15].

Recommendations in the literature are to measure the interincisive distance with maximum mouth opening and the tongue low-placed and with the tip of the tongue placed against the palate, measuring the percentage difference between the two measurements, and to measure the distance from the insertion of the frenulum at the base of the tongue to the tip of the tongue. Kotlow [16, 17] measures the "free tongue", which is defined as "the length of tongue from the insertion of the lingual frenum into the base of the tongue to the tip of the tongue", and considers a normal frenulum length to be >16 mm. Ruffoli *et al.* [18] measure the length of the frenulum itself and classify a normal frenulum length in children aged ⩾6 years to be >20 mm with a mild problem at 16–19 mm. These were our references, with >16 mm our cut-off point for a normal free-tongue length for children aged ⩾3 years [16, 17].

Data collection

All children sent to the clinic underwent a systematic clinical evaluation following pre-established guidelines. The evaluation consisted of a paediatric general evaluation, a clinical sleep medicine evaluation including the paediatric sleep questionnaire and the paediatric daytime sleepiness scale [19, 20], completed by the parents or the child, based on age. Evaluation of possible daytime consequences included diminished alertness, daytime sleepiness and fatigue, cognitive and memory problems, behavioural changes including those evoking cataplexy or seizure disorders, and social impairment. Past medical history was systematically investigated with questions on problems in early infancy regarding sucking, swallowing or masticating, difficulty with elocution and any speech treatment later, history of nasal allergies, abnormal mouth breathing, adenotonsillectomy, teeth problems including teeth agenesis, abnormal growth or early extraction and orthodontic treatment. Family history of short frenula, OSA and symptoms evoking a short frenulum were systematically obtained, and the oral-facial presentation of the family member bringing the child to clinic was systematically evaluated. If a short lingual frenulum in a direct family member was reported, efforts were made to have the family member checked at a follow-up visit of the child.

Standardised scales (the Friedman tonsil scale, the Mallampati–Friedman scale and the "facial harmony" scale) [21–24] and subjective scales, as previously outlined [15] were used during the clinical evaluation.

To evaluate the frenulum, our systematic examination used manoeuvres defined and reported by myofunctional therapists, evaluating for placement of tongue at rest; capability of using the tongue to perform manoeuvres such as trying to touch the nose and chin with the tip of the tongue; making a "cigar tongue" while protruding the tongue; touching the median raphe with the tip of the tongue while maintaining a wide, open mouth and observing whether there is a closing of the upper jaw to perform the manoeuvre; and ability to pronounce some letters and vowels. The opening of the mouth is measured using calipers, with measurement of the maximum opening from the lower left incisor to the upper left incisor, and then measurement with mouth open wide and the tongue tip touching the incisive papilla. This measurement was considered normal if the difference between the two measurements was <50%.

The position of the frenulum was examined and it was considered abnormal if it was attached underneath the tongue at any point between the tongue mid-point and the apex or inserted under the tongue as in a normal subject but short, not reaching the apex. The shape of the tip of the tongue was also noted, indicating a heart shape, a V shape or square. Finally, palpation of the region below the median region of the buccal floor with the bilateral index fingers was used to reveal abnormal genioglossal muscle resistance.

Measurements of the length of the frenulum were performed by measuring between two points; measurements were performed twice: when the short frenulum was recognised and at the end of the clinical evaluation. The mean of the two measurements was recorded in millimetres. All measurements were performed by the same individual.

For the study, we only took into consideration the measurement of the length of the free tongue (*i.e.* the mean of the two measurements performed at time of evaluation), despite the fact that we also measured the length of the frenulum as described by Ruffoli *et al.* [18] (fig. 1).

All children who were suspected of having abnormal breathing during sleep based on the total clinical evaluation, independent of a short lingual frenulum, were recommended to undergo polysomnography (PSG) in a sleep laboratory.

The following variables were systematically monitored during nocturnal sleep: four electroencephalogram leads, two electro-oculogram leads, chin and leg electromyogram (EMG) leads and one ECG lead; respiration was monitored using a nasal cannula pressure transducer, a mouth thermistor, thoracic and abdominal inductive plethysmography bands, a finger oxygen saturation oximeter (Masimo, Irvine, CA, USA) with derivation of oximetry and finger plethysmography signals, a neck microphone, diaphragmatic-intercostal abdominal muscle EMGs and a transcutaneous carbon dioxide electrode; leg EMGs were also monitored. Children were continuously video-monitored during the recording and had one parent present.

Analyses

The different clinical scales were tabulated. The different results of the frenulum evaluation were considered as "indicative", but the only variable interred in the analysis was the mean measured length of the free tongue distance from the frenulum. Sleep and respiratory scoring followed the recommendations of the American Academy of Sleep Medicine (AASM) with hypopnoea scored for either a 3% drop in oxygen saturation or an arousal response [26]. Nasal inspiratory flow limitation [27] was determined using published criteria [28, 29]. The time spent mouth breathing was also calculated as a percentage of total sleep time [30]. The different scoring analyses followed AASM recommendations [26].

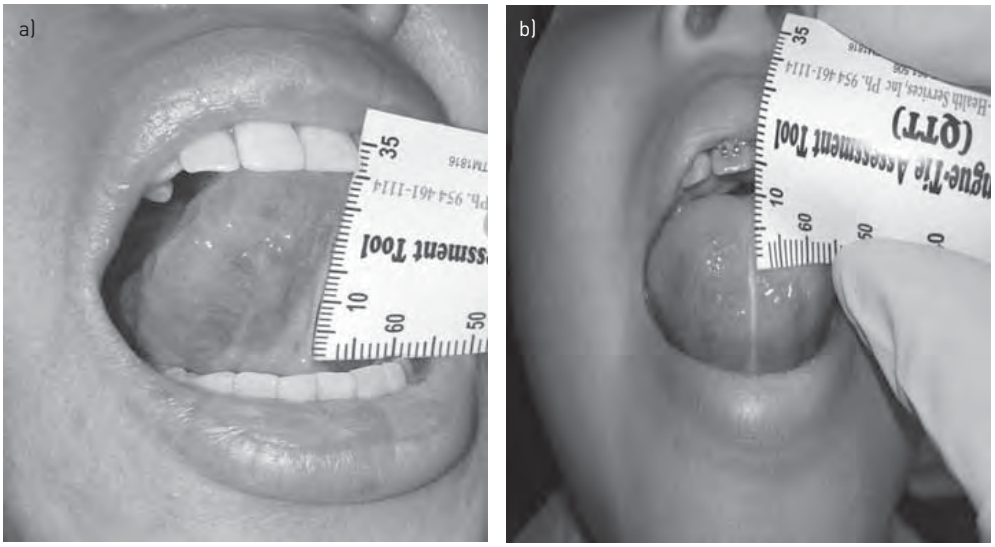

FIGURE 1 Measurement of the frenulum using the commercially available Quick Tongue Tie Assessment Kit (Neo Health Services Inc., Coconut Creek, FL, USA). a) Normal frenulum [9]; b) free tongue [7]. Complete clinical protocols for lingual frenulum investigations for infants [13] and children–adolescents [25] have been published.

All variables were anonymised and submitted for statistical analysis. The continuous variables are presented as mean±SD. A normality test was performed on all continuous variables. If the variables were distributed normally, the paired t-test was used; otherwise, the Wilcoxon rank sum test was computed. A p-value <0.05 was considered statistically significant.

Results

As mentioned, children with neuromuscular disorders, major psychiatric disorders, craniofacial syndromes, major paediatric illnesses (cystic fibrosis, cancers and haematological syndromes such as sickle cell anaemia) and obesity based on body mass index (>28 $kg \cdot m^{-2}$) were excluded from the review.

The data from 150 successively seen children diagnosed with OSAS and with complete charts including PSG results are presented. The children were subdivided into the short lingual frenulum group or the normal lingual frenulum group (based on the short lingual frenulum definition described earlier). In children aged ⩾6 years, we found no difference in classification using KOTLOW [16, 17] or RUFFOLI *et al.* [18] methods: children considered to have a short frenulum were classified as such using both measurements. There was no attempt to define other abnormal aspects of the frenulum (*e.g.* thickness or localisation of the insertion of the frenulum on the tongue) [15] (fig. 2).

Table 1 presents the demographic, clinical, anatomical and PSG findings for all the subjects and for the subgroups with short and normal lingual frenulum. 63 children were in the short frenulum group (aged 9.88±3.21 years) and 87 children were in the normal frenulum group (aged 8.05±3.59 years). Some degree of snoring was reported by parents in 39 (62%) of the children with abnormal frenula and in 59 (66%) children with normal frenula (nonsignificant). Children did not differ in levels of complaints of daytime sleepiness, fatigue or inattention-hyperactivity (the most common complaints from the subjects).

The two groups differed significantly in the anatomical description of the oral cavity (table 1), with the short frenulum group having significantly more frequent reports of a "high and narrow palatal vault" and scores of 4 on the Mallampati–Friedman scale (0–4) (p=0.0001), while the normal frenulum group had a significantly greater frequency of scoring ⩾4 on the Friedman tonsil scale (p=0.0001). The mean tonsil size score was 1.8 in the abnormal frenulum group *versus* 3.2 in the other children. Five children in the short lingual frenulum group had had adenotonsillectomies that had not resolved the OSA, but the short lingual frenulum had been missed at time of the surgery.

A Wilcoxon signed-rank test revealed statistical significance between the average apnoea/hypopnoea index (AHI) of 13.06±4.17 in the short frenulum group *versus* 11.36±5.39 in the normal frenulum group (p=0.025). The short lingual frenulum was predictive of a higher AHI in males (p=0.0069), but not in females (p=0.8615). The average oxygen saturation in the short frenulum group was 89.42±1.52% *versus* 89.85±1.52% (not significant). Again, a short frenulum was only predictive of lower arterial oxygen saturation measured by pulse oximetry (S_{pO_2}) nadir in males (p=0.0060), but not in females (p=0.6089).

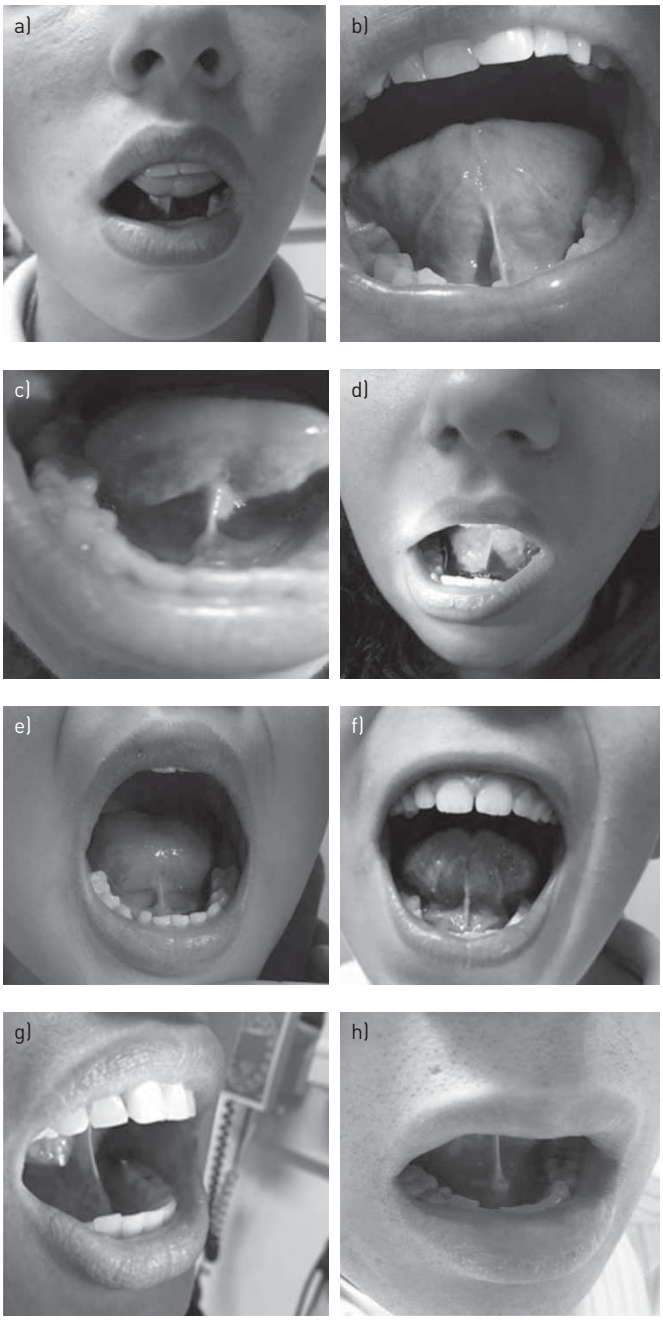

FIGURE 2 a–h) Examples of short frenula in children and teenagers. Consideration was given only to shortness of the frenulum and not difference in presentation of the frenulum. Histological studies have shown that different types of fibres may be present, depending on the individual. Short frenula were found in e) a 40-year-old mother and f) her 14-year-old daughter. The other subjects are aged 3–16 years. All subjects have obstructive sleep apnoea syndrome.

A two-tailed t-test revealed that patients with short lingual frenulae were found to be significantly older (p=0.0015). In addition, qualitative analysis of the age distribution of the short lingual frenulum group shows a unimodal normal distribution of age around a mean of 9.8±3.2 years, whereas the age distribution the normal frenulum group was more evenly distributed across the spectrum (8.05±3.6 years).

A univariate analysis revealed that age, sex and short lingual frenulum were all found to be statistically significant predictors of OSAS severity based on AHI and S_{pO_2} nadir. The association between frenulum abnormality and OSAS severity was more notable among males than females. However, a multivariate analysis with least squares regression analysis showed that age was the only independent predictor of OSAS severity in this series.

The frenulae in all the adults who accompanied the child during the consult were systematically measured; if the family history revealed the presence of SDB in a member not present at the initial evaluation, a request to have the individual present at a follow-up visit was made. This systematic request revealed the presence of a short lingual frenulum in a parent or sibling of 60 out of the 63 index cases in the short

TABLE 1 Demographic and clinical presentation of children with obstructive sleep apnoea syndrome with short and normal lingual frenula

	Subjects	Short frenulum	Normal frenulum	p-value
Subjects	150	63	87	
Age years mean±SD (n/N)	150	9.88±3.21 (63/150)	8.05±3.59 (87/150)	0.0015
Females	58	29/63 (46)	29/87 (33)	0.1288
Symptoms				
Fatigue	147	61/63 (96)	86/87 (98)	0.5725
EDS	73	35/63 (55)	38/87 (43)	0.1859
Inattention/hyperactivity	90	43/63 (68)	47/87 (54)	0.0926
Anatomy				
High and narrow palatal vault	63	56/70 (80)	7/80 (8.75)	0.0001
Friedman tonsil score	150	1.8±0.9	3.2±0.9	0.0001
Mallampati scale score	150	3.4±0.6	2.9±0.7	0.0001
Past medical history	150			
Difficulty sucking		6	0	
Difficulty swallowing		4	0	
Speech problems		31	0	

Data are presented as n, n/N (%) or mean±SD, unless otherwise stated. Feeding and swallowing difficulties were poorly recollected, except in a few cases where the problem was mentioned as "important"; the speech problems were better recalled and were described as "lisp", "stutter" or having led to speech therapy, mostly in school (n=15). Despite speech therapy, the presence of a short lingual frenulum had not been investigated or mentioned to parents. EDS: excessive daytime sleepiness.

frenulum group. The other family members identified as having a short lingual frenulum presented with symptoms or were already being treated for SDB. The short frenulum group included Caucasians (n=34), Far-East Asians (n=23) (the two prominent ethnic groups in the clinic), but also five Mexican-Indians and one African-American (the least represented group in the clinic), indicating the presence of multiethnicity in the short lingual frenulum group.

Discussion

Experiments using monkeys as subjects have demonstrated a continuous interaction between mouth breathing, functions of the tongue and oral-facial growth [31, 32]. The interaction between abnormal bone growth stimulation and the absence of nasal breathing with secondary development of mouth breathing is responsible for an abnormal development of the oral-facial bone structures supporting the upper airway, thus increasing the risk of upper airway collapse during sleep [30]. The abnormal oral-facial growth leading to a reduction of the ideal size of the upper airway will occur at a variable speed, depending on the individual, and abnormal breathing during sleep occurs over time, initially with flow limitation then with progressive worsening toward full-blown OSAS. A short lingual frenulum has been shown to lead to mouth breathing and to abnormal development of the oral cavity [8, 11, 12], increasing the risk of upper airway collapsibility during sleep; interestingly, children with short frenulae in our study were recognised as having SDB later than children who had enlarged tonsils.

Systematic investigation of a short frenulum at birth and clipping in early infancy varies greatly depending on the geographic location of delivery. A short frenulum may lead to speech problems of variable types [8–10, 33], but as shown in our group, children may have had speech therapy without the investigation of the presence of a short frenulum, or an inappropriate treatment of the short lingual frenulum may have been performed. Usually when a child is recognised with speech problems, mouth breathing is commonly associated with either day or night or only during sleep, and speech impairment and mouth breathing (particularly mouth breathing during sleep), will need simultaneous treatment [4, 14].

Our study found a large number of children with both OSAS and a short lingual frenulum. As several siblings with short frenulum and suspicion of OSAS were monitored during the same period, this may have increased the numbers of positive findings, but we only had 12/63 siblings in our survey leaving at least 51 families with short lingual frenulum and OSAS. However, our study is not a general population study and is performed on a specific at-risk group, which is a limitation.

In 95% of our index cases (no family investigation existed for the last 5%), short frenulae were documented upon examination of a direct family member with different clinical presentations. Why short lingual frenula run in families is unknown [34]. Ankyloglossia is considered a congenital anomaly reported

in 4–5% of the general population [34]. It may be inherited as an autosomal X-linked dominant trait (more common in males). A short lingual frenulum has been reported in genetically related syndromes such as Beckwith–Wiedemann, orofacial digital syndrome, cleft palate and Optiz syndrome, but all mutations associated with these syndromes are not known. Genetic studies have been performed on subjects having ankyloglossia and cleft palate relating to a mutation on the TBX22 gene (a T-box transcription factor) and on mice with ankyloglossia looking at the involvement of LGR5, an orphan G-protein coupled receptor [35–38]. Females with such mutations may present with short lingual frenula alone. It is possible that the short frenulum is associated with a malposition of the tongue due to an unknown mutation, but we have no proof to support such a hypothesis.

In our group of children aged ⩾3 years, we found the presence of a short lingual frenulum that had been left untreated despite indications of clinical problems earlier in life in 41 out of 63 subjects. As reported in prior studies, we observed both mouth breathing and abnormal anatomical findings at the time of recording and diagnosis of OSAS. When considering results of several of our investigations performed in children a pattern emerges: a dysfunction early in life involving abnormal nasal breathing, sucking and masticating leads to progressive dysmorphoses favouring increased collapsibility of the upper airway during sleep, which worsens with ageing and leads to the development of SDB over time up to adulthood.

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Toward a functional definition of ankyloglossia: validating current grading scales for lingual frenulum length and tongue mobility in 1052 subjects

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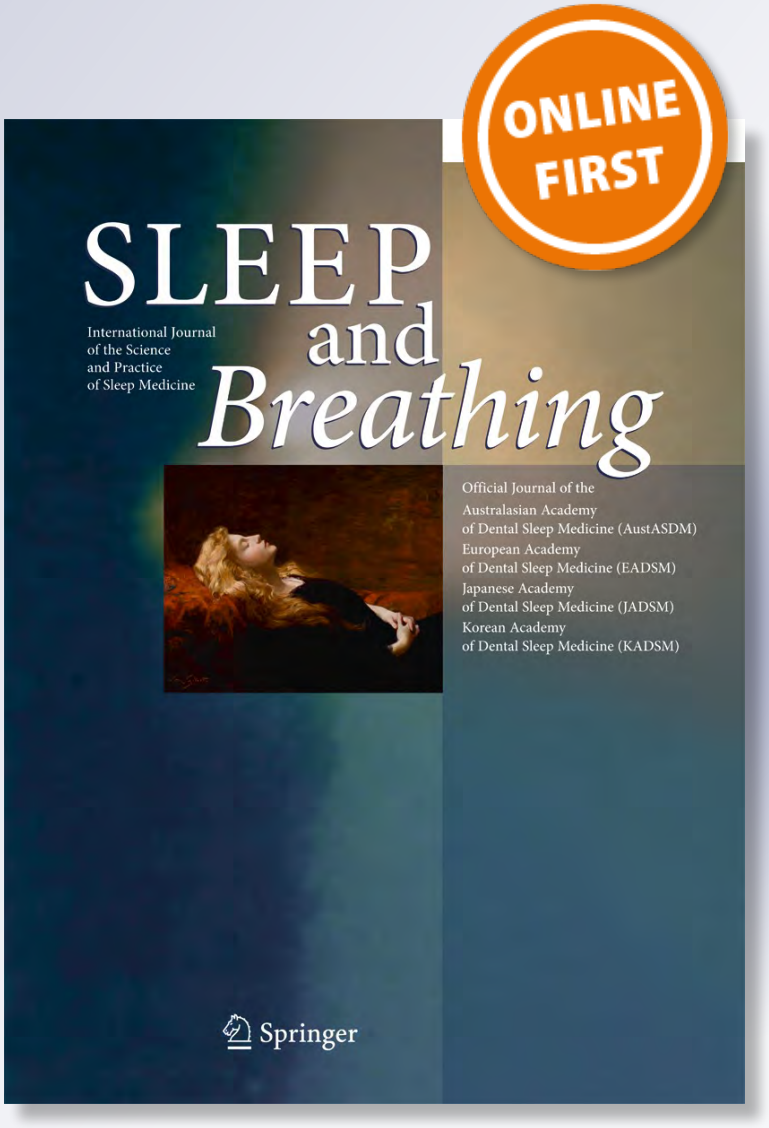

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EPIDEMIOLOGY • ORIGINAL ARTICLE

Toward a functional definition of ankyloglossia: validating current grading scales for lingual frenulum length and tongue mobility in 1052 subjects

Audrey Yoon[1] · **Soroush Zaghi**[2,3] · **Rachel Weitzman**[4] · **Sandy Ha**[5] · **Clarice S. Law**[1] · **Christian Guilleminault**[6] · **Stanley Y.C. Liu**[2]

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Abstract
Purpose Alterations of the lingual frenulum may contribute to oromyofacial dysfunction, speech and swallowing impediments, underdevelopment of the maxillofacial skeleton, and even predispose to sleep breathing disorder. This study aims to assess the utility of existing instruments for evaluation of restricted tongue mobility, describe normal and abnormal ranges of tongue mobility, and provide evidence in support of a reliable and efficient measure of tongue mobility.
Methods A prospective cohort study of 1052 consecutive patients was evaluated during a 3-month period. Age, gender, ethnicity, height, weight, BMI, maximal interincisal mouth opening (MIO), mouth opening with tongue tip to maxillary incisive papillae at roof of mouth (MOTTIP), Kotlow's free-tongue measurement, and presence of severe tongue-tie were recorded. Secondary outcome measures include tongue range of motion deficit (TRMD, difference between MIO and MOTTIP) and tongue range of motion ratio (TRMR, ratio of MOTTIP to MIO).
Results Results indicate that MIO is dependent on age and height; MOTTIP and TRMD are dependent on MIO; Kotlow's free-tongue measurement is an independent measure of free-tongue length and tongue mobility. TRMR is the only independent measurement of tongue mobility that is directly associated with restrictions in tongue function.
Conclusions We propose the use of tongue range of motion ratio as an initial screening tool to assess for restrictions in tongue mobility. "Functional" ankyloglossia can thus be defined and treatment effects followed objectively by using the proposed grading scale: grade 1: tongue range of motion ratio is >80%, grade 2 50–80%, grade 3 < 50%, grade 4 < 25%.

Keywords Ankyloglossia · Frenulum · Tongue tie · Oromyofacial dysfunction · Classification of ankyloglossia · Tongue tie grading scale

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Introduction

The tongue is a dynamic organ that impacts breathing, speech, breastfeeding, and swallowing and thereby plays a critical role in facial development. In utero, the forward growth of the tongue is guided by the lingual frenulum, a thin strip of tissue that attaches the floor of the mouth to the ventral surface of the tongue [1]. During fetal development, the lingual frenulum functions to create a balance between the tongue, lip muscles, and growing facial bones. After birth, as the tongue muscles lengthen, the lingual frenulum retracts and becomes thin [2]. In some cases, the lingual frenulum fails to recede, tethering the tongue to the floor of the mouth. This results in ankyloglossia, commonly described as "tongue tie," a congenital oral anomaly that is characterized by an abnormally short or altered attachment of the lingual frenulum restricting tongue mobility to varying degrees [3].

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Ankyloglossia that functionally limits tongue mobility has tremendous clinical significance. It causes breastfeeding difficulties during infancy, including early weaning, diminished sucking and swallowing functions, and poor weight gain [4]. Ankyloglossia also affects upper and lower jaw development, periodontal tissue maturation, and dental occlusion. In a typically developing child, a balance exists between the lingual and the buccal musculature: the tongue pushes against the dentition and jaw in an expansile fashion, while the buccal musculature counters this force vector. With ankyloglossia, the tethering of the tongue to the floor of the mouth restricts adequate lingual force to expand the dentition and jaws. This leads to altered position and morphology of the jawbone [5]. Specifically, it has been shown that ankyloglossia contributes to maxillary hypoplasia (underdevelopment of the upper jaw bones), which then can predispose toward speech difficulty, nasal obstruction [6], mouth breathing [7], and obstructive sleep apnea [8].

It is important to identify patients with ankyloglossia at an early age, especially during facial development. When there are obvious nursing or speech difficulties in infants or young children, physicians more readily identify a severe lingual frenulum anomaly and direct patients to treatment [9]. However, differentiating the anatomical variations of the altered frenulum and the potential impact of mild to moderate restricted tongue mobility may be more challenging. Various methods to assess the degree of ankyloglossia and limitations in tongue mobility have been described [2, 4, 10–13]. Martinelli et al. have developed a comprehensive validated protocol for assessment of the lingual frenulum in infants that includes clinical history, anatomo-functional, and nutritive and non-nutritive suction evaluations [4, 14]. Similarly, Marchesan et al. have developed a similar protocol for assessment of the lingual frenulum in children and adults that includes clinical history, tongue mobility, anatomical shape, functional assessments, resting tongue position, and speech evaluations [10, 11]. These tools, however, require a time-intensive 30- to 60-min evaluation by a qualified and appropriately trained practitioner to administer. The objective of this study is to (1) validate the existing instruments for measurement of restricted tongue mobility in >1000 consecutive pediatric (6 years and older) and adult patients, (2) describe normal and abnormal ranges of restricted tongue mobility, and (3) propose a simple grading scale for the functional assessment of tongue mobility that is efficient for clinical use as a screening tool applicable in children and adults.

Methods

Study design

This is a prospective cohort study of 1052 consecutive patients evaluated in a private orthodontic office (AY) during the 3-month period from May 1, 2016 to August 1, 2016. Patients who participated in the study signed an informed consent form. Exclusion criteria included patients with a history of frenectomy and those with difficulty in mouth opening such as temporomandibular joint disorder. The institutional review board (IRB) of Stanford University approved the present study (protocol 35054, IRB no. 4947). Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at the Stanford Center for Clinical Informatics. REDCap [15] is a secure, web-based application designed to support data capture for research studies, providing (1) an intuitive interface for validated data entry, (2) audit trails for tracking data manipulation and export procedures, (3) automated export procedures for seamless data downloads to common statistical packages, and (4) procedures for importing data from external sources.

Data Collection method

The following data were prospectively and consecutively collected on all subjects who presented for orthodontic evaluation and provided written consent: age, gender, ethnicity (White, Hispanic, Asian, Indian, Black, Other), height (cm), weight (kg), BMI (kg/m^2), maximal interincisal mouth opening (MIO, mm), interincisal mouth opening with tongue tip to maxillary incisive papillae at roof of mouth (MOTTIP, mm), Kotlow's free-tongue measurement (length from base of tongue insertion of the lingual frenulum to the tip), and presence of severe clinically apparent ankyloglossia using Kotlow's structural guidelines. The quick-tongue tie assessment tool was used for measurements of MIO and MOTTIP, as well as Kotlow's free-tongue measurement (see Fig. 1).

All measurements were obtained with the patient in natural head position, which is a standardized and reproducible position of the head in an upright posture with the eyes focused on a point in the distance at eye level [16]. Natural head position implies that the visual axis is horizontal. For MIO measurement, patients were instructed to "open your mouth." The measurement was obtained on the first mouth opening to avoid jaw protrusion or excessive translation at the temporomandibular joint. Patients were not encouraged to open their mouth "as widely as possible." For MOTTIP measurement, patients were instructed to "touch the tongue to the back of the front two teeth and open your mouth." This measurement is obtained with the tongue at the incisive papillae and not at the incisive foramen which is used as "the spot" landmark during training with myofunctional therapy [17]. Kotlow's free-tongue measurement was obtained as previously reported [12] by measuring the length of the ventral surface of the tongue (while in full extension) from the insertion of the lingual frenulum to the tongue tip. The presence of severe clinically apparent tongue tie was assessed using Ruffoli's classification of levels of ankyloglossia and measurement

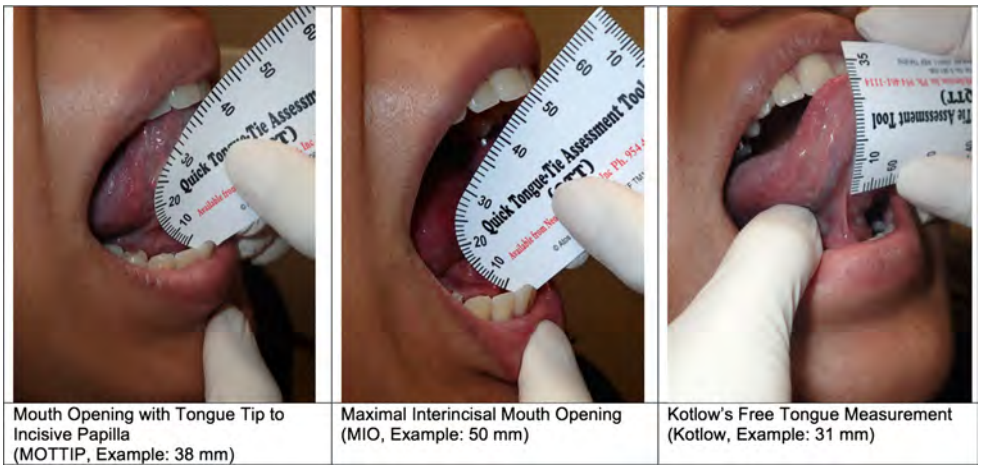

Fig. 1 Examples of tongue functioning and length measurements using the Quick Tongue Tie Assessment Tool (QTT): mouth opening with tongue tip to incisive papilla (MOTTIP), maximal interincisal mouth opening (MIO), and Kotlow's free-tongue measurement. Tongue range of motion deficit (TRMD) is defined as the difference between MIO and MOTTIP. Tongue range of motion ratio (TRMR) is defined as the ratio of MOTTIP to MIO

techniques A. The length of the frenulum was measured by recording the distance between the insertion of the lingual frenulum into oral floor and the tongue. If the length of frenulum was less than 7 mm, it was classified as "severe" in level of ankyloglossia [18].

Outcome measures

Primary outcome measures include MIO, MOTTIP, Kotlow's free-tongue measurement, and presence of severe clinically apparent tongue tie. Secondary outcome measures include tongue range of motion deficit (TRMD) calculated as the difference between the MIO and MOTTIP and tongue range of motion ratio (TRMR) calculated as the MOTTIP divided by MIO.

Statistical analysis

Statistical analyses were performed using JMP Pro 12 (SAS Institute Inc., Cary, NC). Continuous variables are summarized as mean (M) ± standard deviation (SD). Categorical variables are summarized as frequencies and percentages. Univariate analysis with Pearson's Chi square or independent *t* test (continuous variables) was performed to assess for nominal or continuous covariates of tongue measurements including age, gender, height, weight, BMI, and ethnicity. Bonferroni correction was applied to the interpretation of statistical significance due to the testing of multiple variables for each outcome, such that a two-tailed p value <0.0014 was required to achieve statistical significance.

Results

Our study included 1052 subjects with age ranging from 6 to 70 years. Demographic factors include age 20.1 ± 10.3 years (M ± SD); gender 61.7% female; height 162.5 ± 12.5 cm; weight 59.9 ± 17.8 kg; and BMI 22.4 ± 5.8 kg/m^2. Ethnicities include Hispanic 49.1%, Asian 25.8%, white 14.9%, non-Hispanic black 9.8%, and Indian 0.2%. This population includes 140 children (ages 6–11), 436 adolescents (age 12–17), 385 young adults (age 18–35), 84 adults (age 36–64), and 7 seniors (age > 65).

There were 40/1052 (3.8%) patients with severe clinically apparent tongue tie: 7 children, 14 adolescents, 10 young adults, and 9 adults. Measurements of tongue function of all patients are as follows (M ± SD): MIO 52.5 ± 5.4 mm, MOTTIP 33.6 ± 6.9 mm, Kotlow's free-tongue measurement 17.5 ± 5.5 mm, TRMD 18.0 ± 7.7 mm, and TRMR 64 ± 13%. The distribution of these measurements, including minimum, bottom 10% quantile, median, top 90% quantile, and maximum values for each age cohort are displayed in Fig. 2. Quantile box plots for each age cohort are displayed in Fig. 3. Visual assessment of the histograms for measurements of the overall population as shown in Fig. 2 demonstrates (1) MIO—multiple peaks, data symmetrical; (2) MOTTIP—multiple peaks, data skewed left; (3) Kotlow's measurement—single peak, data skewed right; (4) TRMD—multiple peaks, data skewed left; (5) TRMR—single peak, data skewed left, closely fits, and well modeled by the Johnson's S_U-distribution (a transformation of the normal distribution).

When compared to subjects without severe clinically apparent ankyloglossia, 40/1052 patients with severe clinical apparent ankyloglossia showed statistically significant differences in MOTTIP (22.2 ± 5.7 vs. 34.0 ± 6.5, $p < 0.0001$), Kotlow's measurement (12.0 ± 3.8 vs. 17.1 ± 3.8, $p < 0.0001$), TRMD (31.5 ± 7.2 vs. 18.4 ± 7.3, $p < 0.0001$), and TRMR (0.42 ± 0.10 vs. 0.65 ± 0.12, $p < 0.0001$).

Multivariate analysis with Standard Least Squares model shows *age* and *height* to be significant covariates of *MIO* (age: beta −0.08 ± 0.02, $p < 0.001$ and height: beta 0.14 ± 0.03, $p < 0.001$); the effect of these variables was strongest among children and adolescents under 18 years of age (age: beta 0.59 ± 0.08, $p < 0.001$ and height: beta 0.19 ± 0.02,

Cohort	All Patients	Children	Adolescents	Young Adults	Adults	Seniors
Ages (years)	6 - 70	6 - 11	12 - 17	18 - 35	36 - 64	> 65
N	1052	140	436	385	84	7
Maximum Interincisal Mouth Opening (mm)						
Mean	52.5	49.4	53.1	53.1	52	48.4
Std Dev	5.4	5.3	5.2	4.8	5.9	11.4
Min	32	38	38	32	39	33
10% Quantile	46	42	47	48	44.5	33
Median	53	50	53	53	52	53
90% Quantile	60	55	60	60	60	60
Max	70	70	70	65	65	60
Mouth Opening: Tongue Tip to Incisive Papilla (mm)						
Mean	33.6	31	33.1	35.1	33.5	33.7
Std Dev	6.9	6.8	7	6.4	7.2	6
Min	3	13	10	3	8	25
10% Quantile	25	22	23	27	24.5	25
Median	35	31	33	36	35	33
90% Quantile	42	40	42	43	43	42
Max	52	45	52	50	45	42
Kotlow's Measurement (mm)						
Mean	17.5	16.3	16.9	18.6	18	16
Std Dev	5.5	4.4	5.2	6.1	4.9	2.4
Min	2	7	6	2	5	13
10% Quantile	12	11	11	13	13	13
Median	16	16	16	17	17.5	16
90% Quantile	25	22	23.4	26	24.5	20
Max	40	35	35	40	34	20
Tongue range of motion deficit (mm)						
Mean	18.9	18.4	20.1	18.0	18.5	14.7
Std Dev	7.7	7.8	7.9	7.0	8.7	8.4
Min	4	4	5	5	5	5
10% Quantile	10	10	11	10	9.5	5
Median	18	17	19	17	17.5	17
90% Quantile	30	29	32	27	34	28
Max	53	42	45	53	40	28
Tongue range of motion ratio (%)						
Mean	64%	63%	63%	66%	65%	71%
Std Dev	13%	14%	13%	12%	15%	12%
Min	5%	24%	24%	5%	17%	53%
10% Quantile	46%	44%	43%	51%	42%	53%
Median	66%	65%	64%	68%	67%	70%
90% Quantile	80%	80%	79%	80%	81%	88%
Max	91%	90%	90%	91%	90%	88%

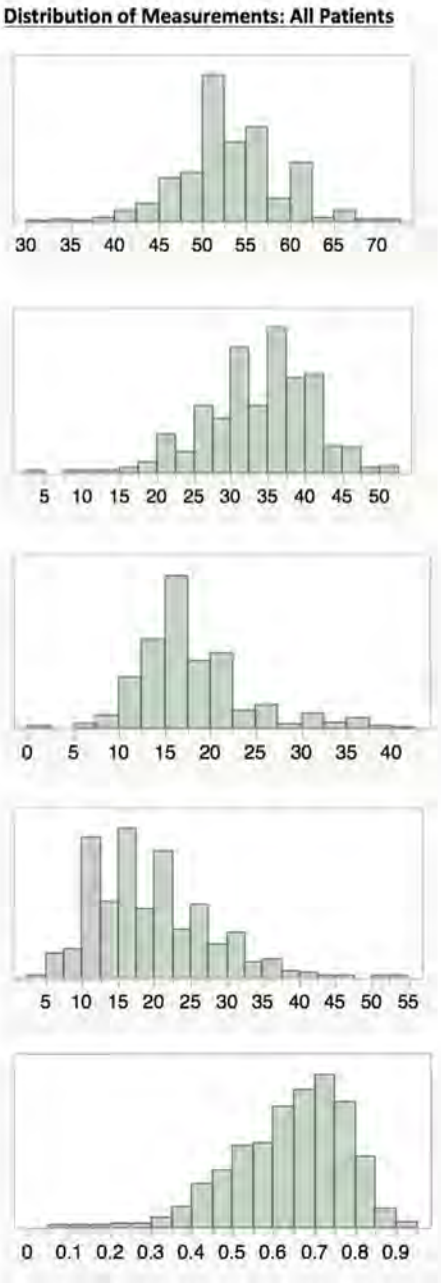

Fig. 2 Distribution of mouth opening, tongue measurements, tongue range of motion deficit, and tongue range of motion ratio by age cohort and overall population

$p < 0.001$). See Fig. 4a, b. *Age* was also a statistically significant covariate of *TRMD* (beta −0.09 ± 0.03, $p = 0.0012$). *Kotlow's free-tongue measurement*, *MOTTIP*, and *TRMR* were independent of age, gender, ethnicity, height, weight, and BMI. *Kotlow's free-tongue measurement* and *TRMR* were independent of *MIO*, whereas *MOTTIP* and *TRMD* had significant linear correlation with the *MIO* variable (R^2 0.05 and 0.25, respectively, $p < 0.0001$). *Kotlow's free-tongue measurement* and *TRMR* correlated with each other more strongly among patients with severe ankyloglossia (R^2 0.485) than those without severe ankyloglossia (R^2 0.314, $p < 0.001$). See Fig. 5.

Discussion

Tongue position and mobility play significant roles in facial skeletal development. Patients with aberrant development of

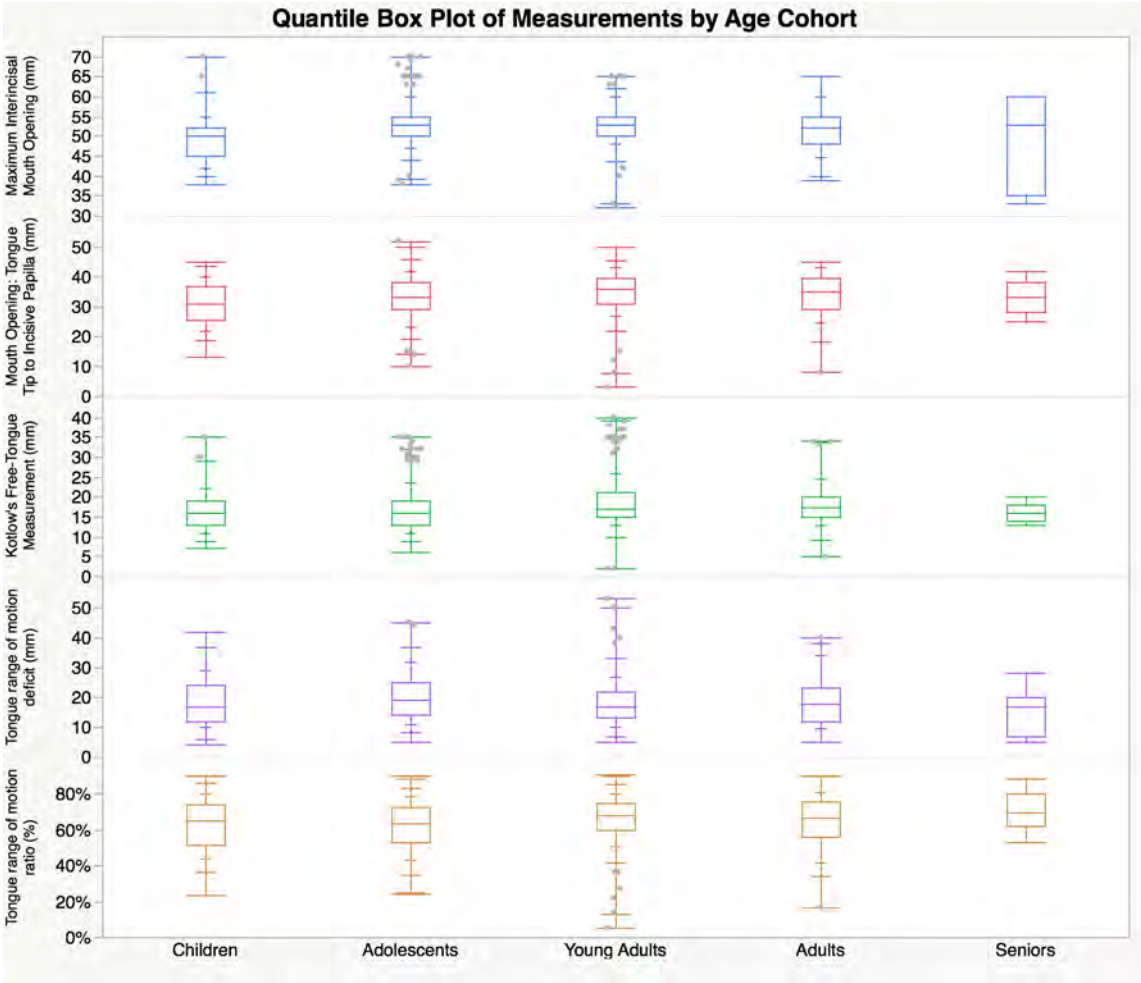

Fig. 3 Quantile box plot of measurements by age cohort: MIO, MOTTIP, Kotlow's free-tongue measurement, TRMD, and TRMR. Children 6–11 years; adolescents 12–17 years; young adults 18–35 years; adults 36–64 years; seniors >65 years

the upper or lower jaws are at increased risk of malocclusion [19], temporomandibular disorders [20], nasal obstruction [7], and obstructive sleep apnea [21]. Most recently, there have been concerted research efforts to explore the role of ankyloglossia and restricted tongue mobility as correctable risk factors of nasal obstruction and sleep-disordered breathing [17, 21, 22].

While the lingual frenulum and tongue mobility have come to the attention of the sleep medicine academic community, there is presently limited published data to guide the differentiation between normal and abnormal ranges of tongue mobility [10, 12, 18]. Here, we built upon the existing tools for assessment of tongue mobility by describing normal and abnormal parameters of tongue function among >1000 consecutive pediatric and adult subjects and provide evidence of a reliable measure of tongue mobility that is quick to use for all clinicians.

Kotlow et al. recognized the need for a classification system of ankyloglossia (tongue tie) over 15 years ago and proposed the free-tongue measurement to identify abnormal lingual frenulum attachments in the pediatric population [12]: 322 children with ages 18 months to 14 years were evaluated, where Boley gauge was used to measure the distance from the tip of the tongue to the insertion of the lingual frenulum. The study proposed that the normal length would be greater than 16 mm. Ankyloglossia was classified as Class I (mild, 12 to 16 mm), Class II (moderate, 8 to 11 mm), Class III (severe, 3 to 7 mm), and Class IV (complete ankyloglossia). A weakness with this method is that the tongue is especially flexible in young children and is difficult to control and stabilize during measurement [12]. To mitigate this weakness, structural guidelines were also used to assist in the determination of functional tongue limitations. Ruffoli et al. followed with a validation study in 200 children aged 6 to 12 years to describe normal and abnormal ranges of frenulum measurement (normal ≥ 20 mm, mild ankyloglossia 16–19 mm, moderate 8–15 mm, severe ≤ 7 mm) as well as MOTTIP (normal ≥ 23 mm, mild ankyloglossia 17 to 22 mm, moderate 4 to 16 mm, severe ≤3 mm) [18].

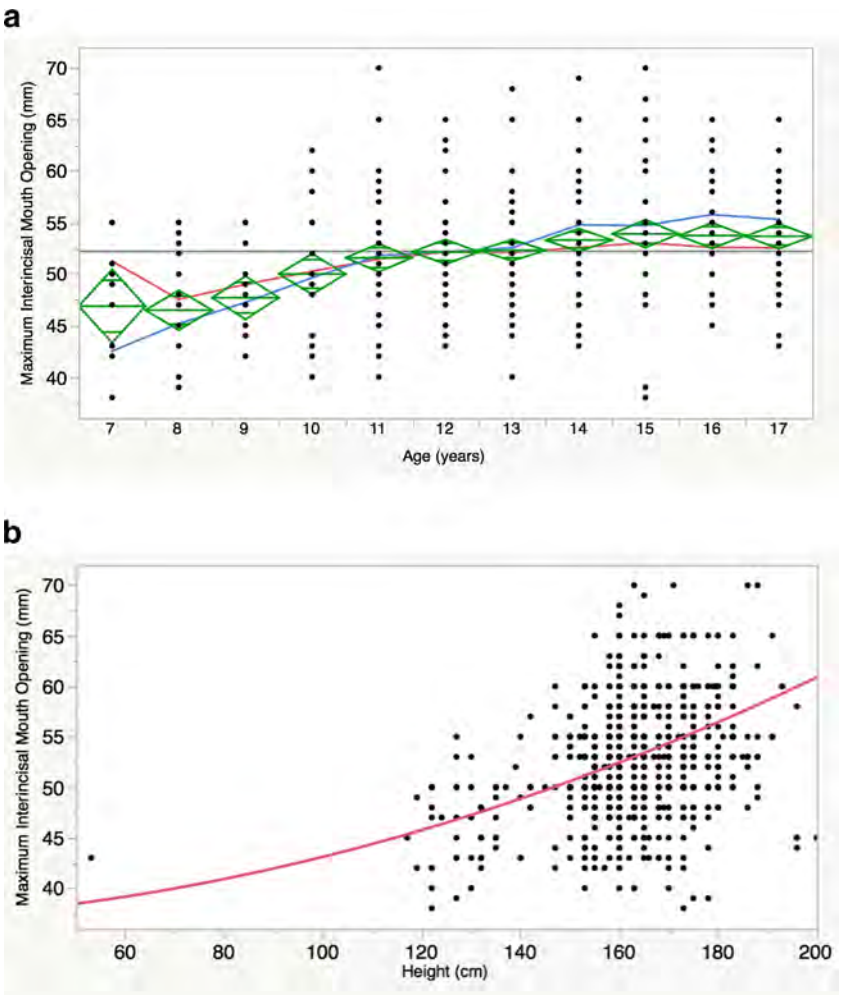

Fig. 4 Measurement of maximal interincisal mouth opening was found to be dependent on patient age and height. **a** Maximum interincisal mouth opening (mm) by age (years). The *red line* represents female gender, the *blue line* represents male gender, and the *green line* shows the mean diamond including the mean with 95% confidence interval of the mean for each age in years. **b** Maximum interincisal mouth opening (mm) by height (cm) for age <18 years

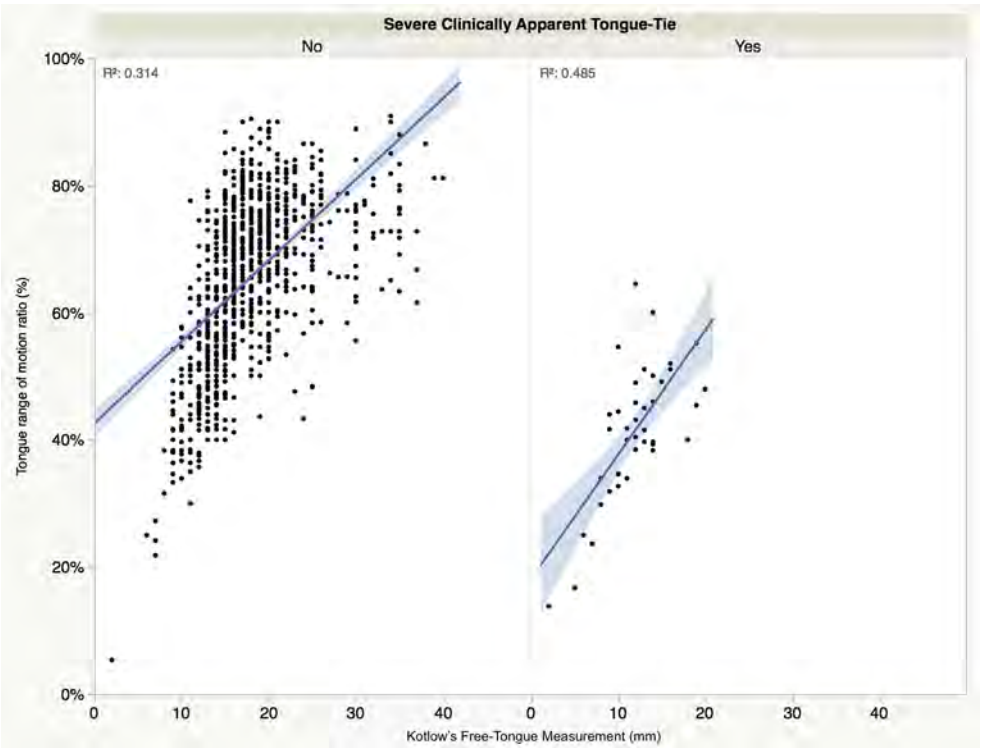

Fig. 5 Kotlow's free-tongue measurement vs. assessment of functioning with tongue range of motion ratio (TRMR). Kotlow's free-tongue measurement correlates only modestly with tongue range of motion (functioning). Kotlow's free-tongue measurement <20 mm was found to have 16.1% sensitivity and 77.6% specificity as a tool to predict below average tongue functioning in this series (TRMR grades 3–4). Among 295/1052 (28.0%) subjects with Kotlow's free-tongue measurements in the normal range (> 20 mm), there were still found to be 66 subjects with below average tongue functioning

Hazelbaker et al. developed a lingual frenulum measurement for use in breast-feeding infants. The Hazelbaker Assessment Tool for Lingual Frenulum Function (HATLFF) is based on clinical observations from lactation counselors [13]. HATLFF consists of five structural and seven functional criteria that have been validated by multiple groups with moderate reliability. [23–25] However, HATLFF only applies to infants.

Marchesan et al. developed a quantitative method to classify the lingual frenulum in adults for assessment of speech-language pathology [10]. Based on 98 adult subjects, they characterized the relationship between maximal interincisal mouth opening (MIO) to tongue tip movement toward the incisal papilla (TTIP). This is described either by (1) the difference between MIO and TTIP (TRMD) or (2) the ratio of TTIP to the MIO (TRMR). Among 16 subjects with short frenulum and 82 patients with normal frenulum, MIO was 46.6 ± 5.1 vs. 47.9 ± 6.9 mm (NS); MOTTIP was 28.1 ± 4.7 vs. 33.1 ± 5.0 (p = 0.0005); TRMD was 19.4 ± 7.7 vs. 13.4 ± 6.1 (p = 0.0056); and TRMR was 50 vs. 60%. A limitation of this study in adults was the sample size. Marchesan et al. then followed up with the same protocol to assess the lingual frenulum in more than 1400 adults [11] and infants [4] age 8 months to 62 years. [26] This allowed for the development of a comprehensive qualitative tool. [11].

To date, our study is the largest quantitative validation of Kotlow's free-tongue measurement and Marchesan's MOTTIP, TRMD, and TRMR measurements in 1052 subjects with age ranging from 6 to 70 years. Our results indicate that (1) MIO is dependent on age and height, especially for children and adolescents under 18 years of age (consistent with prior reports [27]). Hence, the covariates age and height need to be considered when determining quantile cutoffs for MOTT and TRMD as these measurements are dependent on MIO; (2) Kotlow's free-tongue measurement and Marchesan's TRMR are independent measures of free-tongue length and tongue mobility respectively and are not significantly influenced by age, gender, height, weight, ethnicity, or MIO; (3) Kotlow's free-tongue measurement has low sensitivity (16.1%) and only modest specificity (77.6%) for the diagnosis of functional ankyloglossia (tongue-tie); and (4) Marchesan's TRMR is the only independent measurement of tongue mobility that is directly associated with restrictions in tongue function.

Limitations to the study include (1) unblinded single-rater measurements based on one clinical encounter, (2) disproportionate racial ethnic groups (although this can be a strength as compared to previous studies which had more homogeneous ethnic populations), (3) cross-sectional nature of the study (where long-term longitudinal follow-up studies may be most ideal but not feasible), (4) no patients under the age of 6, and (5) analysis based on subjective "clinically significant" ankyloglossia.

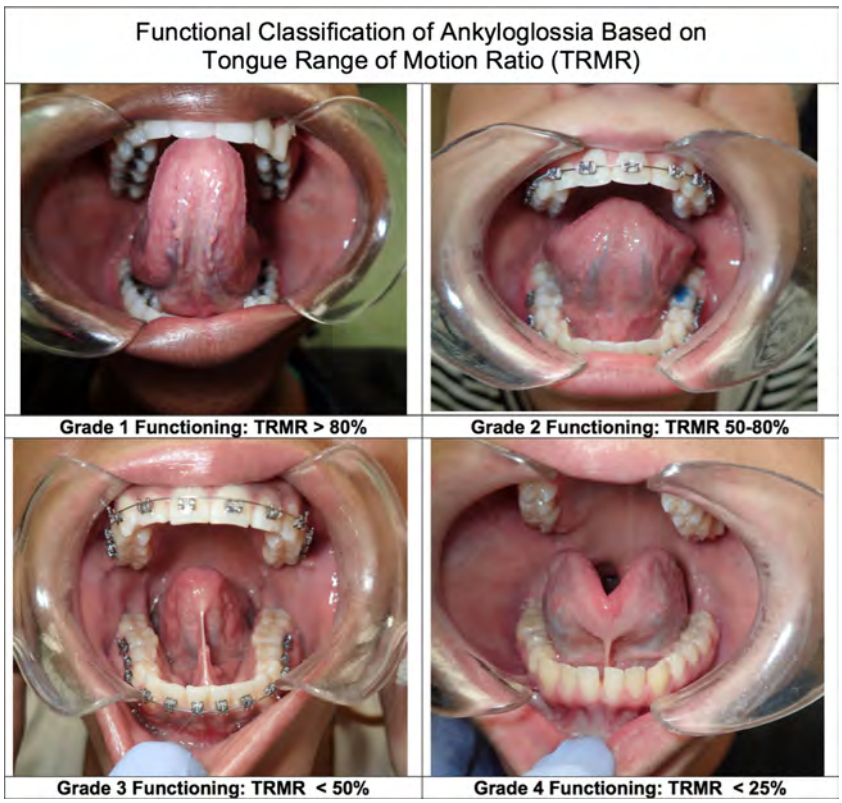

Fig. 6 A grading scale for the functional classification of ankyloglossia is proposed based on the TRMR (ratio of MOTTIP to MIO) building on the classification of Ferrés-Amat et al. [28]. Grade 1: tongue range of motion ratio is >80%, grade 2 50–80%, grade 3 <50%, grade 4 <25%. Higher grades reflect decreased tongue mobility and increased severity of tongue tie. The *photos* here demonstrate the deficit in the mobility of the tongue tip relative to MIO. With increasing ankyloglossia, the tongue tip is unable to touch the incisive papilla unless the mouth opening is closed to some extent. Considering grade 3, mouth opening is limited to 50% of maximal opening in order for the tongue tip to reach the incisive papilla. For grade 4, mouth opening is limited to 25% of MIO for the tongue tip to reach the incisive papilla

Conclusion

We propose the use of TRMR as an initial screening tool to assess for restrictions in tongue mobility, where a normal value for TRMR is between 51 and 77% (this represents the M ± 1 SD to include 68% of the population). Values below 46% can be considered significantly below average (bottom 10%), and values greater than 80% represent significantly above average functioning (top 10%). A functional TRMR grading scale based on our findings is proposed in Fig. 6: grade 1 = >80%, grade 2 = 50–80%, grade 3 = <50%, grade 4 = <25%. With the high reliability and precision of TRMR in assessing tongue mobility, our proposed grading scale enables a functional definition of ankyloglossia that can be used to assess treatment effects of myofunctional therapy and frenulum surgery. The grading scale allows clinicians to effectively communicate tongue mobility and associated nasal and oral function as they pertain to facial development. Further studies are needed to characterize the specific alterations to the lingual frenulum that render functional impairments.

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Author contributions All the authors met the four criteria for authorship established by the International Committee of Medical Journal Editors: Audrey Yoon, Soroush Zaghi, and Stanley Liu were responsible for the conception, design, analysis; drafting and revising the work; and reviewing the manuscript. Rachel Weitzman and Sandy Ha had substantial contributions to the acquisition of data for the work as well as in drafting and revising the work and reviewing the manuscript. Clarice S. Law and Christian Guilleminault had substantial contributions to data analysis, interpretation of data for the work, and revising the work critically for important intellectual content. Additionally, all authors provided final approval of the version to be published and agreed to be accountable for all aspects of the work including ensuring the accuracy and/or integrity of the work.

Compliance with ethical standards

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Conflict of interest The authors declare that they have no conflict of interest.

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Comments

Otolaryngologists and pediatricians pay close attention to the frenulum status of newborns to enable breastfeeding. Dentists can evaluate for functional tongue tie and contribute to proper growth and development of the maxilla. This article gives us an easy way to make a judgment, but it mostly will help the dentist pay attention.

Steve Carstensen
Washington, USA

MYOFUNCTIONAL THERAPY TO TREAT OSA: REVIEW AND META-ANALYSIS

Myofunctional Therapy to Treat Obstructive Sleep Apnea: A Systematic Review and Meta-analysis

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Objective: To systematically review the literature for articles evaluating myofunctional therapy (MT) as treatment for obstructive sleep apnea (OSA) in children and adults and to perform a meta-analysis on the polysomnographic, snoring, and sleepiness data.

Data Sources: Web of Science, Scopus, MEDLINE, and The Cochrane Library.

Review Methods: The searches were performed through June 18, 2014. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement was followed.

Results: Nine adult studies (120 patients) reported polysomnography, snoring, and/or sleepiness outcomes. The pre- and post-MT apnea-hypopnea indices (AHI) decreased from a mean ± standard deviation (M ± SD) of 24.5 ± 14.3/h to 12.3 ± 11.8/h, mean difference (MD) −14.26 [95% confidence interval (CI) −20.98, −7.54], P < 0.0001. Lowest oxygen saturations improved from 83.9 ± 6.0% to 86.6 ± 7.3%, MD 4.19 (95% CI 1.85, 6.54), P = 0.0005. Polysomnography snoring decreased from 14.05 ± 4.89% to 3.87 ± 4.12% of total sleep time, P < 0.001, and snoring decreased in all three studies reporting subjective outcomes. Epworth Sleepiness Scale decreased from 14.8 ± 3.5 to 8.2 ± 4.1. Two pediatric studies (25 patients) reported outcomes. In the first study of 14 children, the AHI decreased from 4.87 ± 3.0/h to 1.84 ± 3.2/h, P = 0.004. The second study evaluated children who were cured of OSA after adenotonsillectomy and palatal expansion, and found that 11 patients who continued MT remained cured (AHI 0.5 ± 0.4/h), whereas 13 controls had recurrent OSA (AHI 5.3 ± 1.5/h) after 4 y.

Conclusion: Current literature demonstrates that myofunctional therapy decreases apnea-hypopnea index by approximately 50% in adults and 62% in children. Lowest oxygen saturations, snoring, and sleepiness outcomes improve in adults. Myofunctional therapy could serve as an adjunct to other obstructive sleep apnea treatments.

Keywords: exercise therapy/methods, myofunctional therapy/methods, obstructive sleep apnea, sleep apnea syndromes

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INTRODUCTION

Several medical and surgical treatment modalities exist as treatment for obstructive sleep apnea (OSA).[1–3] Four pathophysiological traits seen in patients with OSA are: the passive critical closing pressure of the upper airway (Pcrit), arousal threshold, loop gain, and muscle responsiveness (PALM) with categories of 1, 2, 2a, 2b, and 3.[4] It has been demonstrated that patients in four of five PALM categories will benefit from anatomic interventions.[4] Because the dilator muscles of the upper airway play a critical role in maintaining an open airway during sleep, researchers have explored exercises and other airway training (singing, didgeridoo, instrument playing) that target oral cavity and oropharyngeal structures as a method to treat OSA.[5–7] Myofunctional therapy (MT) and proper tongue positioning in the oral cavity have been described since 1918 to improve mandibular growth, nasal breathing, and facial appearance.[8] Guimaraes has proposed MT as a treatment for OSA since the 1990s.[9] MT is composed of isotonic and isometric exercises that target oral (lip, tongue) and oropharyngeal structures (soft palate, lateral pharyngeal wall).[7,10] There have been an increasing number of studies evaluating the effect of MT in the form of case studies, case series, and most recently, two randomized controlled trials.[7,10–13]

The most comprehensive MT exercises are described by Guimaraes et al.[7] and involve the soft palate, tongue, and facial muscles and address stomatognathic functions. For soft palate exercises, patients pronounce oral vowel sounds either continuously (isometric exercises) or intermittently (isotonic exercises).[7] Tongue exercises include moving the tongue along the superior and lateral surfaces of the teeth, positioning the tongue tip against the anterior aspect of the hard palate, pressing the entire tongue against the hard and soft palate, and forcing the tongue onto the floor of the mouth.[7] Facial exercises address the lip (i.e., contraction and relaxation of the orbicularis oris), buccinators (i.e., suction movements and application of intraoral finger pressure against the buccinator muscles), and jaw muscles (i.e., lateral jaw movements).[7] In addition, stomatognathic functions are addressed by instructing patients to inhale nasally and exhale orally without and then with balloon inflation, and performing specific swallowing and chewing exercises (i.e., swallowing with the teeth clenched together, tongue positioned in the palate and without contraction of

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perioral muscles; alternating chewing sides).[7] A newer study describes a device that conditions and strengthens oral and tongue muscles.[12]

The objective of this study is to systematically review the literature for articles evaluating MT or oral/oropharyngeal exercises as treatment for OSA in both children and adults and to perform a meta-analysis on the available polysomnographic and sleepiness data.

METHODS

Search Strategy

A search was performed on Web of Science, Scopus, MEDLINE, and The Cochrane Library, initially January 18, 2014, with an update on June 18, 2014. MeSH terms and keywords used for the search included various combinations of the following: "myofascial reeducation," "myofunctional therapy," "obstructive sleep apnea," "orofacial myotherapy," "oral myotherapy," "oropharyngeal exercises," "sleep," "sleep apnea syndromes," "speech therapy," "upper airway exercises," and "upper airway remodeling." One example of a MEDLINE search is: ((("Myofunctional Therapy"[MeSH]) AND "Sleep Apnea Syndromes"[MeSH])) OR ("sleep" AND ("myofascial reeducation" OR "myofunctional therapy" OR "orofacial myotherapy" OR "oral myotherapy" OR "oropharyngeal exercises" OR "speech therapy" OR "upper airway exercises" OR "upper airway remodeling")).

For each of the searches, the titles and abstracts were screened and the full text versions of articles that met criteria were downloaded. Full texts were reviewed and any referenced articles that were not already obtained were ordered and obtained. "Related citations" were also reviewed during the searches, and the "cited by" function on Google Scholar was also used to identify any additional studies.

Study Selection

Criteria for inclusion included peer-reviewed studies (published articles or abstracts) evaluating oral or oropharyngeal MT as an isolated treatment for either adult or pediatric OSA; studies needed to report quantitative polysomnographic, snoring, and/or sleepiness data pretreatment and posttreatment or they needed to report the percentage of difference between pretreatment and posttreatment outcomes. All languages were included. Exclusion criteria included studies evaluating singing, instrument playing, and studies without quantitative data. If individual patient data were reported and patients lost 10% or more of their body weight, then those patients were excluded. Studies in which the MT patients also underwent additional interventions such as continuous positive airway pressure therapy, mandibular advancement device therapy, sleep apnea surgery, allergy management, weight loss management, or any other intervention that could also contribute to improved sleep apnea outcomes were excluded (unless the additional interventions were performed in control groups and the data were provided separately for both MT and control groups).

Data Abstraction and Study Quality Assessment

Authors MC, JA, and SZ independently performed a search of the literature and screened titles and abstracts and downloaded the articles for inclusion. The decision to include the articles was made by consensus, and if necessary the final decision was made by author MC. Data collected included patient age, body mass index (BMI), polysomnographic data (AHI, lowest oxygen saturation), snoring, and sleepiness data. If data were missing from the articles, then the corresponding author was contacted in an attempt to obtain the data. The corresponding author of the study by Suzuki et al.[12] was contacted and confirmed that the reported oxygen saturation data were for lowest oxygen saturation and that tongue training was involved as part of the MT device training.

The National Institute for Health and Clinical Excellence (NICE) quality assessment tool was used to evaluate the quality of the included studies. The instrument consists of eight items that are assessed for each individual study.

Statistical Analysis

The statistics were performed with the IBM Statistical Package for Social Sciences software (SPSS) version 20.0 (Armonk, New York, USA). Means and standard deviations were calculated before and after myofunctional therapy. Studies providing raw patient data without means and standard deviations were manually input into SPSS for calculation; or if individual scatterplots with pretreatment and posttreatment data were available, the estimated data point values were used to calculate the means and standard deviations. The null hypothesis for this study is that there is no difference in outcome data before and after myofunctional therapy. For combining data, a two-tailed, paired t test was performed ($P < 0.05$ was the cutoff for significance). Review Manager (RevMan) [Computer program] Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for meta-analysis. A random-effects model was used if heterogeneity existed and a fixed-effects model was used if no heterogeneity existed. When pooling the data in studies, the means, standard deviations, and 95% confidence intervals (CI) were calculated by REVMAN. Heterogeneity was assessed by I^2 statistic (inconsistency levels: low = 25%, moderate = 50% and high = 75%)[14] and the Cochran Q statistic (with significant heterogeneity being considered when $P \leq 0.1$ was obtained).[15] If heterogeneity existed, then a sensitivity analysis was performed by removing each of the studies individually to identify the source(s).

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were downloaded and followed during this review.[16]

RESULTS

A total of 226 studies were screened for relevance, and 204 were excluded. After identification of 22 potentially relevant studies, they were downloaded and the reviews of the reference lists yielded an additional 6 studies, for a total of 28 studies.[7–13,17–36] Nine were review articles,[8,20,22,27,30,32–34,36] two reported no intervention,[24,31] two studied lip exercises and the effect on lip thickness,[21,37] one reported breathing exercises not involving oral cavity or oropharyngeal structures,[28] one was a letter to the editor,[11] and two studies were abstracts in which data were later reported in the authors' journal articles.[19,25] Eleven studies met criteria and were included in

this review. Individual patient data were reported by one pediatric study[35] and one adult study,[12] whereas the remaining nine studies reported outcomes with means and standard deviations.[7,9,10,13,17,18,23,26,29] Figure 1 summarizes the flow for study selection.

Methodological Quality of the Included Studies

The studies included in this review included one abstract,[26] one retrospective case report,[23] three retrospective case series,[9,10,18] three prospective case series,[12,17,29] one randomized trial,[35] and two randomized controlled trials.[7,13] Most of the studies satisfied four to six of the eight NICE quality assessment tool items (presented in Table S1 of supplemental material). The main limitations were that the total number of patients in most studies was low, the studies were at single institutions (except one that was multicentered) and most studies did not explicitly state that patients were consecutive.

Adult Studies

A total of nine adult studies (120 patients, age 44.5 ± 11.6 y, BMI 28.9 ± 6.2 kg/m^2) reported polysomnography and/or sleepiness outcomes (Table 1). Baz et al.[17] reported using American Academy of Sleep Medicine (AASM) scoring criteria but did not specify which year, Diaferia et al.[13] and Guimaraes et al.[7] reported using 1999 AASM scoring criteria, Suzuki et al.[12] scored based on the 2005 update to AASM scoring criteria, and the remaining five studies did not specify which polysomnography scoring criteria were used.[9,18,23,26,29]

The pre- and post-MT AHI mean ± standard deviation (M ± SD; 82 patients) decreased from 24.5 ± 14.3/h to 12.3 ± 11.8/h, with a mean difference (MD) of −14.26 [95% CI −20.98, −7.54], Z score of 4.16 (P < 0.0001) (Figure 2). Both the I^2 statistic (91%) and the Q statistic (value of < 0.00001) demonstrated significant heterogeneity; therefore, studies were individually excluded to identify the source(s). Exclusion of the studies by Suzuki et al.[12] and Berreto et al.[18] resulted in no heterogeneity in the remaining 73 patients, with the I^2 statistic = 0% and the Q statistic value of 0.6. The mean difference for the remaining studies was −10.49 26 [95% CI −12.67, −8.31]. In adult studies in which MT was performed for at least 3 mo, the mean AHI reduced from 25.2 ± 14.6/h to 12.6 ± 12.2/h, which is a 50% reduction.

The lowest oxygen saturation improved in 82 patients from 83.9 ± 6.0% to 86.6 ± 7.3%, MD of 4.19 [95% CI 1.85, 6.54], with an overall Z score of 3.5 (P = 0.0005); see Figure 3. Both the I^2 statistic (59%) and the Q statistic (value of 0.05)

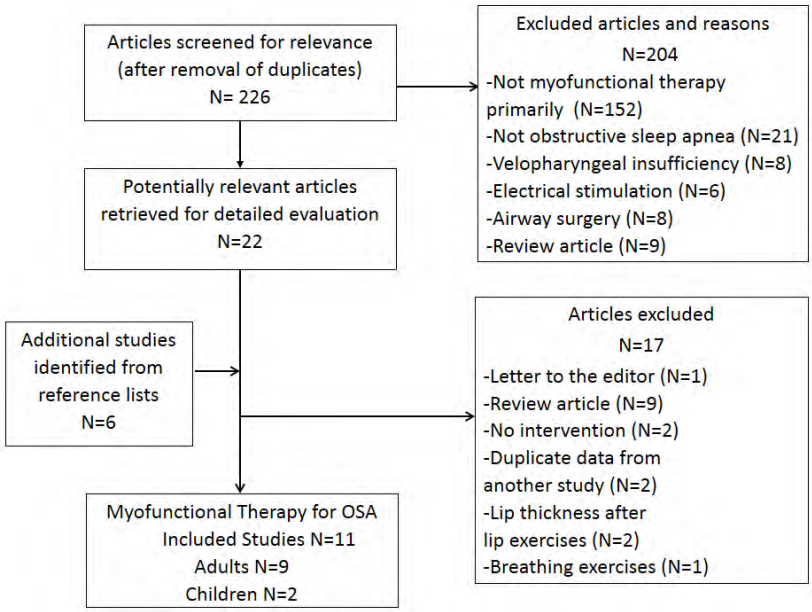

Figure 1—Flow diagram demonstrating myofunctional therapy for obstructive sleep apnea (OSA) study selection. N, number of articles.

Table 1—Adult pre- and post-myofunctional therapy outcomes.

Authors, Year	Study Design	N	Age (years)	BMI (kg/m^2)	AHI (events/h)		low O_2 (%)		ESS	
					Pre-MT	Post-MT	Pre-MT	Post-MT	Pre-MT	Post-MT
Suzuki et al., 2013*	PCS	6	22.0 ± 0.5	23.8 ± 1.8	15.1 ± 3.4	9.2 ± 1.5	90.0 ± 2.9	96.8 ± 0.8	–	–
Kronbauer et al., 2013	PCS	8	(40–65)	–	–	–	–	–	11.75	4.25
Diaferia et al., 2013	RCT	27	45.2 ± 13.0	25.0 ± 7.4	28.0 ± 22.7	13.9 ± 18.5	83.7 ± 7.7	84.9 ± 8.8	13.7 ± 3.2	7.5 ± 3.7
Baz et al., 2012	PCS	30	44.1 ± 7.5	33.6 ± 2.0	22.3 ± 4.5	11.5 ± 5.4	84 ± 4	87 ± 5	16.4 ± 2.0	9.3 ± 2.9
Guimaraes et al., 2009	RCT	16	51.5 ± 6.8	29.6 ± 3.8	22.4 ± 4.8	13.7 ± 8.5	83 ± 6	85 ± 7	14 ± 5	8 ± 6
de Paula Silva et al., 2007	RCR	1	60	23.3	44	3	83	92	–	–
Berreto et al., 2007	RCS	2	46 ± 12.7	24.2 ± 2.9	44.5 ± 5.7	6.0 ± 3.7	78 ± 1.4	85 ± 2.8	12.5 ± 0.7	4.5 ± 3.5
Guimaraes et al., 2003	ABS	10	–	–	36.1	11.3	–	–	11	7.6
Guimaraes et al., 1999	RCS	20	(33–55)	–	–	−48%	–	–	–	–
Total		120	44.5 ± 11.6	28.9 ± 6.2	24.5 ± 14.3	12.3 ± 11.8	83.9 ± 6.0	86.6 ± 7.3	14.8 ± 3.5	8.2 ± 4.1

*Study authors confirmed the reported oxygen saturation data was for lowest oxygen saturation. –, not reported, %, percent; ABS, abstract; AHI, apnea-hypopnea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; events/h, events per hour; kg/m^2, kilograms per meter squared; low O_2, lowest oxygen saturation; MT, myofunctional therapy; N, number of myofunctional therapy patients in the study; PCS, prospective case series; RCR, retrospective case report; RCS, retrospective case series; RCT, randomized controlled trial.

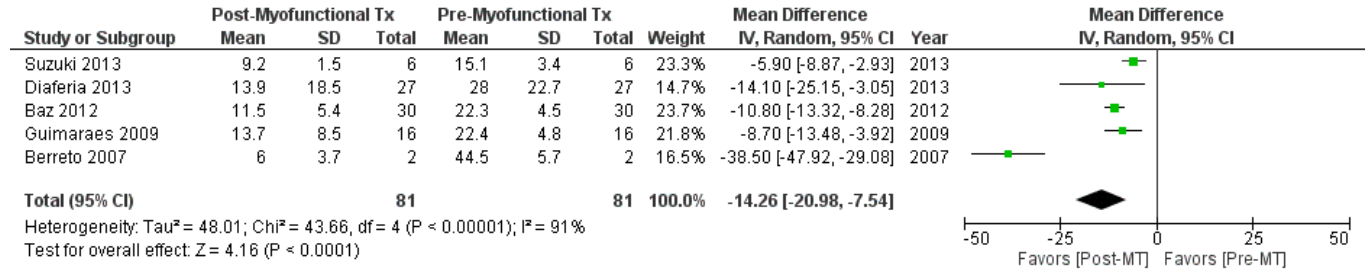

Figure 2—Adult premyofunctional and postmyofunctional therapy outcomes for apnea-hypopnea index (events per hour). CI, confidence interval; MT, myofunctional therapy; SD, standard deviation; Tx, treatment.

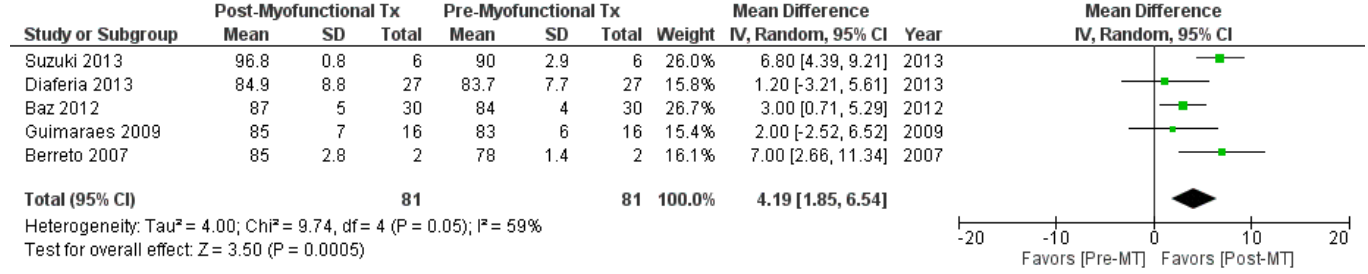

Figure 3—Adult premyofunctional and postmyofunctional therapy outcomes for lowest oxygen saturation (percent). CI, confidence interval; MT, myofunctional therapy; SD, standard deviation; Tx, treatment.

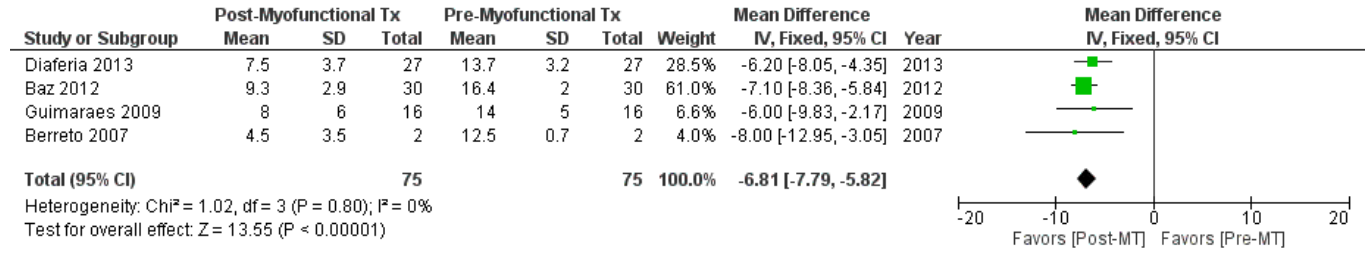

Figure 4—Adult premyofunctional and postmyofunctional therapy outcomes for Epworth Sleepiness Scale. CI, confidence interval; MT, myofunctional therapy; SD, standard deviation; Tx, treatment.

demonstrated significant heterogeneity, therefore, studies were individually excluded to identify the source(s). Exclusion of the studies by Suzuki et al.[12] and Berreto et al.[18] resulted in no heterogeneity in the remaining 73 patients, with the I^2 statistic = 0% and the Q statistic value of 0.56. Oxygen desaturation index was reported by one study, and demonstrated a reduction from 14.53 ± 5.04 to 9.27 ± 4.27, pre- and post-MT, respectively.[17] Sleepiness decreased in all studies reporting the outcome. The Epworth Sleepiness Scale (ESS)[38] decreased in 75 patients from 14.8 ± 3.5 to 8.2 ± 4.1, MD of −6.81 [95% CI −7.79, −5.82], with an overall Z score of 13.55 (P < 0.00001); see Figure 4. Both the I^2 statistic (0%) and the Q statistic (value of 0.8) demonstrated no heterogeneity.

Snoring

Snoring changes were evaluated by 4 studies, Baz et al.,[17] Berreto et al.,[18] de Paula Silva et al.[23] and Guimaraes et al.[7]; see Table 2. Baz et al.[17] reported that 30 patients snored before therapy and 16 snored after therapy, P = 0.008 (yes versus no; article did not specify if patient or bed partner was asked) and the polysomnography demonstrated that the percent of total sleep time spent snoring decreased from 14.05 ± 4.89% to 3.87 ± 4.12% (before and after, respectively), P < 0.001.[17] Guimaraes et al.[7] found snoring frequency decreased by 25% (article did not specify if patient or bed partner was asked) from 4 to 3 (based on 0 = never to 4 = everyday), P = 0.001, and the snoring intensity decreased by 66% from 3 to 1 (based on 1 = similar to breathing and 3 = very loud) with P = 0.001; whereas the control groups had no change in snoring frequency or intensity. The case study by de Paula Silva et al.[23] demonstrated a decrease in snoring intensity after 8 sessions. Berreto et al.[18] described two patients who decreased from a (bed partner) snoring score of 3 down to 2 (0 = snoring absence, 1 = heavy breathing, 2 = light snoring, 3 = snoring that disturbs the bed partner and 4 = snoring that can be heard outside the bedroom).

Table 2—Snoring outcomes based on mean values pre and post-myofunctional therapy.

		Subjective Snoring		PSG %TST Snoring	
Authors, Year	**N**	**Pre-MT**	**Post-MT**	**Pre-MT**	**Post-MT**
Baz et al., 2012	30	Yes = 30; No = 0	Yes = 16; No = 14	14.05 ± 4.89%	3.87 ± 4.12%
Guimaraes et al., 2009	16	Very loud	Similar to breathing	–	–
de Paula Silva et al., 2007	1	Snoring	Decreased snoring	–	–
Berreto et al., 2007	2	Disturbs bedpartner	Light snoring	–	–

MT, myofunctional therapy; %TST, percentage of total sleep time. Snoring outcomes are based on quantified definitions pre- and post-myofunctional therapy by all studies except de Paula Silva et al. (case report).

Pediatric Studies

A total of two pediatric studies (25 patients, age 8.4 ± 3.1 y) reported polysomnography and/or sleepiness outcomes. Both pediatric studies reported using 2007 AASM scoring criteria, and Guilleminault et al.[10] also specified that hypopneas were scored with a 50% reduction in nasal cannula curve and an associated 3% or more reduction in oxygen saturation and/or with associated arousals, while Villa et al.[35] did not specify the hypopnea scoring criteria. The study by Villa et al.[35] was a prospective randomized controlled trial in which postadenotonsillectomy patients were randomized to either oropharyngeal exercises or control group. The treatment group in this study consisted of 14 patients and the pre- and post-MT AHI was evaluated after 2 mo of oropharyngeal exercises. The AHI M ± SD reduced from 4.87 ± 3.0/h to 1.84 ± 3.2/h, P = 0.004 (a 62% reduction).[35] The control group had minimal change in AHI during the 2-mo period (4.56/h down to 4.11/h).[35] The study by Guilleminault et al.[10] was a retrospective chart review, evaluating 24 children who were cured by the combination of adenotonsillectomy and palatal expansion (AHI 0.4 ± 0.3); and 11 of the children received MT (intervention group) and 13 children did not receive MT (controls).[10] At the 4-y follow-up, the children who practiced MT over the long term remained cured of OSA (AHI 0.5 ± 0.4), compared to children who were never trained to perform the exercises and subsequently had a recurrence of OSA (AHI 5.3 ± 1.5/h).[10] Although both pediatric MT studies compared the intervention groups to control groups, neither study reported pretreatment and posttreatment lowest oxygen saturation or sleepiness outcomes.

DISCUSSION

This systematic review and meta-analysis of nine adult and two pediatric studies evaluating the effect of MT on OSA has five main findings. First, MT provides a reduction in AHI of approximately 50% in adults and 62% in children. The pre- and post-MT AHI for adults decreased from 24.5 ± 14.3/h to 12.3 ± 11.8/h, MD of −14.26 [95% CI −20.98, −7.54] (P < 0.0001). For pediatric patients, the pre- and post-MT M ± SD for AHI decreased from 4.87 ± 3.0/h to 1.84 ± 3.2/h, P = 0.004. Additionally, the study by Guilleminault et al.[10] reported that 11 children remained cured of OSA (AHI of 0.5 ± 0.4/h) after continuing MT for 4 y. There was heterogeneity, and the studies by Suzuki et al.[12] and Berreto et al.[18] were shown to be the sources. The study by Suzuki et al.[12] had six patients, who used an oral exercise device to help train, but the length of time between polysomnography was 2 mo, whereas the remaining adult studies reporting AHI had a follow-up duration of at least 3 mo between polysomnography studies. Had the study been extended to 3 mo, there may have been additional improvement in AHI. In studies with control groups, there was little to no improvement in the AHI for the control groups compared to improvement in the MT intervention group. There is also a clear improvement in lowest oxygen saturation by approximately 3–4%, with the meta-analysis of 81 patients demonstrating a mean difference pre- and post-MT of 4.19%, [95% CI 1.85, 6.54]. The oxygen desaturation index (ODI) was only reported by Baz et al.,[17] demonstrating a 36% reduction, but the article did not specify whether the ODI in the study was based on 3% or 4% desaturation.

Second, MT decreases snoring both subjectively and objectively. Four studies compared the pre- and post-MT outcomes and it was noted that snoring decreased after therapy (three of four studies quantified the snoring). The polysomnography demonstrated a 72.4% reduction in snoring pre- versus post-MT (14.05 ± 4.89% to 3.87 ± 4.12%, before and after, respectively), P < 0.001.[17] With regard to subjective improvement in snoring intensity, the three studies quantifying the outcomes reported that during posttreatment there was a decrease in snoring to either light snoring, or the sound was similar to normal breathing.

Third, subjective sleepiness also improves post-MT as demonstrated by a clear reduction in ESS score for the 93 patients in which it was administered, with a reduction from 14.8 ± 3.5 to 8.2 ± 4.1 (in 75 patients in whom M ± SDs were reported).[7,13,17,18,26,29] The posttreatment ESS is below the threshold for hypersomnia, which is generally considered to be 11 or higher on the scale.[39] Additionally, the 1999 study by Guimaraes[9] reported a subjective reduction in sleepiness; however, the use of a validated sleepiness scale was not specified.[9]

Fourth, despite the heterogeneity in oral and oropharyngeal exercises, overall the improvements in polysomnographic outcomes and sleepiness were consistent. MT was performed for as little as 5 min, twice daily, 4 days a week for 2 mo[12] to as many as 10 min, three to five times daily for 3 mo.[17] The longest published experience with MT for adult OSA has been that of Guimaraes,[9] which is 6 mo. Guimaraes[9] has also published thorough instructions for performing the exercises that involve the soft palate, tongue, facial muscles, and stomatognathic functions to be performed 30 min a day.[7]

Fifth, future research is needed to help explain the pathophysiology and mechanism of action of MT as treatment for

OSA. It can be hypothesized that the exercises improve oral and/or oropharyngeal muscle tone and also may decrease the amount of fatty deposition of the tongue, but this has not been proven. It can be recommended that future researchers consider using the standardized exercises, which have been developed and used over a period of several years by Guimaraes et al.[7] because they have the most experience with the therapy. As pointed out by Guimaraes et al.,[7] because MT is based on an integrative approach with several exercises, it is not possible to determine the effects of specific exercises to determine which ones contribute the most to improvement in outcomes[7]; therefore, future studies could consider exploring the effect of individual exercises. Individual patient data were not available for most studies; therefore, a subanalysis could not be performed for BMI, AHI, age, etc. based on the current literature. However, with regard to BMI, Guimaraes et al.[7] and Baz et al.[17] had significant reductions in AHI in overweight (BMI M ± SD 29.6 ± 3.8) and obese patients (BMI M ± SD 33.6 ± 2.0). With regard to age, the MT has been shown effective in children and adults of all ages studied thus far, ranging from 3 to 60 y.

Limitations

A total of 145 patients (including 25 children) were included in this meta-analysis; however, the magnitude of the effects was highly significant. Although there were nine adult studies, a significant limitation for pediatric studies is that currently only two articles have been published. Additionally, long-term follow-up for more than 6 mo is limited. Except the study by Guilleminault et al,[10] which followed patients for 4 y, all of the other studies spanned 2 to 6 mo. The study by Guilleminault et al.[10] demonstrates a long-term (4 y) maintenance of reduction in AHI and alleviation of OSA symptoms in patients who continued to perform MT exercises, compared to the control group that had recurrence of symptoms and recurrence of an elevated AHI at 4-y follow-up.[10] Because this is the only study that has reported outcomes longer than 6 mo after initiation of MT exercises, additional long-term studies are needed to demonstrate the lasting effects of continued MT. Questions that have not been addressed that could be studied in the future include whether there is a relationship with the tongue exercises and changes in the tongue and palatal muscle tone and/or strength, tongue size (tongue fat), and overall upper airway volume changes pretreatment and posttreatment.

CONCLUSION

Current literature demonstrates that myofunctional therapy decreases AHI by approximately 50% in adults and 62% in children. Lowest oxygen saturation, snoring, and sleepiness outcomes improve in adults. Myofunctional therapy could serve as an adjunct to other OSA treatments.

DISCLOSURE STATEMENT

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SUPPLEMENTAL MATERIAL

Table S1—General characteristics of included patients and quality criteria of included studies.

General Characteristics							Quality Assessment of Included Studies[a]							
Authors, Year	**Site**	**Design**	**N**	**Follow-up**	**BMI**	**Outcomes Analyzed**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Pediatric Studies														
Villa et al., 2014	Italy	RT	14	2 mo	21.6	AHI, O_2 sat	No	Yes	Yes	Yes	Yes	No	Yes	Yes
Guilleminault et al., 2013	USA	RCS	11	4 y	–	AHI, O_2 sat	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Adult Studies														
Suzuki et al., 2013	Japan	PCS	6	2 mo	23.8	AHI, O_2 sat	No	Yes	Yes	Yes	Yes	No	Yes	No
Kronbauer et al., 2013	Brazil	PCS	8	2.5 mo	–	ESS, physical measurements	No	Yes	No	Yes	Yes	No	Yes	No
Diaferia et al., 2013	Brazil	RCT	27	3 mo	25.0	AHI, AI, ESS, O_2 sat	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Baz et al., 2012	Egypt	PCS	30	3 mo	33.6	AHI, ESS, O_2 sat, snoring	No	Yes	Yes	Yes	Yes	No	Yes	No
Guimaraes et al., 2009	Brazil	RCT	16	3 mo	29.6	AHI, AI, ESS, O_2 sat, snoring	No	Yes	Yes	Yes	Yes	No	Yes	Yes
de Paula Silva et al., 2007	Brazil	RCR	1	–	23.3	AHI, O_2 sat, sleepiness, snoring	NA	NA	NA	NA	NA	NA	NA	NA
Berreto et al., 2007	Brazil	RCS	2	4 mo	24.2	AHI, ESS, O_2 sat, snoring	No	No	No	Yes	No	No	No	No
Guimaraes et al., 2003	Brazil	ABS	10	–	–	AHI, ESS	NA	NA	NA	NA	NA	NA	NA	NA
Guimaraes et al., 1999	Brazil	RCS	20	6 mo	–	AHI, sleepiness	No	Yes	No	Yes	Yes	No	Yes	No

[a]Quality assessment of cases series studies checklist from National Institute for Health and Clinical Excellence (NICE): (1) Case series collected in more than one center,i.e.,multicenter study? (2) Is the hypothesis/aim/objective of the study clearly described? (3) Are the inclusion and exclusion criteria (case definition) clearly reported? (4) Is there a clear definition of the outcomes reported? (5) Were data collected prospectively? (6) Is there an explicit statement that patients were recruited consecutively? (7) Are the main findings of the study clearly described? (8) Are outcomes stratified? (e.g., by disease stage,abnormal test results, patient characteristics)? –, not reported; AI, apnea index; AHI, apnea-hypopnea index; ESS, Epworth Sleepiness Scale; mo, months; N, number of patients with intervention; NA, not applicable; O_2 sat, oxygen saturation; PCS, prospective case series; RCR, retrospective case report; RCS, retrospective case series; RCT, randomized controlled trial; RT, randomized trial; y, years.

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REVIEW ARTICLE

Oropharyngeal and tongue exercises (myofunctional therapy) for snoring: a systematic review and meta-analysis

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Abstract

Purpose Oropharyngeal and tongue exercises (myofunctional therapy) have been shown to improve obstructive sleep apnea. However, to our knowledge, a systematic review has not been performed for snoring. The study objective is to perform a systematic review, with a meta-analysis, dedicated to snoring outcomes after myofunctional therapy.

Methods PubMed/MEDLINE and three other databases were searched through November 25, 2017. Two authors independently searched the literature. Eligibility (1) patients: children or adults with snoring, (2) intervention: oropharyngeal and/or tongue exercises, (3) comparison: pre and post-treatment data for snoring, (4) outcomes: snoring frequency and snoring intensity, (5) study design: publications of all study designs.

Results A total of 483 articles were screened, 56 were downloaded in their full text form, and nine studies reported outcomes related to snoring. There were a total of 211 patients (all adults) in these studies. The snoring intensity was reduced by 51% in 80 patients from pre-therapy to post-therapy visual analog scale values of 8.2 ± 2.1 (95% CI 7.7, 8.7) to 4.0 ± 3.7 (95% CI 3.2, 4.8). Berlin questionnaire snoring intensity reduced by 36% in 34 patients from 2.5 ± 1.0 (95% CI 2.2, 2.8) to 1.6 ± 0.8 (95% CI 1.3, 1.9). Finally, time spent snoring during sleep was reduced by 31% in 60 patients from 26.3 ± 18.7% (95% CI 21.6, 31.0) to 18.1 ± 20.5% (95% CI 12.9, 23.3) of total sleep time.

Conclusions This systematic review demonstrated that myofunctional therapy has reduced snoring in adults based on both subjective questionnaires and objective sleep studies.

Keywords Snoring · Myofunctional therapy · Systematic review · Meta-analysis

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Introduction

There have been several treatments developed over the years to treat snoring and obstructive sleep apnea (OSA) [1–4]. Of the current techniques to treat snoring and OSA, many of them are invasive and involve either performing surgery or wearing a device during sleep [5–7]. A technique that can serve either as a primary treatment or as an adjunct treatment to treat primary snoring that does not require either surgery or wearing a device would be beneficial. Tongue exercises and oropharyngeal exercises (myofunctional therapy) have improved OSA in children and adults [8]. In a previous meta-analysis evaluating myofunctional therapy, apnea-hypopnea index was reduced by 50% in adults and 62% in children [8]. The sub-analysis, evaluating patients with sleep study snoring, demonstrated a significant reduction from 14.05 ± 4.89% to 3.87 ± 4.12% of total sleep time, p value < 0.001 [8].

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Since the publication of the meta-analysis for OSA, there have been several studies evaluating oropharyngeal exercises and tongue exercises and their outcomes for snoring; however, to our knowledge, there has been no systematic review or meta-analysis evaluating the effect on snoring. To provide the most up-to-date information, a systematic review would be required. Therefore, the objective of this study was to perform a systematic review for snoring, specifically using the PICOS acronym, as follows: (1) *Patients* (*P*) adults or children who snore; (2) *Intervention* (*I*) oropharyngeal exercises and/or tongue exercises; (3) *Comparison* (*C*) data pre and post-exercises; (4) *Outcomes* (*O*) snoring frequency, snoring index, percentage of night spent snoring, visual analog scale (VAS), and Likert scales; (5) *Study design* (*S*) any study type or design. After obtaining the studies, the pre- and post-oropharyngeal exercises and tongue exercises snoring data were analyzed.

Methods

The preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement were reviewed and used as a guide during this study [9].

Protocol

Our Institutional Department of Clinical Investigation was contacted, and a protocol was submitted and was approved. For this type of study, formal consent is not required.

Eligibility criteria

The inclusion criteria for this review: (1) studies with adult or pediatric patients who were treated with oropharyngeal exercises and tongue exercises as the sole intervention and (2) the publication provided both pre- and post-oropharyngeal exercises and tongue exercises quantitative outcomes for snoring. Exclusion criteria: studies with additional treatments performed, studies using devices, and studies without data for myofunctional therapy alone.

Information sources

We searched PubMed/MEDLINE, Google Scholar, The Cochrane Library and Cumulative Index to Nursing and Allied Health (CINAHL).

Search

Authors M. C. and M. W. N searched through May 8, 2017 initially, and provided additional updating through November 25, 2017. An example of a search strategy is the one used for PubMed/MEDLINE: [(Snoring OR Sleep) AND ("tongue exercise" OR "tongue exercises" OR "orofacial" OR "myotherapy" OR "speech therapy" OR "oropharyngeal exercises" OR "myofascial reeducation" OR "myofunctional therapy" OR "upper airway exercises" OR ("Myofunctional Therapy"[MeSH]))]. For the remaining databases, we applied very similar keywords and terms, just tailored to the specific databases.

Authors extracted the snoring data from the studies meeting the predefined selection criteria. If a study did not provide the information necessary to include it in the review, then the study authors were emailed at least twice in an attempt to obtain the data.

Risk of bias and heterogeneity

If there are sufficient summary measures provided, then an analysis for bias and heterogeneity would be performed using REVMAN.

Summary measures

Study measures collected include the means, standard deviations (SD), medians, and other summary measures provided by the individual studies.

Results

A total of 483 articles were screened, 56 were downloaded in their entirety, and nine studies [10–18] with 211 patients met the inclusion criteria, see Supplementary Fig. 1. The studies provided data for snoring frequency, snoring intensity, snoring severity, and bedpartner visual analog scale scores, see Table 1. The studies that used Berlin questionnaire and values for snoring frequency were rated as follows: 0 = never, 1 = 1–2 times a month, 2 = 1–2 times a week, 3 = 3–4 times a week, and 4 = every day [19]. Values for snoring intensity were 0 = no snoring, 1 = similar to breathing, 2 = as loud as talking, 3 = louder than talking, and 4 = very loud, and can be heard in adjacent rooms [19].

For the 211 patients who performed myofunctional therapy, the mean snoring frequency and snoring intensity were reduced, see Table 2. In 80 patients, the snoring intensity reduced by 51%, from pre-therapy to post-therapy using the VAS values [from 8.2 ± 2.1 (95% CI 7.7, 8.7) to 4.0 ± 3.7 (95% CI 3.2, 4.8)]. A sub-analysis was performed for VAS using random effects modeling, which demonstrated a mean difference of -3.67 [95% CI -4.44, -2.90], overall effect $Z = 9.34$, p value < 0.00001, Q statistic p value $= 0.64$, and $I^2 = 0\%$ (Fig. 1). The VAS standardized mean difference was -1.46 (95% CI -1.81, -1.11), overall effect $Z = 8.15$,

Table 1 General characteristics and quality criteria of included studies

Author, year, *N*	General characteristics			Quality assessment of included studies							
	Country	Design	Snoring data	1	2	3	4	5	6	7	8
Diaferia et al. 2016, *N* = 27	Brazil	RCT	SF, SI, (VAS)	N	Y	Y	Y	Y	Y	Y	Y
Mohamed et al. 2016, *N* = 30	Egypt	PCS	SF, SI	N	Y	Y	Y	Y	N	Y	N
Verma et al. 2016, *N* = 20	India	PCS	SI	N	N	Y	Y	Y	N	Y	N
Ieto et al. 2015, *N* = 19	Brazil	RCT	SF, SI (VAS)	N	Y	Y	Y	Y	N	Y	Y
Kayamori et al. 2015, *N* = 30	Brazil	RCT	SF, SI	N	Y	Y	Y	Y	N	Y	Y
Nemati et al. 2015, *N* = 53	Iran	PCS	SS, VAS	N	N	Y	Y	N	N	Y	N
Baz et al. 2012, *N* = 30	Egypt	PCS	SF, SI	N	Y	Y	Y	Y	N	Y	N
Guimaraes et al. 2009, *N* = 16	Brazil	RCT	SF, SI	N	Y	Y	Y	Y	N	Y	Y
Berreto et al. 2007, *N* = 2	Brazil	RCS	SS	N	N	N	Y	N	N	N	N

Columns: (1) case series collected in more than one center, i.e. multi-center study? (2) Is the hypothesis/aim/objective of the study clearly described? (3) Are the inclusion and exclusion criteria (case definition) clearly reported? (4) Is there a clear definition of the outcomes reported? (5) Were data collected prospectively? (6) Is there an explicit statement that patients were recruited consecutively? (7) Are the main findings of the study clearly described? (8) Are outcomes stratified? (e.g., by abnormal results, disease stage, and patient characteristics)?

PCS prospective case series, *RCS* retrospective case series, *RCT* randomized control trial, *SF* snoring frequency, *SI* snoring intensity, *SS* snoring severity, *VAS* visual analog scale

Table 2 Demographic and snoring data before and after oropharyngeal exercises and tongue exercises

Study, authors, year	*N*	Age	BMI	Pre-SF	Post-SF	Pre-SI	Post-SI	% Change SI
Diaferia et al. 2016	27	45 ± 13	25.0 ± 7.4	8.5 ± 2.3[‡V] [7.6–9.4]	4.9 ± 3.2[‡V] [3.7–6.1]	7.7 ± 2.3[‡V] [6.8–8.6]	4.3 ± 2.8[‡V] [3.2–5.4]	− 44.2%
Mohamed et al. 2016	30	46.9 ± 6.4	27.9 ± 2.0	464 ± 168 [401–527][‡SN]	396 ± 172 [331–460][‡SN]	38.5 ± 19.5[‡P] [31.5–45.5]	32.3 ± 20.6[‡P] [24.9–39.7]	− 16.2%
Verma et al. 2016	20	41 ± 11	25.6 ± 3.1	–	–	2.8 ± 0.5[‡B] [2.6-3.0]	1.7 ± 0.6[‡B] [1.4-2.0]	− 39.3%
Ieto et al. 2015	19	48 ± 14	28.1 ± 2.7	4 (3–4)[‡B]	2 (1.5-3)[‡B]	4 (2.5-4)[‡B]	1 (1–2)[‡B]	− 75%
Kayamori et al. 2015	14	42 ± 13	28.9 ± 4.3	2.7 ± 1.4[‡B] [2.0-3.4]	2.6 ± 1.3[‡B] [1.9–3.3]	2.0 ± 1.4[‡B] [1.3–2.7]	1.5 ± 1.0[‡B] [1.0–2.0]	− 25%
Nemati et al. 2015	53	45 ± 10	26.5 ± 5.2	91%	36%	8.5 ± 1.9[‡V] [8.0–9.0]	4.7 ± 2.9[‡V] [3.9–5.5]	− 44.7%
Baz et al. 2012	30	44 ± 8	33.6 ± 2.0	100%	53.3%	14.1 ± 4.9[‡P] [12.3–15.9]	3.9 ± 4.1[‡P] [2.4–5.4]	− 72.3%
Guimaraeset al. 2009	16	52 ± 7	29.6 ± 3.8	4 (4–4)[‡B]	3 (1.5–3.5)[‡B]	3 (3–4)[‡B]	1 (1–2)[‡B]	− 66.6%
Berreto et al. 2007	2	46 ± 13	24.2 ± 2.9	–	–	3 ± 0[‡G] [3–3]	2 ± 0[‡G] [2–2]	33.3%

BMI body mass index, *N* number of patients, *SF* snoring frequency, *SI* snoring intensity, – not reported

[] Denotes lower and upper 95% confidence intervals

[‡B] Berlin score, 0–10

[‡V] Visual analog scale, 0–10.0

[‡SN] Snores per hour

[‡G] Grading scale, 0–4

[‡P] Percent of night based on sleep study

p value < 0.00001, Q statistic p value = 0.54, and $I^2 = 0\%$ (Fig. 1).

In studies that used the Berlin questionnaire, snoring intensity reduced in 34 patients from 2.5 ± 1.0 (95% CI 2.16, 2.84) to 1.6 ± 0.8 (95% CI 1.33, 1.87). A sub-analysis was performed for Berlin scores for snoring using random effects modeling, which demonstrated a mean difference of − 0.95 (95% CI − 1.46, − 0.44], overall effect $Z = 3.67$, p value = 0.0002, Q statistic p value = 0.22, and $I^2 = 33\%$ (Fig. 2). The Berlin scores for snoring using standardized

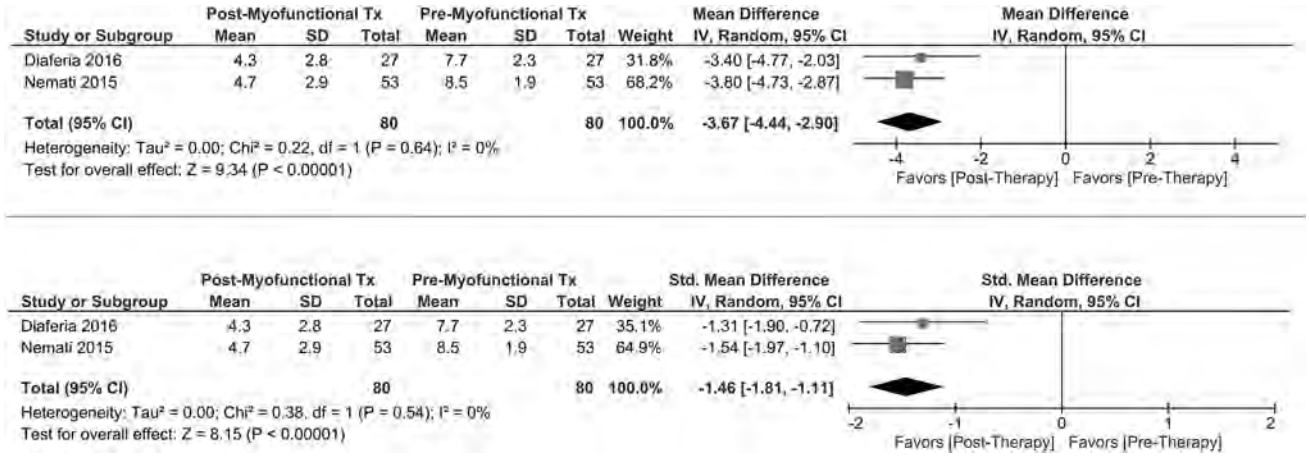

Fig. 1 Pre- and post-myofunctional therapy visual analog scale for snoring intensity. Mean difference (top) and standardized mean difference (bottom)

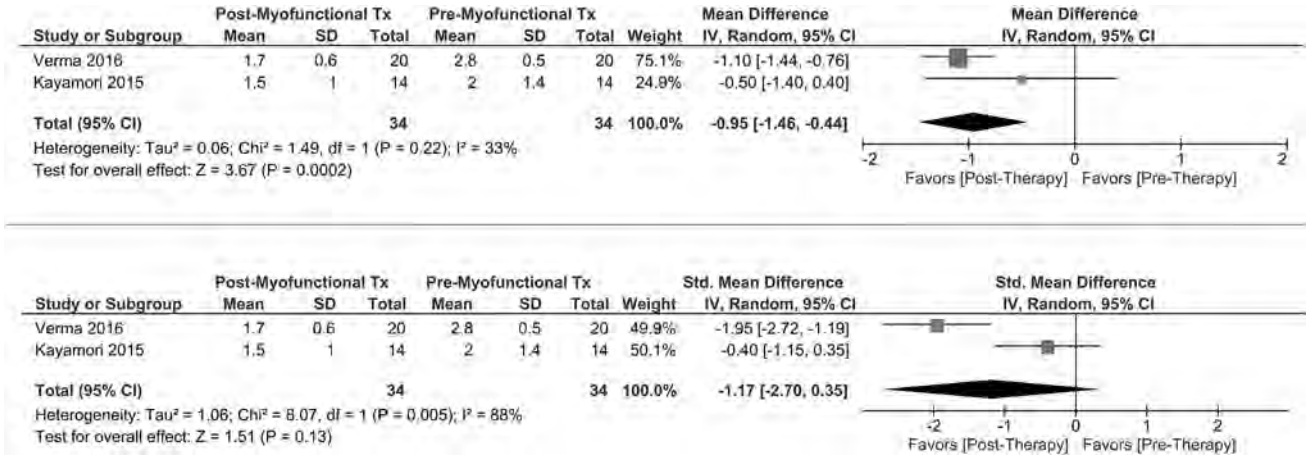

Fig. 2 Pre- and post-myofunctional therapy Berlin score for snoring intensity. Mean difference (top) and standardized mean difference (bottom)

mean difference were − 1.17 (95% CI − 2.70, 0.35), overall effect $Z = 1.51$ p value = 0.13, Q statistic p value = 0.005, and $I^2 = 88\%$ (Fig. 2).

Time spent snoring during sleep was reduced by 31.2% in 60 patients from 26.3 ± 18.7% (95% CI 21.6, 31.0) to 18.1 ± 20.5% (95% CI 12.9, 23.3) of total sleep time. A subanalysis was performed for percentage of time spent snoring with random effects modeling, demonstrating a mean difference of − 10.01 percent of the night (95% CI − 12.24, − 7.78), overall effect $Z = 8.79$, p value < 0.0001, Q statistic p value = 0.45, and $I^2 = 0\%$ (Fig. 3). The percentage of time spent snoring's standardized mean difference was − 1.26 (95% CI − 3.14, 0.63) (large effect using Cohen's guidelines), overall effect $Z = 1.31$ p value = 0.19, Q statistic p value < 0.00001, and $I^2 = 95\%$.

Overall, the exercises described were generally performed for 3 months and consisted of four main locations, the soft palate, the tongue, facial exercises, pharyngeal exercises, jaw exercises, and stomatognathic exercises [10–18]. Soft palate exercises generally consisted of saying vowels, which recruits the palatoglossus, palatopharyngeus, tensor veli palatini, levator veli palatini, and the uvula [12]. Tongue exercises generally consisted of moving the tongue in different directions with or without sticking the tongue out, pressing against bony and soft tissue structures within the oral cavity, sucking the tongue against the palate, and other tongue movements with or without resistance [10–18]. Facial exercises generally involve recruitment of the buccinator muscles by placing a finger into the oral cavity and pressing in an outward direction and puckering, closing or moving the lips [10–18]. Jaw exercises involve opening/closing/exercising the jaw. Pharyngeal exercises can involve swallowing exercises. Finally, stomatognathic functional exercises can involve sucking through a narrow straw, inflating balloons and swallowing and chewing exercises.

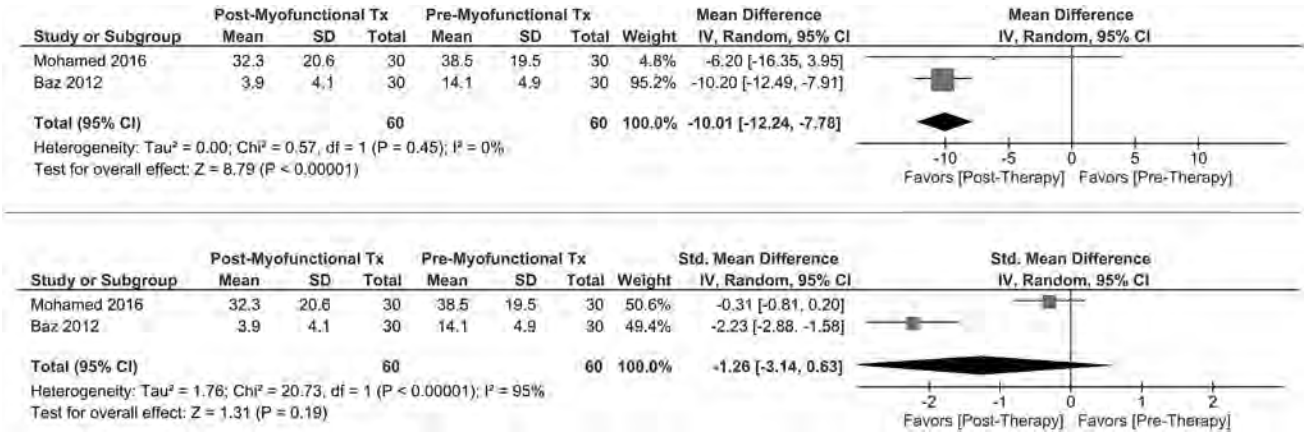

Fig. 3 Pre- and post-myofunctional therapy percentage of time spent snoring during the sleep study. Mean difference (top) and standardized mean difference (bottom)

Individual studies

Diaferia et al. [12] evaluated 100 patients who were randomized into various treatments and 27 were placed into the myofunctional therapy treatment arm. The myofunctional therapy consisted of tongue, soft palate, stomatognathic function, and facial exercises [12]. The patients performed the exercises three times daily, for 20 min sessions, a total of 3 months [12]. The snoring frequency using the visual analog scale was 8.5 ± 2.3 and 4.9 ± 3.2 (42% reduction) before and after myofunctional therapy [12]. The snoring intensity reduced from 7.7 ± 2.3 to 4.3 ± 2.8 before and after treatment, corresponding to a 44% reduction) [12].

Mohamed et al. [18] treated 30 patients with OSA by having them perform oropharyngeal exercises (soft palate, tongue, facial muscles, and stomatognathic function exercises) [18]. Exercises were performed for at least 10 min, three to five times a day for 3 months. The patients were divided into two groups (Group 1 with moderate OSA and Group 2 with severe OSA) [18]. Snoring index in patients with moderate OSA reduced by 24%, and the percent time spent snoring during the sleep study decreased by 37%. However, in patients with severe OSA, the snoring index only reduced by 10%, and the percent time spent snoring during the sleep study only reduced by 9%.

Verma et al. [17] evaluated 20 patients who were treated with myofunctional therapy. The exercises were performed five times daily, for 3 months [17]. The exercises performed included tongue exercises, jaw exercises, lip exercises, and soft palate exercises [17]. The researchers used the Berlin scoring for snoring. The snoring intensity was reduced from 2.8 ± 0.5 before myofunctional therapy down to 1.7 ± 0.6 after myofunctional therapy (a 39% reduction) [17].

Ieto et al. [14] treated nineteen patients with myofunctional therapy to include tongue exercises, palate exercises, facial exercises, and chewing/swallowing exercises. The patients performed the myofunctional therapy exercises for approximately 8 min daily for 3 months [14]. The researchers used the Berlin scoring. The median values for snoring frequency were reported and were 4 (3–4) before myofunctional therapy and 2 (1.5–3) after myofunctional therapy [14]. The snoring intensity reduced from 4 (2.5–4) before treatment, down to 1 (1–2) after treatment [14].

Kayamori and Filho [15] had 14 patients who underwent myofunctional therapy and had data that could be analyzed. The exercises were performed three times a day for 3 months [15]. Exercises included tongue exercises, soft palate exercises, facial exercises, and chewing/swallowing exercises [15]. The researchers used the Berlin scoring. The authors found that the snoring frequency did not change significantly 2.7 ± 1.4 to 2.6 ± 1.3 (4% reduction); however, the snoring intensity did decrease from 2.0 ± 1.4 to 1.5 ± 1.0 (25% reduction) [15].

Nemati et al. [16] reported treating 53 patients with primary snoring with myofunctional therapy for 30 min sessions, 5 days a week for 3 months. Patients performed soft palate exercises, tongue exercises, and facial exercises [16]. The researchers used the Lim and Curry snoring scale score (SSS) [20], frequency of snoring (every night, most nights, some nights, and seldom/never), the duration of snoring (all night long, most hours of the night, or some hours of the night), and the visual analog scale (0–10) [16]. The snoring severity scale demonstrated a reduction in snoring from 7.0 ± 1.7 to 3.1 ± 2.7 (56% reduction) [16]. The frequency of snoring based on the percentage of patients who snored every night or most nights was reduced from 91 to 36% [16]. The visual analog scale demonstrated an improvement in snoring from 8.5 ± 1.9 to 4.7 ± 2.9 (45% reduction) [16].

Baz et al. [10] evaluated 30 patients based on symptoms and a sleep study. The patients performed exercises for at

least 10 min, 3–5 times daily for 3 months [10]. The myofunctional therapy included tongue exercises, the soft palate exercises, and pharyngeal exercises. Before myofunctional therapy, 100% of patients snored and afterwards 53% snored [10]. The sleep study demonstrated a reduction in the total time spent snoring from 14.1 ± 4.9% down to 3.9 ± 4.1%, which is a 72% reduction [10].

Guimaraes et al. [13] reported outcomes for 16 patients who were treated with myofunctional therapy for 3 months. Exercises performed included the tongue exercises, soft palate exercises, facial exercises, and stomatognathic function exercises [13]. The snoring frequency and intensity were obtained using the Berlin questionnaire. The median values for snoring frequency reduced from 4 (4–4) down to 3 (1.5–3.5) [13]. The median values for snoring intensity reduced from 3 (3–4) down to 1 (1–2), a 67% reduction [13].

Berreto et al. [11] had two patients who performed myofunctional therapy for 16 weeks. Exercises included tongue exercises, facial exercises, soft palate exercises, pharyngeal exercises, jaw exercises, and stomatognathic function exercises. Snoring was grades 0–4, where 0 = no snoring, 1 = heavy breathing, 2 = light snoring, 3 = snoring that disturbs the bedpartner, and 4 = snoring that disturbs the family [11]. The snore score decreased from 3 to 2 for both patients, corresponding to a 33% reduction [11].

Discussion

There are three main findings from this systematic review. First, the systematic review has demonstrated an improvement in snoring by approximately 50% after myofunctional therapy. An improvement is seen in all the study measures (Berlin questionnaires, VAS, and snoring during the sleep study). The studies have all been in adult patients thus far, and to our knowledge, a pediatric study has not reported outcomes for snoring. Interestingly, the 50% improvement in snoring seen in adults is consistent with the improvement seen in OSA (also 50%) in the meta-analysis performed for myofunctional therapy and OSA [8]. In addition, there was objective improvement in snoring based on polysomnography, with a 31% improvement in the percentage of time spent snoring.

Second, pediatric studies are lacking. Although there are no pediatric studies evaluating snoring, there was a significant improvement in pediatric OSA after myofunctional therapy in the previous meta-analysis [8]. Therefore, it is likely that the improvement in snoring would have also been noted in children; however, we cannot generalize, since there were no studies identified. Anecdotally, a few of the authors' (MC, CG, and SZ) pediatric patients undergoing myofunctional therapy as adjunct or primary treatment for snoring or OSA have been noted to have significant decreases in the snoring intensity and frequency. Interestingly, there is debate regarding snoring in pediatric patients: younger children have a greater chance of sleeping closer to their parents, while older pre- and peri-pubertal children usually sleep farther away from where parents sleep; therefore, the parents are more likely to hear younger children. This snoring phenomenon is even more true for pubertal and post-pubertal teenagers: therefore, there is a clear change in the possibility of perception of snoring during childhood and this has been pointed out in different pediatrics studies. In adults, there is a bias on reporting given that snoring complaints are bedpartner driven; therefore, adults who sleep alone generally do not have people complain unless they share a room for some reason. This bedpartner phenomenon presents a risk of bias concerning snoring outcomes, but despite this potential bias, the studies were consistent in their findings of decreased snoring noted after myofunctional therapy.

Third, although there are improvements in snoring, the mechanism of action as to why myofunctional therapy improves snoring are not completely understood. Given that the lips, facial muscles, tongue, soft palate, oral cavity, and pharynx are exercised by the techniques used in the studies in this manuscript, we hypothesize that the training improves both tone and positioning. An analogy could be seen in people who have never lifted weights and want to start weight training; initially, they will not be able to lift as much weight, but after lifting for 3 months, they will have improved strength and tone. It is possible, therefore, that the myofunctional therapy can help improve the tone and strength of the oral cavity, tongue, soft palate, and pharynx analogous to the improvement in strength and tone that is seen with weight training. Friberg et al. demonstrated that heavy snorers have a neuropathy of the soft palate when compared to control patients and there is even more neuropathy in patients with OSA [21]. Engelke et al. explored orofacial training and hypothesized that it promotes a closed oral rest position which can help to keep the tongue in contact with the palate and lead to an intraoral negative pressure which may help stabilize the pharynx into a more open position (and may also reduce the neuromuscular activity necessary to maintain the open airway) [22].

Limitations

As with all systematic reviews, we are limited to the currently published studies. It is possible that authors who have not seen a difference in snoring outcomes for their patients did not submit their findings, or if they did submit their findings, then maybe their study was not accepted secondary to publication bias against negative studies.

Conclusions

This systematic review demonstrated that myofunctional therapy has reduced snoring in adults based on both subjective questionnaires and objective sleep studies. No pediatric studies were identified. Additional research is recommended based on these initial encouraging results.

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Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study, formal consent is not required. There is no additional need for informed consent as no identifying information is included in this article.

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Can we avoid development of a narrow upper airway and secondary abnormal breathing during sleep?

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The origins of paediatric sleep-disordered breathing are still not completely understood, and more intriguingly, what exists of our understanding is scattered among a variety of fields, some of which traditionally have little professional interaction with one another. Among busy clinicians, time might not permit curiosity about development of sleep-disordered breathing beyond the obvious: adenotonsillar hypertrophy, frequently dispatched by surgical resection with the possibility for short-term clinical improvement in at least some domains.[1] That no long-term (ie, >12–24 months) evidence shows that adenotonsillectomy has any residual benefit, either in terms of sustained symptom improvement or preventing representation of sleep apnoea in later childhood or adulthood, ought to give one pause. Long-term outcomes of adenotonsillectomy for paediatric sleep-disordered breathing have simply not been well studied, though the scarce evidence that does exist does not suggest that the short-term gains of adenotonsillectomy are retained.[2,3] More practically speaking, a notable challenge is that normally developing children and many adults have sleep-disordered breathing in the absence of lymphoid tissue hypertrophy or obesity. Fully understanding the other origins of sleep-disordered breathing is crucial in the pursuit of early identification and further development of interventions that might prevent the development of sleep-disordered breathing in childhood and into adulthood. This concept is truly radical: primary and secondary prevention during childhood of one of the most common serious chronic medical disorders of adulthood.[4]

Such thinking presupposes important developmental and genetic contributions to the disorder, for which a great deal of evidence exists. Craniofacial development, in particular maxillomandibular development, has been shown to be negatively affected by chronic nasal obstruction and mouth breathing in early childhood,[5,6] and chronic nasal obstruction is quite common in children with atopy, an established risk for sleep-disordered breathing. The maxillary hypoplasia, narrowed palatal structure, and steep mandibular plane resulting in children with chronic mouth breathing has been observed clinically for at least 150 years as adenoidal facies, or more colloquially termed long face syndrome. These alterations in craniofacial growth are associated with sleep-disordered breathing,[7] and such features are wholly retained after adenoidal tissue reduction from surgery, anti-inflammatory medications, or the passage of time. Mouth breathing during a critical developmental period in childhood leaves an indelible stamp on craniofacial architecture that lasts a lifetime, and 60% of facial growth is complete before the age of 6 years. Fortunately, in the last two decades, growing evidence has shown that orthodontic approaches can improve to some degree this skeletal and occlusal maldevelopment.[8] Even still, without attention to the continued effects of accompanying oromotor dysfunction to correct mouth breathing, the work of orthodontic expansion and surgery might be in vain.

Although the familial nature of sleep apnoea is well known, specific genetic pathways have not been established. Nonetheless, observations in some genetically based disorders are intriguing. For example, Ehlers-Danlos syndrome, which is secondary to either an autosomal-dominant, autosomal-recessive, or X-linked mutation of genes, is associated with alterations of endochondral growth. Clinically, Ehlers-Danlos syndrome is often marked by an abnormally long face, narrow and high hard palate, and cross-bite, which are physical features highly associated with sleep-disordered breathing. Although initially only abnormalities of the nasomaxillary complex might be seen, as patients enter adulthood they might develop worsening sleep-disordered breathing. Observations of increased occurrence of sleep-disordered breathing in other genetically linked disorders, including dental agenesis and short lingual frenulum syndromes, underscore the importance of bidirectional structure–function relationships to airway stability.[9]

Developmentally, in addition to nasal obstruction and subsequent mouth breathing and abnormal muscle action on the developing upper airway, other early-life factors have been linked to sleep-disordered breathing in children and adults. Poor muscle function (hypotonia) and subsequent poor

suck and swallow from birth have been indicated to be the mechanism for abnormal craniofacial growth and sleep-disordered breathing in premature infants, in whom developmental craniofacial alterations are readily apparent. Those with a history of term birth marked by hypotonia, short frenulum, or other sources of oromotor dysfunction also have an increased risk of sleep-disordered breathing—though some do not present until well into adulthood, at which point such historical details are not usually sought clinically. Myofunctional therapy has recently come into focus as an important domain in the maintenance of long-term, stable improvements in craniofacial architecture and in sleep-disordered breathing, and seems one way to span both developmental and genetic aspects of sleep-disordered breathing.[10]

Recently the European Respiratory Society Task Force on the diagnosis and management of obstructive sleep-disordered breathing in childhood included orthodontic treatment in addition to adentonsillectomy and anti-inflammatory treatment for management of paediatric sleep-disordered breathing. It might be the first step of evolution toward a model of creating long-term stable improvements in craniofacial aberrancies that are present from childhood and that can lead to sleep-disordered breathing in adulthood. But challenges remain: visionary prevention of sleep-disordered breathing is hampered by the well guarded silos of the health-care system, topped by a healthy dollop of future discounting. Of course it can be said that prevention of all chronic diseases is subject to such vagaries, but for sleep-disordered breathing, not only must disparate specialties connect, but a truly joint medical and paediatric approach to the clinical syndrome is needed. Since few sleep centres see patients at all stages and ages of life, the experience and observations that might be learned by following members of three or even four generations of families might not materialise. What's more, such division produces the most dogged of handicaps; our own ignorance of what we do not know.

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We declare no competing interests.

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Critical role of myofascial reeducation in pediatric sleep-disordered breathing

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ABSTRACT

Background: Limited studies suggest that pubertal development may lead to a recurrence of sleep-disordered breathing (SDB) despite previous curative surgery. Our study evaluates the impact of myofunctional reeducation in children with SDB referred for adenotonsillectomy, orthodontia, and myofunctional treatment in three different geographic areas.

Methods: A retrospective investigation of children with polysomnographic analysis following adenotonsillectomy were referred for orthodontic treatment and were considered for myofunctional therapy. Clinical information was obtained during pediatric and orthodontic follow-up. Polysomnography (PSG) at the time of diagnosis, following adenotonsillectomy, and at long-term follow-up, were compared. The PSG obtained at long-term follow-up was scored by a single-blinded investigator.

Results: Complete charts providing the necessary medical information for long-term follow-up were limited. A subgroup of 24 subjects (14 boys) with normal PSG following adenotonsillectomy and orthodontia were referred for myofunctional therapy, with only 11 subjects receiving treatment. Follow-up evaluation was performed between the 22nd and 50th month after termination of myofunctional reeducation or orthodontic treatment if reeducation was not received. Thirteen out of 24 subjects who did not receive myofunctional reeducation developed recurrence of symptoms with a mean apnea–hypopnea index (AHI) = 5.3 ± 1.5 and mean minimum oxygen saturation = 91 ± 1.8%. All 11 subjects who completed myofunctional reeducation for 24 months revealed healthy results.

Conclusion: Despite experimental and orthodontic data supporting the connection between orofacial muscle activity and oropharyngeal development as well as the demonstration of abnormal muscle contraction of upper airway muscles during sleep in patients with SDB, myofunctional therapy rarely is considered in the treatment of pediatric SDB. Absence of myofascial treatment is associated with a recurrence of SDB.

1. Introduction

Obstructive sleep apnea (OSA) has become increasingly recognized as a notable health concern in children given its consequences on behavior, function, and quality of life. The importance of early recognition and treatment in children is paramount to maximizing resolution of symptoms and potential avoidance of OSA syndrome during adulthood. Adenotonsillectomy and palatal expansion have established their roles in the treatment of OSA after demonstrating considerable improvement related to adenoid or tonsillar hypertrophy, maxillary or mandibular deficiency, and orthodontic or craniofacial abnormalities. However, the implementation of other treatment modalities such as myofascial reeducation also may play a role in the optimization of sleep-disordered breathing (SDB).

Functional myofascial reeducation in children has been well-established in the treatment of abnormal orofacial development for more than 40 years [1]. However, few studies have been published supporting the benefits of orofacial reeducation compared to the numerous studies reinforcing the utility of surgical and orthodontic treatments in SDB [2]. Although the role of orofacial education remains largely variable between institutions, the most notable results have been described when myofunctional therapists and orthodontists worked in collaboration to manage orofacial weakness. Although promising, the efficacy of myofunctional therapy in combination with surgical and orthodontic treatment is unclear. The purpose of our study was to evaluate the impact of myofunctional reeducation protocols on orofacial muscle weakness and the treatment of SDB in children following surgical and orthodontic optimization.

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2. Methods

Our retrospective analysis involving prepubertal children diagnosed with OSA, who were referred for orthodontic treatment after presenting with residual symptoms of abnormal breathing following adenotonsillectomy, could only draw a small number of subjects.

Data collection was performed in three different regions of the world, including the San Francisco Bay area, Taiwan, and France. Our analysis involved three different pediatric sleep centers working with otolaryngologists, orthodontists, and functional therapists. The three sleep centers performed all sleep monitoring and were referral centers for large geographic areas. The participating sleep clinics and the orthodontic practices had a collaborative working relationship spanning from 6 to 14 years.

Retrieval of health information for children was variable but targeted those initially seen between the ages of 3 and 6 years preceding confirmation of SBD by nocturnal polysomnography (PSG). If a child was confirmed to have OSA by PSG, the second step was to determine the presence of adequate follow-up and appropriate documentation including subsequent PSGs and documentation from other specialists. Most charts did not fulfill these criteria and were excluded from our study. Charts that had systematic PSG at different phases of follow-up were those of children seen by orthodontists either postadenotonsillectomy or without otolaryngologic intervention. Children often were referred to both a functional reeducation specialist and to an orthodontist in an effort to perform the investigation where myofunctional therapy was practiced. Children were followed in sleep medicine and orthodontic clinics with variable schedules.

Despite being followed in these clinics, postorthodontic treatment PSG records often were unavailable and complete documentation often was absent, excluding a large number of cases. Once the necessary clinical data and PSG reports were confirmed, identifiers were removed and data were extracted (Fig. 1). Anonymous analyses of clinical and polysomnographic data were performed. Retrospective analyses of unidentified PSG and of clinical information were approved by the internal review boards.

All surveyed subjects were prepubertal children between the ages of 3.6 and 6.6 years at the time of their initial visit. Initial assessment of each child included clinical interview, pediatric and sleep clinical evaluation, completion of the pediatric sleep questionnaire (PSQ), a questionnaire validated in different languages [3,4], and nocturnal PSG. Following clinical and PSG evaluation, all children diagnosed with OSA were referred to otolaryngology for surgical evaluation. All subjects except for one had adenotonsillectomy performed and all were followed up after surgery with repeat clinical evaluation and PSG. Subjects with residual OSA detected on postsurgery PSG were sent for orthodontic evaluation [5]. Once the decision regarding orthodontic treatment was made (i.e., rapid maxillary expansion or bimaxillary expansion), recommended myofunctional reeducation also was performed [1].

Subjects were followed at an orthodontic practice during the application of orthodontic treatment and also were followed at their sleep clinics 6 to10 months following initiation of their orthodontic treatment. Concomitant use of myofunctional reeducation was documented as being implemented or as recommendation not followed. Repeat PSG was performed following orthodontic treatment with or without functional reeducation. Data from myofunctional reeducation clinics were used solely to monitor compliance with follow-up appointments and to monitor duration of treatment. Subjects were most often seen during their scheduled orthodontic follow-up. Less frequently they were seen several years after initiation of orthodontic treatment due to planned follow-up visits or due to recurrence of sleep-related symptoms; in this case, they were referred back to sleep clinics. During long-term follow-up visits, the reassessment always involved clinical interviews, PSQ, clinical pediatric evaluation and sleep evaluation, determination of height and weight based on body mass index, sleep medicine examination, myofunctional orofacial status, and nocturnal PSG.

All long-term follow-up PSGs (i.e., last investigation performed) were transferred to new compact discs with recordings formatted in European Data Format. This transfer allowed analysis of all PSGs performed on various sleep programs to be anonymously rescored by a single scorer. PSG rescoring could not be performed on the initial PSGs in the same fashion. However, all centers used the same atlases and guidelines for scoring sleep and breathing variables.

All subjects were evaluated by full-night PSG performed in a sleep laboratory and included the following electrophysiologic parameters, electroencephalogram (EEG) (three channels), electrooculogram (two channels), electrocardiogram, chin electromyogram (EMG), leg EMG (one channel), nasal pressure cannula, oral thermistor, thoracic and abdominal belts, snoring sensor, pulse oximetry, position sensor, and video recording. Variations to the montage included an additional second leg EMG, a fourth EEG, transcutaneous CO_2 or end-tidal CO_2, and the thoracic and abdominal belts were either piezoelectric or inductive plethysmography. All recordings lasted a minimum of 7.5 hours. Individuals were assigned corresponding identification numbers and their data were compiled using the Microsoft Excel program to perform statistical analyses of the results.

Myofunctional reeducation specialists were trained in various countries and were divided into two categories of either speech therapists or specialists in muscle reeducation. Speech therapists were trained in the United States, whereas muscle reeducation specialists were trained outside of the United States. Myofunctional specialists obtained university degrees in functional reeducation with a subspecialty in myofunctional reeducation and practiced validated therapeutic protocols. Treatment protocols are similar in different countries [1]. In the United States, if not sanctioned by a diploma, courses are administered (particularly in California) by trained individuals often trained in other countries. The myofunctional re-educators involved in the three participating sleep centers had similar myofunctional reeducation training, including several years of experience with treatment modalities and use of the same type of report forms. Similar exercise regimens and daily durations of treatment were recommended to parents. Frequency of visits varied not with the sleep center but with the individual and were based on the needs of each case. Visits were more frequent at the initiation of treatment and less frequent as time passed. Daily exercise performance was recorded by parents in a log and reviewed by re-educators at visits. Reeducation programs were completed after 2 years.

3. Reeducation

Myofunctional reeducation involves strengthening of the tongue and orofacial muscles by teaching individuals how to reposition muscles to the appropriate position. The tongue should be kept in a high position during sleep with its dorsal-terminal end in constant contact with the palatine striae located on the anterior aspect of the palate. Reeducation typically is easier in children ages 6 years and older, but it is largely related to the degree of effort parents make in reinforcing a subject to perform his or her exercises. Exercises are initially repeated several times per day with a quick initial increase in frequency during the earliest phase of treatment. This phase requires the subject and one parent to frequently follow-up with a specialist during the first 6 months and less frequently thereafter. The amount of follow-up depends on the duration of therapy needed, but once the subject has gained the desired tongue position along with appropriate strength the

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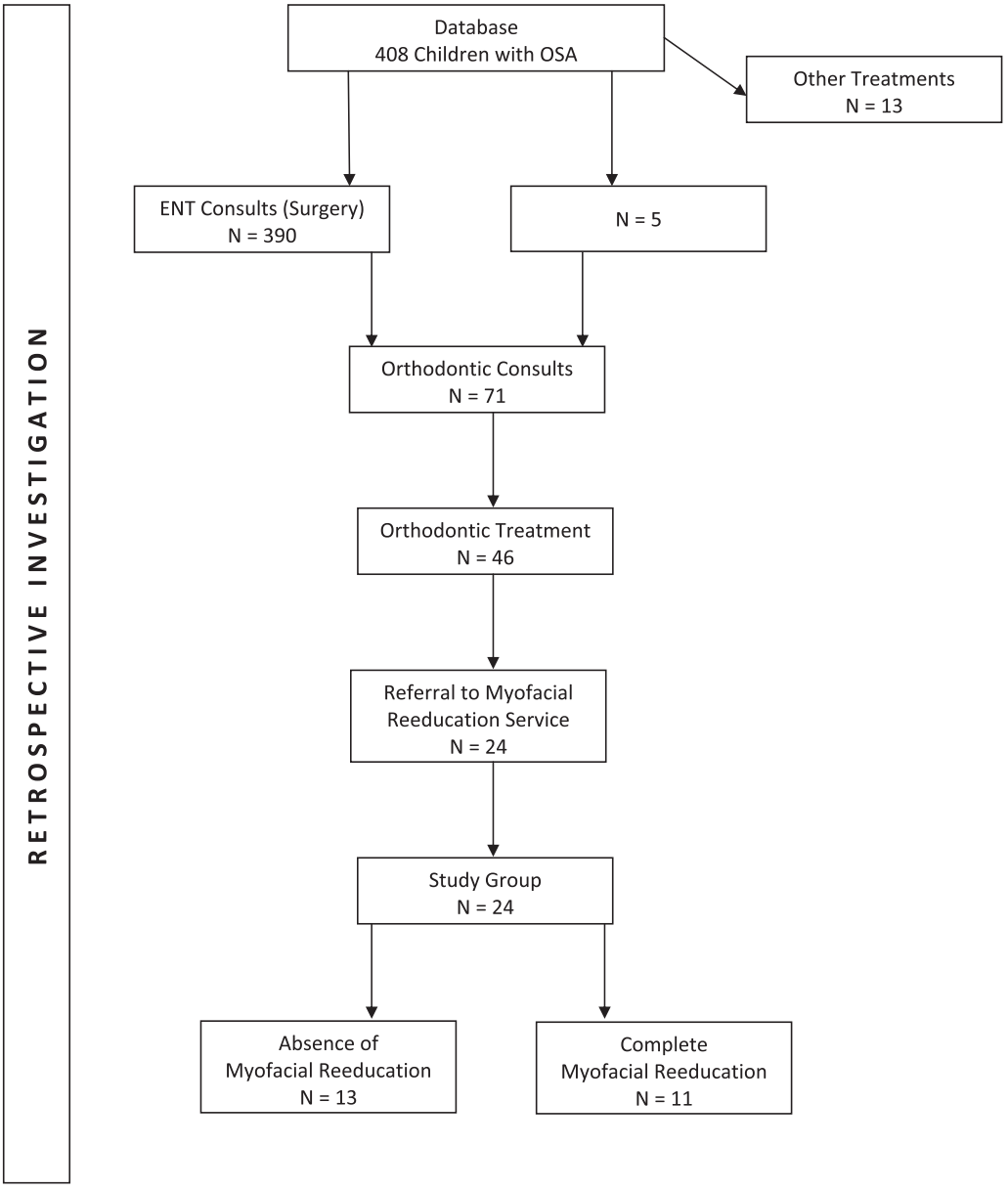

Fig. 1. Graph of initial charts retrieved for study. The graph documents the poor follow-up that occurred for a long time in the past after diagnosis and initial treatment of obstructive sleep apnea (OSA). Many children had no sleep follow-up and absence of sleep recordings postadenotonsillectomy. Seventy one children were seen again posttreatment and had systematic investigation by both a sleep specialist and an orthodontist. Evaluation indicated validity of performing orthodontic treatment in 46 children. Rapid maxillary expansion and bimaxillary treatments were recommended (32 rapid maxillary expansion; 14 bimaxillary treatments). Only 26 children had good documentation of treatment at follow-up. Myofunctional therapy had been recommended in 24 of them in association with orthodontic treatment. However, myofunctional therapy was only performed in 11 children and 13 either did not follow the recommendations or quickly dropped out of the study.

frequency of follow-up can be extended. The subject is then primarily monitored to insure continued appropriate development until the completion of treatment. The investigation took place between the 22nd and 50th month following termination of the myofunctional treatment program, independent of the amount of time spent in the program. If the program was never implemented, subjects were seen for follow-up between the 28th and 34th month following termination of orthodontic treatment.

4. Analysis

The information collected for our study included gender, age at time of each treatment phase and testing, clinical concerns and symptoms, PSQ results, and results of clinical orofacial evaluation. Description of the nasofacial and orofacial examination included Friedman classification tonsil size [6]; modified Mallampati score [7,8]; calculated overjet (mm); evaluation of the hard palate, which was categorized as high and narrow, low lying, or normal; and the presence of enlarged inferior nasal turbinates categorized as occupying less than 50% or 50% or more of the space inside the nostrils. The presence or absence of nasal valve collapse, deviated septum, small mandible, overbite, and awake-mouth breathing also were documented. Absence of anterior short frenulum was affirmed. Head posture was noted in lateral position [9,10] but nuchal Solow angle was not calculated. Clinical information that was recorded during follow-up evaluation but was unavailable at initial presentation included preferential chewing to one side, presence of visualized facial asymmetry, presence of palpable asymmetry of masseteric muscles at maximum clinching, and results of myofunctional evaluation performed by a reeducation specialist. Such information was retrieved from orthodontic and myofunctional reeducation charts. Individual

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orthodontists and myofunctional re-educators worked as a team with one orthodontist working with one preferred re-educator.

The long-term follow-up PSG recording was scored blindly by a single investigator, whereas all other PSG results were reported without access to the actual recording. The scoring was based on the manual for sleep scoring by Rechtschaffen and Kale [11], the American Sleep Disorders Association recommendation for EEG arousal scoring [12], and the American Academy of Sleep Medicine criteria for scoring hypopneas and apneas [13]. Hypopneas were defined by a 50% reduction in nasal cannula curve amplitude and an associated drop of 3% or more in oxygen saturation. The usual subdivision of obstructive, mixed, and central events was followed. Events defined as postarousal central apneas were eliminated from the apnea–hypopnea index (AHI) score. There was additional scoring of flow limitation based on the definition of Hosselet et al. [14]. The nasal cannula curve was compared to published patterns involving flattening or truncation of the curve during inspiration [15]. The percentage of flow limitation was determined by the number of 30-second epochs containing the presence of flow limitation [16]. An epoch was scored with flow limitation if it was present for more than 15 seconds (i.e., more than 50% of the scored PSG epoch). The percentage of flow limitation was calculated by dividing the total flow limited sleep time (i.e., number of 30-s epochs scored with flow limitation multiplied by two) by the total sleep time [16]. The score of flow limitation was not available for the initial recordings in many subjects and was only systematically obtained in the reports from the postorthodontic treatment and the rescored recordings.

Presence or absence of mouth breathing was noted in the results of each PSG based on the mouth thermistor tracing but was not quantified. As previously mentioned the long-term follow-up PSGs were scored by a single-blinded scorer. Comparisons of PSG results between the subjects with and without myofunctional treatment were performed using Wilcoxon signed rank tests and χ^2 tests.

5. Results

5.1. Subjects involved in retrospective survey

An initial database of 408 pediatric cases diagnosed with OSA by PSG was established and was evaluated by an otolaryngologist who performed surgery and who subsequently had a postsurgical PSG. As previously mentioned many charts were incomplete when looking for further follow-up and were excluded. From this database, 71 subjects with documented visits to an orthodontist postadenotonsillectomy were retrieved. Children seen by orthodontists for evaluation had better documentation than those seen in other places, reflecting the higher representation of this subgroup in the follow-up survey. Children lacking the syndromic presentation but who had close orthodontic follow-up led to closer evaluation and anatomic findings observed in subjects recognized with SDB. Documented charts revealed that 46 of these subjects were considered for orthodontic treatment and simultaneous myofascial reeducation due to persistent OSA at PSG, even if improvement was noted postadenotonsillectomy. Of these 46 subjects, 24 had retrievable follow-up documentation including myofunctional treatment information (Fig. 1 [graph]). These 24 nonoverweight subjects (14 boys) (17% of initial database) formed the study group of those who satisfied the inclusion parameters being evaluated.

5.2. Evaluation at entry

The results at entry are presented in Tables 1 and 2. All subjects presented with clinical concerns, symptoms, and anatomic findings consistent with OSA, with the PSG confirming the diagnosis. Anatomic investigation at entry showed that out of the 24 cases, 23 had a tonsil-size scale of three or four. Twenty-three subjects had a modified Mallampati scale score of three or four, and one subject had a modified Mallampati scale score of two. Inferior nasal turbinates were scored with occupying nasal space >50% in 13 cases. Nasal septum deviation was found in 14 cases, and all of them had a narrow palatal vault. Fourteen subjects had been referred and treated for nasal allergies with treatment consisting of nasal steroids, allergic desensitization, or both. Of the 401 initial nonoverweight subjects being evaluated, 90% had a tonsil score of three or four, 73% had a modified Mallampati scale score of three or four, and 48% were mentioned to have a high and narrow palatal vault. Statistics revealed from the χ^2 test indicated that the 24 studied subjects were significantly different in Mallampati scale score three and four ($P = .01$) and presence of high and narrow palatal vault ($P = .001$), but the initial anatomic description was similar in 46% of the cases.

5.3. Initial treatment

Twenty-three subjects had adenotonsillectomy (T&A). Additionally, five subjects had radiofrequency ablation of the inferior nasal turbinates performed at the time of T&A. One girl was felt to have small tonsils that would not benefit from surgery but was directly referred for orthodontia, given her high and narrow arched hard palate. None of the subjects had an abnormally placed anterior frenulum.

The data retrieved postadenotonsillectomy and postorthodontia treatments are presented in Tables 1 and 2, including the one girl subject who was sent directly for orthodontia treatment. Although symptoms were reportedly improved in all 23 cases following surgery, clinical concerns and symptoms were not completely eliminated, and the persistence of abnormal breathing was confirmed with PSG analysis. The presence of mouth breathing was noted in all postsurgical cases but was not quantified. All 24 subjects were sent to orthodontists and in all cases were expected to benefit from orthodontic treatment.

Following orthodontic evaluation rapid maxillary or bimaxillary expansion was performed, and orthodontic equipment was kept in place for 8 to12 months. Follow-up evaluation in the sleep clinic with follow-up PSG was performed near the time of orthodontic equipment removal (Tables 1 and 2). Clinical concerns and symptoms related to SDB were absent with the exception of one subject with persistence of attention deficit and hyperactivity disorder that may not have been related to SDB. Despite noted improvement in symptoms following treatment, persistence of intermittent agitated sleep with teeth clenching was reported, for which the subject was referred back to the orthodontist. PSG showed a normal AHI and oxygen saturation. However, in seven cases presence of mouth breathing without indication of frequency was identified in the PSG. Parents also had been referred to myofunctional re-educators. Review of charts indicated that parents regularly followed up for orthodontic treatments. Of the 24 subjects, 10 did not go to myofunctional reeducation and three children missed routine appointments and training sessions, did not adhere to the requested exercise regimen, or did not participate in long-term follow-up with re-educators. Conversely 11 subjects were adherent to myofunctional treatment and were compliant with routine follow-up with their orthodontists. None of the subjects had begun puberty throughout the follow-up period and all remained Tanner stage 1. Children at end of treatment were told to have a yearly orthodontic follow-up to assure persistence of healthy oral development. As part of this follow-up, as subjects were growing orthodontists recommended a follow-up evaluation at the sleep clinic; the timing of this postorthodontic treatment reevaluation ranged between 38 and 50 months postorthodontic treatment.

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Table 1
Clinical concerns reported by parents.

	Entry	Post-AT	Postorthodontics	Follow-up study
No. of children (*n*)	24	23	24	24
Age (y)	5.5 ± 1.2	5.10 ± 1.3	7.3 ± 1.5	11.6 ± 1.2
Snoring	24	2	0	5
Agitated sleep	22	11	1	5
EDS	10	0	0	0
Fatigue	15	23	0	11
Insomnia	5	2	0	5
Hyperactivity and inattention	7	2	1	11
Poor school performance	0	0	0	11
Parasomnia	10	0	0	0
Bruxism	3	3	1	3
Morning headache			0	2

Abbreviations: AT, adenotonsillectomy; *n*, number of children; y, years; EDS, excessive daytime sleepiness. One child never had adenotonsillectomy (see text).
The number in each column represents the number of children of which the clinical concern was mentioned by parents.
Parents did not report of school performance concerns in younger children, but they did report concerns of attention and hyperactivity, children often were considered to have possible attention-deficit/hyperactivity disorder.
As previously reported, parental concerns associated with obstructive sleep apnea vary with age [36].

Table 2
Sleep-disordered breathing documented with polysomnography.

	Entry	Post-AT	Postorthodontics	Follow-up study	
				No reeducation	Reeducation
No. of children (n)	24	23	24	13	11
Age (y)	5.5 ± 1.2	5.10 ± 1.3	7.3 ± 1.5	11.8 ± 1.4	11.5 ± 1.2
AHI (event/h)	10.5 ± 2.6	4.3 ± 1.6	0.4 ± 0.3	5.3 ± 1.5	0.5 ± 0.4*
Lowest SaO_2 (%)	90 ± 1.5	92 ± 1	95 ± 1	91 ± 1.8	96 ± 1**
Flow limitation (% TST)	–	–	10 ± 10	72 ± 14	5 ± 8***

Abbreviations: AT, adenotonsillectomy; *n*, number of individuals affected; y, years; AHI, apnea–hypopnea-index; TST, total sleep time.
Percent of flow limitation was determined based on number of 30-second epochs of sleep with abnormal nasal cannula contour not responding to definition of hypopnea with flattening of curve.
If abnormal pattern was present for more than 50% of sleep epoch, epoch was scored as flow limited. The percentage was calculated by number of flow-limited epochs × 2 (i.e., number of min) divided by TST in minute. The percentage was extracted from this calculation. Flow limitation was unavailable in most of the initial reports and initial posttreatment recordings. Flow limitation was introduced in polysomnography scoring later on, and the scoring criteria and definition used were those of the Stanford center, which had trained scorers [33].
Myofunctional treatment: significant differences between treated and untreated children Wilcoxon signed rank test.
* Significant difference ($p = .001$).
** χ^2 test ($p = .01$).
*** χ^2 test ($p = .0001$).

5.4. Evaluation at long-term follow-up

Results are presented in Tables 1 and 2. There was a clear difference between the subjects who had valid myofunctional reeducation and those who did not. Clinically, none of the 11 subjects with reeducation reported clinical concerns related to sleep disorders, and their PSG showed no evidence of breathing abnormalities during sleep. All subjects had continuous nasal breathing noted on PSG. Wilcoxon rank sum test showed that the AHI was significantly different between the two groups ($P = .001$) and χ^2 test statistics showed that the percentage of lowest oxygen saturation and the percentage of flow limitation also were significantly different ($P = .01$ and $P = .0001$, respectively) At the long-term follow-up, the 13 other subjects reported persistent daytime concerns; parents indicated presence of school difficulties including inattention in school and in some degree attributed these to fatigue in the subject. Interviews and questionnaires also indicated that specific sleep concerns persisted in some subjects, including the presence of snoring, agitated sleep, symptoms of sleep-phase delay, and morning headaches (Table 1). Children with the highest amount of flow limitation (Fig. 2) and the highest AHI scores reported more frequent concerns. All 13 subjects in this subgroup displayed mouth breathing during sleep, as demonstrated by analysis of the mouth thermistor curve on the PSG (Fig. 3). Clinical evaluation reported abnormal head posture in four of the subjects during the daytime (Fig. 4), and the previous improvements noted at the time of removal of the orthodontic equipment were lost after development of a counter-clockwise rotation of the maxilla and high and narrow palatal vault. Such findings were confirmed on evaluation by an orthodontist. These anatomic presentations were not found in the 11 subjects with normal breathing during sleep.

Myofunctional evaluation of the orofacial region showed that subjects had an abnormally low tongue position in the mouth while awake. Among the subjects, 12 were unable to perform appropriate clicking sounds with the tongue, 10 were unable to protrude their tongue upward when asked to try to touch their nose with the tip of their tongue, four had difficulties holding a button between their lips, and one had difficulties swallowing while drinking quickly. All subjects acknowledged having a preferential side for mastication, and nine subjects presented with slight asymmetry of masseteric muscles when evaluated during active contraction. At the end of the evaluation by re-educators, all subjects were scored with abnormal orofacial muscle tone while awake. All subjects without clinical concerns had been scored as normal at myofunctional testing.

6. Discussion

Our retrospective study has typical limitations associated with retrospective studies, particularly when evaluating subjects diagnosed with OSA years ago. First despite the many subjects with

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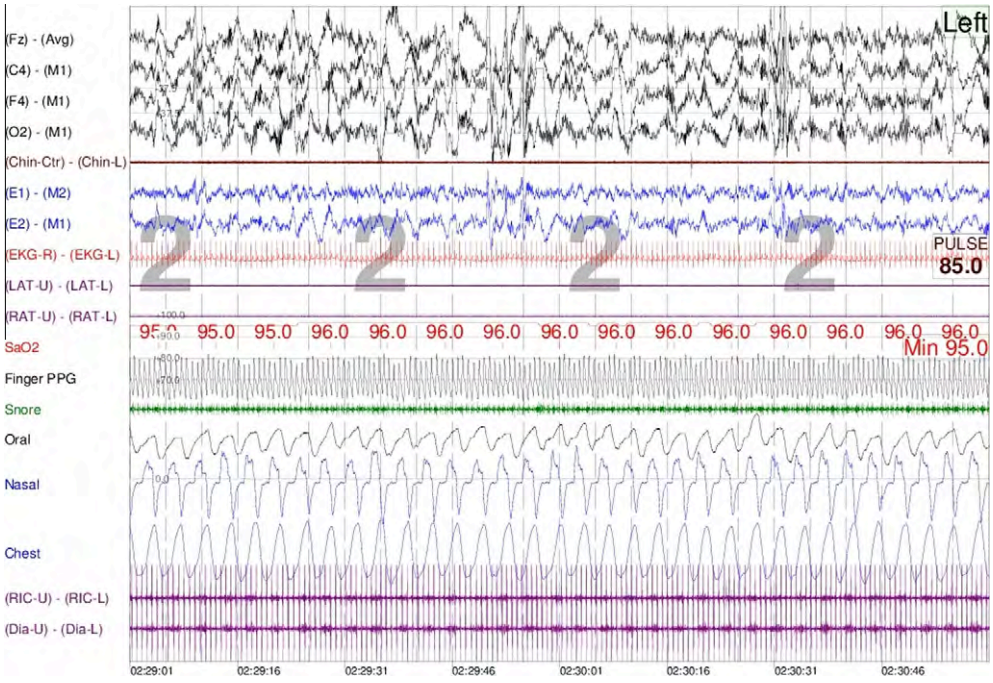

Fig. 2. Example of polysomnography (PSG) segment of a subject with recurrent symptoms postadenotonsillectomy and with orthodontic treatment but without myofunctional therapy. Note the continuous flow limitation expressed as an abnormal curve of the nasal cannula recording (#14 from top).

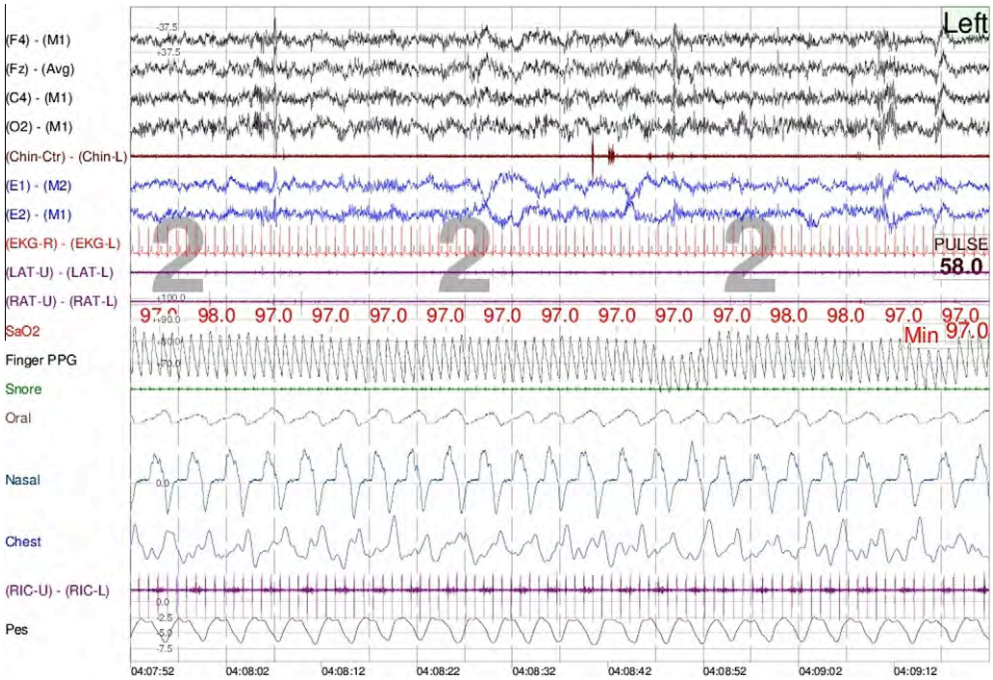

Fig. 3. PSG segment of mouth breathing and flow limitation. In a subject with recurrent symptoms, PSG showed abnormal nasal curve recording contour (tracing from nasal cannula) with flattening of the curve (#14 from top), presence of continuous nasal breathing as indicated by mouth thermistor recording (#13 from top), and presence of continuous increase effort indicated by esophageal manometry (Pes) (#17 from top) with a peak end–inspiratory pressure oscillating approximately 8-cm H_2O compared to baseline supine with normal breathing of 3-cm H_2O.

OSA treated with adenotonsillectomy alone or with adenotonsillectomy and orthodontics, this is a retrospective study with a relatively small number of subjects. This small sample was largely due to the few subjects having the documented data necessary for analysis and the absence of long-term follow-up in OSA patients. Obtaining information from three different locations with differing referral patterns also was challenging. Our goal was to assess the role of myofunctional reeducation, and medical records were not always easily retrievable. Although the different locations worked together in data collection and analyses for other investigations involving pediatric subjects with OSA, the different locations may have created variability in data collection and results. Rescoring of all follow-up PSG records obtained at the last sleep clinic visit was performed by a single-blinded scorer in an effort to avoid interlaboratory and interscorer variability. However, the initial diagnostic PSGs from all the subjects was unavailable for

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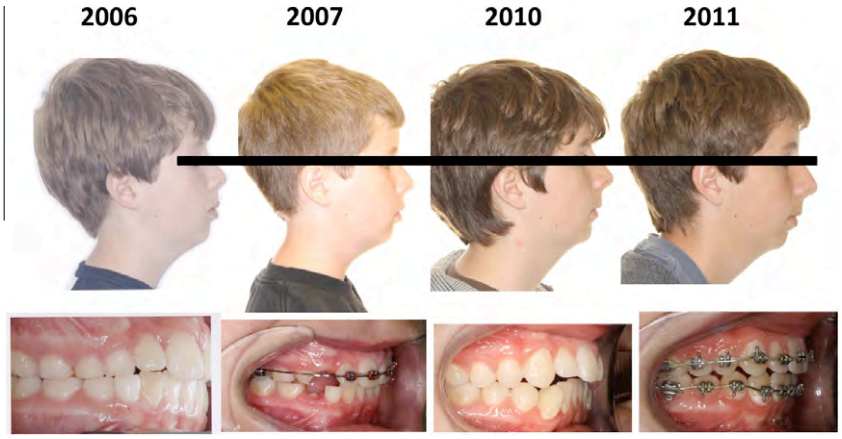

Fig. 4. Abnormal head position during wakefulness with abnormal breathing during sleep. Note the progressive change in head position over time associated with the development of an abnormal nuchal angle. The angle was normal in 2007 with progressive development of abnormal head position associated with abnormal breathing and OSA despite absence of snoring but the presence of mouth breathing during sleep. The last photo clearly shows the abnormal head-neck posture related to the sleep-disordered breathing.

review and results solely relied on the PSG reports kept on file. Finally the different laboratories were affiliated with different healthcare systems that may have influenced subjects' ability to accept or adhere to treatment recommendations. The cost of myofunctional reeducation could have been free, covered by medical insurance, or paid entirely out of pocket. Numbers may have been higher if this type of study had been performed in Brazil where such treatment is routinely included in the management of patients with OSA [2]. Additionally most of the data obtained were from children seen at orthodontic clinics, likely adding another bias. We do not claim that all children with OSA should have myofunctional reeducation, and our study does not show the role of myofunctional treatment performed without orthodontic treatment postadenotonsillectomy; however, clearly more studies are needed. Despite these biases, our study is the first retrospective study investigating myofunctional reeducation and underlining its benefits in the treatment of SDB in the pediatric population. Approximately 46% of nonoverweight children initially diagnosed with OSA had similar anatomic risk factors as in our 24 children. It is possible that adenotonsillectomy itself led back to nasal breathing during sleep, but such changes should be objectively documented several months' postsurgery. The intricate relationship between nasal breathing and orofacial growth has been studied for several years [17–28], and myofunctional reeducation programs were established with the understanding and intention of optimizing orofacial development and breathing in children. Mouth breathing is associated with malposition of the tongue, which further reinforces impaired development and growth of the maxilla and mandible. The intricate relationship between breathing and orofacial growth was studied for many years, supported by experimental animal models that were extensively studied in the 1970s. Harvold et al. [17], Miller et al. [18], and Vargervik et al. [19] showed that abnormal nasal breathing leads to abnormal EMG discharges in tongue and orofacial muscles with secondary impact on the facial skeleton and dentition. Impairment of nasal breathing also has been investigated in children and has demonstrated an impact on facial growth, head posture, and general medical consequences [20–29]. Swedish researchers also have suggested that early mouth breathing without appropriate humidification of air through the nose leads to repetitive tonsillar trauma [29]. Such trauma may lead to an inflammatory response of the tonsils, previously histologically demonstrated and also may lead to progressive enlargement of an already narrow airway.

With the understanding of these implications, treatment programs were established with the goal of optimizing orofacial development to improve breathing in children. The benefits of the combination of orthodontic and myofunctional reeducation on breathing, speech, swallowing, orofacial growth, and the elimination of abnormal head-neck posture, with a focus on eliminating tongue and orofacial muscle hypotonia, have been published particularly in the orthodontic literature [2]. This movement also has led to the development of myofunctional reeducation specialists whose expertise is sanctioned in many countries. There is no systematic prospective study involving myofunctional therapy in children with OSA, but there has been an abundance of literature on the benefits of myofunctional treatment on growth and orthodontic development for more than 20 years [1]. This literature emphasizes the importance of nasal breathing and obtaining good orofacial muscle tone to maintain orthodontic gains in children. It also stresses maintenance of obtained gains during pubertal years. However, none of these studies involved systematic PSG evaluation, and the reports emphasized orthodontic development rather than nocturnal breathing. SDB invariably involves abnormal nasal breathing and impaired facial growth associated with mouth breathing. Unfortunately, this concern often has been ignored. Our report indicates that a combined treatment approach including adenotonsillectomy and orthodontia with myofunctional reeducation can be crucial in the elimination of OSA. This finding is especially critical, as the failure to eliminate oral breathing will lead to the reappearance of the OSA syndrome in children. A recent prospective follow-up study [30] lasting 36 months that included clinical and PSG data had followed 67% of an initial OSA children cohort and showed that 68% of the children still involved in the study had either worsening abnormal breathing if adenotonsillectomy had not fully resolved the concern (with complete OSA resolution defined as AHI <1) or had reappearance of OSA, even if complete resolution had been obtained postadenotonsillectomy. Mean AHI of the cohort was approximately six events per hour and none of the children had been monitored for mouth breathing or received myofunctional therapy. Treatment achieving a normal upper airway in children does not guarantee normal tongue position or normal tongue and orofacial muscle strength during sleep. This in turn affects the development of the airway as demonstrated in monkey models [17–19]. Persistence of oral breathing during sleep directly affects tongue position and strength as well as that of the orofacial muscles, leading to abnormal airway development unless myofunctional reeducation is performed to avoid this evolution.

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Despite its deficiencies our study highlights the importance of influencing normal facial growth by using the available tools and resources to optimize orofacial development in children with abnormal breathing during sleep. As previously mentioned, although integrated care between myofunctional re-educators and orthodontists may be routine in some countries, such as France, Belgium, Brazil, or Taiwan, this is not the case in all parts of the world. The lack of understanding of these interactions leads to the misconception that pediatric OSA is an upper airway syndrome and not a facial growth dysfunction with secondary impact on the upper airway.

Finally, our study shows that scoring only apneas and hypopneas is not sufficient to recognize abnormal breathing during sleep. Flow limitation [14] is a much more adequate indicator of abnormal breathing in our patients. Previous studies have shown the involvement of flow limitation in parasomnias and in abnormally high amounts of cyclic alternating pattern phases A2 and A3 [31]. Chervin et al. [32] showed that abnormal breaths that do not meet criteria for defined apneas and hypopneas still may have a disrupting effect on the sleep EEG. Recently it was shown that young women with an abnormal amount of flow limitation and a low or normal AHI had the same clinical presentation as women with pathologic AHIs [33]. It also is imperative that we recognize abnormal breathing in children during sleep and have the knowledge to select the appropriate indices to detect SDB [33]. This knowledge requires increased attentiveness for abnormal breathing, as many of our children had no snoring likely due to prior treatment, yet clearly displayed flow limitation disrupts their sleep along with persistent symptoms. We must treat children to optimize and insure normal development of the airway, orofacial muscle strength, and positioning, and in turn normal breathing during sleep. Myofunctional reeducation may be considered to treat adult patients with OSA; however, as demonstrated by Guimaraes et al. [2] even if it is effective, it has a limited impact in adulthood. This finding further reinforces the importance of early identification and intervention during childhood development to optimize normal growth of the airway and to insure a lasting impact in the treatment of SDB. With the help of orthodontists and myofunctional therapists and appropriate testing of nasal resistance in children, we may be able to recognize and treat children at risk for SDB early in life [1,34].

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2013.01.013.

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Original Article

Effect of myofunctional therapy on children with obstructive sleep apnea: a meta-analysis

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ABSTRACT

Objective: To systematically review the current literature for articles describing the effect of myofunctional therapy on pediatric obstructive sleep apnea (OSA) and to perform a meta-analysis on the sleep study data.
Methods: Three authors (A.B., K.K. and M.C.) independently searched from inception through April 20, 2020 in PubMed/MEDLINE, Scopus, Embase, Google Scholar and The Cochrane Library. Mean difference (MD), standard deviations and 95% confidence intervals were combined in the meta-analysis for apnea-hypopnea index (AHI), mean oxygen saturations, and lowest oxygen saturations (nadir O2).
Results: 10 studies with 241 patients met study criteria and were further analyzed. The AHI reduced from 4.32 (5.2) to 2.48 (4.0) events/hr, a 43% reduction. Random effects modeling demonstrated a mean difference in AHI of −1.54 (95% CI -2.24,-0.85)/hr, z-score is 4.36 ($p < 0.0001$). Mean oxygen saturation increased by 0.37 (95% CI 0.06,0.69) percent, z-score is 2.32 ($p = 0.02$). There was no significant increase in nadir O2.
Conclusions: Despite heterogeneity in exercises, myofunctional therapy decreased AHI by 43% in children, and increased mean oxygen saturations in children with mild to moderate OSA and can serve as an adjunct OSA treatment.

1. Introduction

Obstructive sleep apnea (OSA) can affect 1–6% of children [1]. OSA is characterized by repeated episodes of upper airway obstruction during sleep [2]. Untreated OSA can lead to adverse cardiovascular, neurocognitive outcomes and lower quality of life [3,4]. Pathophysiology of pediatric OSA differs significantly from adult OSA [5]. Children with OSA report narrower maxilla, mandibular retrognathia, longer lower facial height, caudal placement of hyoid bone, larger adenoids, tonsils and soft palate [6,7]. Facial growth in pediatric OSA is influenced by route of breathing. Mouth breathing induces morphological skeletal changes in the maxilla and mandible which is at least partially reversible after treatment [8,9]. In children, the primary cause of OSA is thought to be hypertrophy of upper airway lymphoadenoid tissue [10]. This is not seen in adults. Consequently, adenotonsillectomy is regarded as the first line of treatment for pediatric OSA [11]. However, there is a high prevalence of residual OSA despite adenotonsillectomy [12]. Causes for residual OSA may be due to (1) abnormal craniofacial anatomy, (2) increased tissue deposition/infiltration or (3) due to increased airway collapsibility. Decreasing airway collapsibility by strengthening airway muscles has been utilized in myofunctional therapy (MT) [13,14]. A meta-analysis of myofunctional therapy demonstrated reduction in severity of OSA in adults and children [15]. However, this meta analysis included only two pediatric studies [14,16]. Another recent meta analysis concluded that there is a high level of heterogeneity of myofunctional therapy interventions and high risk of bias due to low quality evidence [17]. Due to intrinsic differences in the pathophysiology of OSA between adults and children, it is important to look at the pediatric data separately.

Myofunctional therapy was first described in 1918, to increase mandibular growth and improve nasal breathing [18]. In 1999, it

Institution where the work was primarily performed: Riley Hospital for Children at Indiana University Health.

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was proposed as a new therapy for management of OSA [13]. The premise of this therapy is built on isotonic and isometric exercises that promote the sensitivity, proprioception, mobility, coordination and strength of orofacial structures [19]. MT include different types of soft palate, tongue and facial muscle exercises. These exercises are performed daily and lead to strengthening of the tongue and orofacial muscles thereby realigning to the correct intraoral position. It is relatively easy to teach and has very few complications. However, it relies on patient co-operation and adherence for optimal benefit. Recently, some studies have used a passive MT through an intra-oral device instead of an active exercise structure and is expected to have improved compliance. However, no study has evaluated the effect of active and passive MT separately on OSA in children.

The objective of this study is to systematically review the literature for articles evaluating active and passive MT as treatment for OSA in children and to perform a meta-analysis on the available polysomnographic data.

2. Methods

The **inclusion criteria** for this study were as follows (with the PICOS acronym):

- *Patients:* any child (<18 years) with OSA
- *Intervention:* myofunctional therapy, active or passive
- *Comparison:* pre- and postintervention sleep study data
- *Outcomes:* apnea-hypopnea index (AHI), mean oxygen saturation, nadir oxygen saturation (LSAT), prevalence of mouth breathing (determined by study PI)
- *Study Design:* case series, case–control, cohort, and/or randomized controlled trials

Studies were included if outcome data was reported before and after myofunctional therapy was implemented. Post intervention study should have been conducted at the conclusion of myofunctional therapy.

2.1. Information source

Databases include the Ovid Medline, Embase, Cumulative Index to Nursing and Allied Health, Cochrane Library, Scopus searched from inception through May 1st, 2020.

2.2. Search strategy

- Terms related to obstructive sleep apnea, obesity hypoventilation, snoring, sleep disordered breathing, or upper airway resistance/obstruction were searched, and combined with terms for myofunctional therapy, myotherapy, myology, myofacial, myofascial. Additionally, facial anatomical terms (lip, tongue, facial muscles) and speech therapy or exercises were also searched.
- Refined for children 0–18 years old in addition to text word searching for keywords related to children.

The detailed search strategy has been outlined for Ovid Medline in supplemental data.

2.3. Data extraction

Search strategy was discussed by all three participants at the onset of the study. Once search study was finalized, librarian KK ran the search and provide all the references to both reviewers in an Endnote file.

Both reviewers (AB and MC) independently screened the titles, abstracts and relevant full text articles and finalized the articles to be included, containing primary outcome (AHI).

AB extracted data and entered it in Review manager 5.3 for each of the outcomes. MC checked the extracted data.

2.4. Data included

1. Study design and methodology (prospective, retrospective, case control, randomized controlled trial)
2. Participant demographics and baseline characteristics including age, gender, prior history of adenotonsillectomy, orthodontic treatment
3. Intervention: Data was collected on the nature of the intervention, including, whether it was active or passive in nature.
4. Outcomes: mean (SD) AHI, mean oxygen saturations, nadir oxygen saturations prior to myofunctional therapy as well as post intervention. Number of patients with mouth breathing (determined by study PI) before and after mouth breathing.

2.5. Data items

If a study reported outcomes for obstructive AHI and overall AHI, we selected obstructive AHI, as this number includes only the obstructive component derived from the sleep study.

Secondary outcome included mouth breathing. Although mouth breathing should be assessed by polysomnogram, several studies have measured mouth breathing indirectly by using Iowa Oral Performance Instrument (IOPI) to evaluate tongue endurance and muscle strength.

Any disagreement between individual judgments was resolved by a discussion between AB and MC. Final inclusion was decided by MC.

Missing data (unreported or clarifications) was handled by contacting the first author via email. A second email was sent in two weeks if no response was received. If no response was received after the second email, then a third email was sent to the last author. If no response was received, then that particular study was excluded from the analysis for the missing outcome.

2.6. Data synthesis

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were utilized for this review as much as possible [20].

Data was synthesized using Review Manager 5.3 software. The data collected for meta-analysis included means, standard deviations, mean differences, standardized mean differences and 95% confidence intervals (95% CI). To determine the standardized mean differences' magnitudes of effect, we used the guidelines outlined by Cohen: 0.2, a small effect, 0.5 a medium effect and 0.8 a large effect [21].

2.7. Statistical analysis

Means and standard deviations were calculated before and after myofunctional therapy for AHI, mean oxygen saturations and nadir oxygen saturations. Studies providing raw patient data without means and standard deviations were manually calculated or the respective authors were contacted for the data. The null hypothesis for this study is that there is no difference in outcome data before and after myofunctional therapy. For the meta-analysis, the program: Review Manager (RevMan) (Computer program) Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane

Collaboration, 2014) was used. A random-effects model was used throughout the meta-analysis. The means, standard deviations, and 95% confidence intervals (CI) were calculated by REVMAN. I^2 statistic was used for determining the inconsistency (inconsistency levels: low = 25%, moderate = 50% and high = 75%) [22]. The Cochran Q statistic was used for determining heterogeneity, with a $P \leq 0.1$ being considered as significant heterogeneity [23]. If inconsistency and/or heterogeneity were identified, then a sensitivity analysis was performed by individually removing one study at a time.

Forest plots were created after extracting pre and post myofunctional therapy data for each of the primary outcomes. Mean difference and effect estimate were combined using random effects meta-analysis for AHI, mean oxygen saturations and nadir oxygen saturations pre and post MT. Odds ratios were combined using a random effects meta-analysis for mouth breathing. Effect estimate was reported for all four outcomes.

A funnel plot to assess for risk of publication bias was performed if at least 10 studies report a specific variable (as recommended by Cochrane collaboration).

3. Results

A total of 598 studies were screened for relevance and 470 were excluded as they did not meet study criteria. After identification of 128 potentially relevant studies, they were downloaded, and abstracts were reviewed. Ten studies met criteria and were selected for this review [14,16,24–31]. We were unable to obtain outcome measures from one of these studies, despite contacting the authors. This study was removed from our quantitative analysis [14]. Fig. 1 summarizes the flow for study selection. One study was a case report [24], two studies were retrospective case series [14,28], three studies were prospective case series [25,29,31], one study was a prospective case control [26] and three studies were randomized controlled trials [16,27,30]. None of the randomized controlled trials were blinded and none gave details on randomization.

Table 1 depicts details of the selected studies. three studies used passive myofunctional therapy [25,26,29], six studies used active myofunctional therapy while one study had three arms, dividing the cohort into passive, active myofunctional therapy and control groups [27]. 285 children were included in this review, of which 241 received myofunctional therapy and the remaining were 44 children were controls [26,28,30]. If the same authors published more than two articles, they were contacted to ask whether data from any of the recruited children in one study overlapped with another study or not [16,28]. One of the articles, did not provide outcome measures on the children who received myofunctional therapy. The authors were contacted and data was obtained [28]. Five authors were contacted for secondary outcome measures and data was obtained from four of the authors [16,25,29,31]. We were unable to obtain data from one of the articles so excluded the study from quantitative analysis [14]. All studies were performed on children who had residual OSA after adenoidectomy, tonsillectomy or adenotonsillectomy except three studies which included children with OSA without adenotonsillar hypertrophy [26,27,29] and one study which did not report previous history of surgery [30].

3.1. Compliance

Six studies did not report compliance for myofunctional therapy [14,16,24,25,29]. Lee [28] reported that only nine, out of the 35 patients referred to myofunctional therapy, (25.7%) pursued it. Chuang [26] reported 80% compliance. Von Lukowicz [31] reported 100% compliance for one week intense therapy. Huang [27] reported that 10 of 23 children (43.4%) had good compliance with active myofunctional therapy while 50 of 56 (89%) children had good compliance with passive myofunctional therapy. Huang [27] reported data only on the 50 children who reported good compliance.

3.2. Comorbidities

While two studies specifically mentioned that the included children were non syndromic, the rest of the studies did not report this comorbidity [14,29]. one study was performed entirely on children with Down syndrome [31]. BMI was reported in three studies [25–27] and was within normal range. One study reported that the children were normal weight [28]. Villa reported mean BMI centile of 81.85 (29.94)[16] and in another study reported prevalence of obesity to be 2% [30]. The rest of the four studies did not report data on weight. Chuang reported data on prematurity, while the rest of the studies did not report this data [25].

3.3. Polysomnogram

Three studies utilized home sleep study [24,29,31], while the rest of the six studies were performed in-laboratory. four studies reported using AASM criteria for scoring studies [14,16,30,31], while the rest of the studies did not report the criteria they utilized.

3.4. AHI

After myofunctional therapy, AHI decreased by 1.54 events/hr (95% CI -2.24,-0.85), Z score of 4.36 ($p < 0.0001$) (Fig. 2a). Both the I^2 (72%) and Q statistics ($p = 0.0003$) suggested significant heterogeneity. Studies were individually excluded to identify the source. Exclusion of studies by Alexander [24], active myofunctional therapy subgroup of Huang [27] and Lee [28], resulted in no heterogeneity in the remaining 160 children with I^2 of 0% and Q statistic value of 0.48. The mean decrease in AHI for the remaining studies was 2.22 events/hr (95% CI -2.87,-1.57) ($Z = 6.69$, $P < 0.00001$). This has been shown in Fig. 2b. After excluding study by von Lukowicz, which performed one week intense myofunctional therapy in children with Down syndrome, there was a sustained decrease in AHI by 2.26 events/hr (95% CI -2.92, −1.59)[31] ($z = 4.34$, $p < 0.00001$). After excluding all the studies performing home sleep studies, there was a decrease in AHI by 2.35 events/hr (95% CI -3.26,-1.44) in 133 children [24,29,31] ($z = 4.41$, $p < 0.0001$).

Next, we analyzed change in AHI in children with residual OSA. 72 children were included in the study [16,24,25,28,31]. There was a significant decrease in AHI by 1.61 events/hr (95% CI -2.70,-0.53), $z = 2.91$, $p = 0.004$. There was significant heterogeneity with $I^2 = 79\%$ and Q statistic value of 0.0009. We also analyzed change in AHI in 122 children with OSA without adenotonsillar hypertrophy [26,27,29]. There was a significant decrease in AHI by 1.58 events/hr (95% CI -2.73,-0.44), $z = 2.71$, $p = 0.007$. There was significant heterogeneity ($I^2 = 70\%$, Q statistic = 0.02).

3.5. Mean saturations

After myofunctional therapy, there was a significant increase in mean oxygen saturations 0.37 percent (95% CI 0.06,0.69), z score 2.32 ($p = 0.02$) (Fig. 3a).There was significant heterogeneity, I^2 (57%) and Q statistics (p-0.02). After removing study by Villa [30], there was no heterogeneity ($I^2 = 0\%$, Q statistic value of 0.53) and the remaining 178 children still had an increase of 0.2 percent (95% CI 0.00, 0.39)% ($z = 1.99$,$p = 0.05$). This has been shown in Fig. 3b.

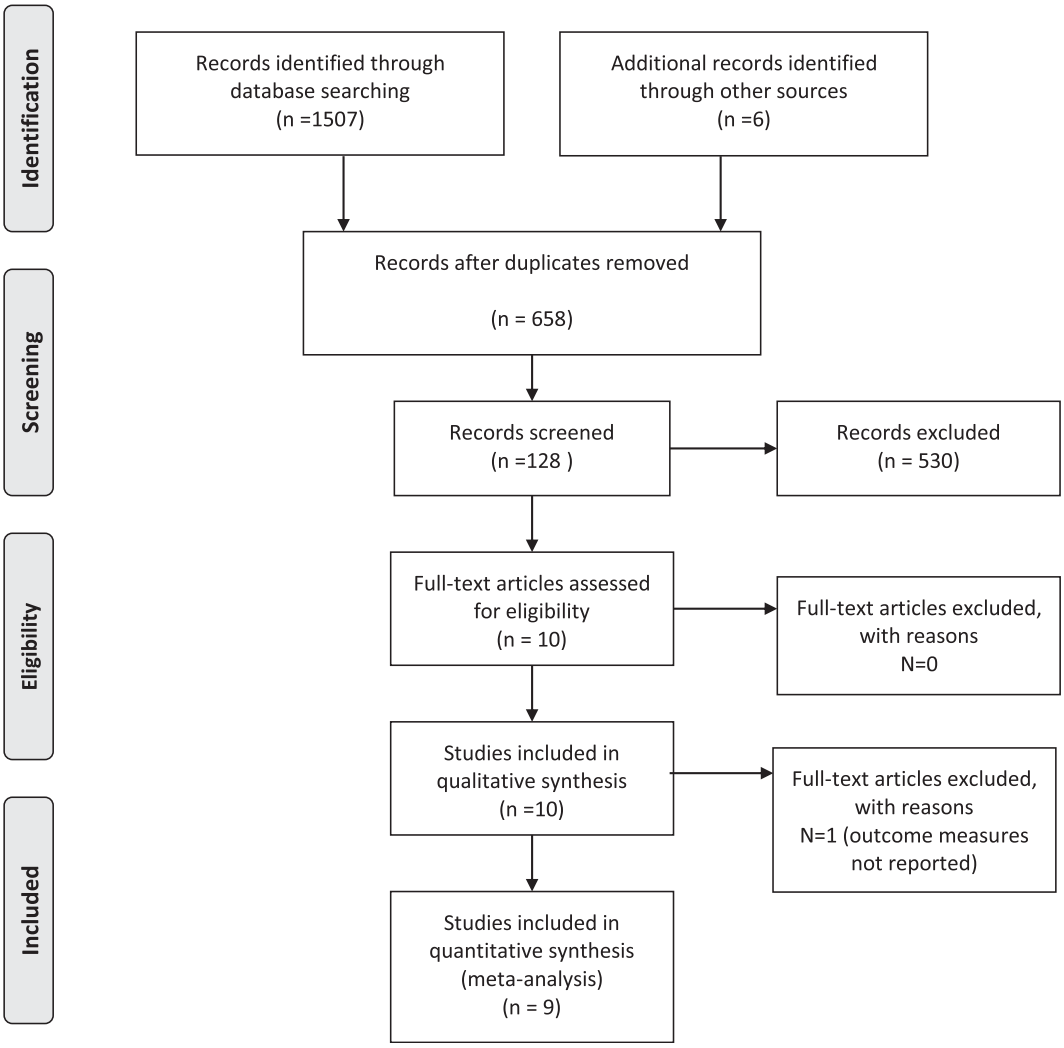

Fig. 1. PRISMA 2009 flow diagram effect of myofunctional therapy on children with obstructive sleep apnea: A meta-analysis.

3.6. Nadir saturations

After myofunctional therapy, there was no significant increase in nadir oxygen saturations with significant heterogeneity ($I^2 = 87\%$, Q statistics of $p < 0.0001$) (Fig. 4). This was sustained, even after removing studies [29,30] to reduce heterogeneity.

3.7. Mouth breathing

Three studies reported mouth breathing. Two studies reported mouth breathing based on a myofunctional therapist evaluation [16,30]. One of those two studies reported using a separate myofunctional therapist for evaluations to avoid observer bias [30]. Another study reported mouth breathing using an oral scoop [28]. In our review, children who received MT had a decreased odds ratio of persistent mouth breathing, OR 0.03 (95% CI 0.01,0.10). There was no heterogeneity with $I^2 = 0\%$ and Q statistics ($p = 0.49$) (Fig. 5).

3.8. Passive myofunctional therapy

We separately analyzed the subgroup who received passive myofunctional therapy [25–27,29]. After passive myofunctional therapy, AHI decreased by 2.14 events/hr (95% CI -2.87, −1.4), Z score of 5.69 ($p < 0.00001$) (Fig. 6) in 128 children. Both the I^2 (4%) and Q statistics ($p = 0.37$) suggested no significant heterogeneity. In contrast, 66 children who received active myofunctional therapy, had a decrease in AHI by 1.04 events/hr (95% CI -1.98,-0.09), z score of 2.15 ($p = 0.03$). There was significant heterogeneity, $I^2 = 80\%$ and Q statistics ($p = 0.0004$). Exclusion of two studies, showed low heterogeneity, $I^2 = 37\%$ and Q statistics ($p = 0.21$) and showed a decrease of AHI by 1.87 events/hr (95% CI -2.98,-0.75) in 41 children [24,27].

There was no significant increase in mean oxygen saturations in the subgroup who received passive myofunctional therapy.

4. Discussion

Our systematic review and meta-analysis of ten studies is the first to report the effect of MT in children with OSA. Myofunctional therapy, active and passive, decreased AHI and increased mean oxygen saturations in children with mild to moderate OSA. Myofunctional therapy decreased odds ratio of persistent mouth breathing in children with mild to moderate OSA.

Our study showed a small yet significant decrease in AHI after myofunctional therapy, even after removing studies causing heterogeneity, study on syndromic children as well as study utilizing home sleep studies. This decrease is lower compared to adult literature [15]. This is an interesting observation, since there is a

Table 1
Characteristics of studies on myofunctional therapy in children with obstructive sleep apnea.

Authors, Year	Study design	N	Age (years)	BMI (kg/m2)	Residual sleep apnea	Treatment	MT	Length of treatment	length of follow up PSG	AHI (events/hr) pre-MT	AHI (events/hr) post−MT
Alexander N, 2019	Two case reports	2	9	not reported	Yes	not reported	Active	3 month	12 month	1.25 (0.35)	1.05 (0.05)
Huang 2019	randomized controlled trial	23	7.02 (2.44)	15.61 (1.74)	Yes, or children with OSA without adenotonsillar hypertrophy	20 min daily exercise	Active	6 months	6 months	2.47 (1.31)	2.26 (1.84)
		50	7.97 (3.08)	17.82 (4.45)	Yes, or children with OSA without adenotonsillar hypertrophy	Oral appliance	Passive	12 months	6 months	5.56 (6.65)	2.85 (2.45)
von Lukowicz, 2019	prospective case series	18	6.3 (2.5)	not reported	30% had prior surgery	three 45 min session based on Padovan method	Active	1 week	1 week	6.4 (8.6)	6.4 (10.8)
Chuang 2019	prospective case control	57 (17 control)	7.86 (3.09)	18.09 (3.84)	yes (18 in treatment group and 10 in control group had prior surgery)	oral appliance	Passive	12 months	12 months	3.75 (2.48)	2.16 (1.8)
Levrini 2018	prospective case series	9	not reported	not reported	Yes, or children with OSA without adenotonsillar hypertrophy	wore myofunctional appliance for 1−2 h during day and at nigh time when sleeping	Passive	3 months	3 month	3.2 (2.2)	0.7 (0.69)
Chuang LC, 2017	prospective case series	29	9.76 (3.54)	18.2 (5.4)	Yes	oral mandibular device with bead for passive MT	Passive	6 months	6 months	5.4 (5.9)	1.9 (2.5)
Villa 2017	Randomized controlled trial	54 (18 control)	7.1 (2.5)	not reported	not reported	3 times a day 10−20 repetitions	Active	2 months	2 month	1.5 (1−2.8)	
Villa 2015	Randomized controlled trial	14	6.01 (1.55)	not reported	yes	3 times a day 10−20 repetitions; nasal breathing rehabilitation, labial seal and lip tone exercise, tongue posture exercise	Active	2 months	2 month	4.87 (2.96)	1.84 (not reported)
Lee 2015	retrospective case series	18 (9 controls)	not reported	not reported	yes	education on negative impact of mouth breathing and resources for myofunctional therapy	Active	6 months	6 months	2.69 (0.68)	1.91 (1.36)
Guilleminault 2013	Retrospective case series	11	11.5 (1.2)	Not reported	yes	myofacial re-education	Active	38−50 months	50 months	0.4 (0.3)	0.5 (0.4)
Total		**241**	**7.9 (3.1)**	**17.6 (4.25)**						**4.32 (5.1)**	**2.48 (4.0)**

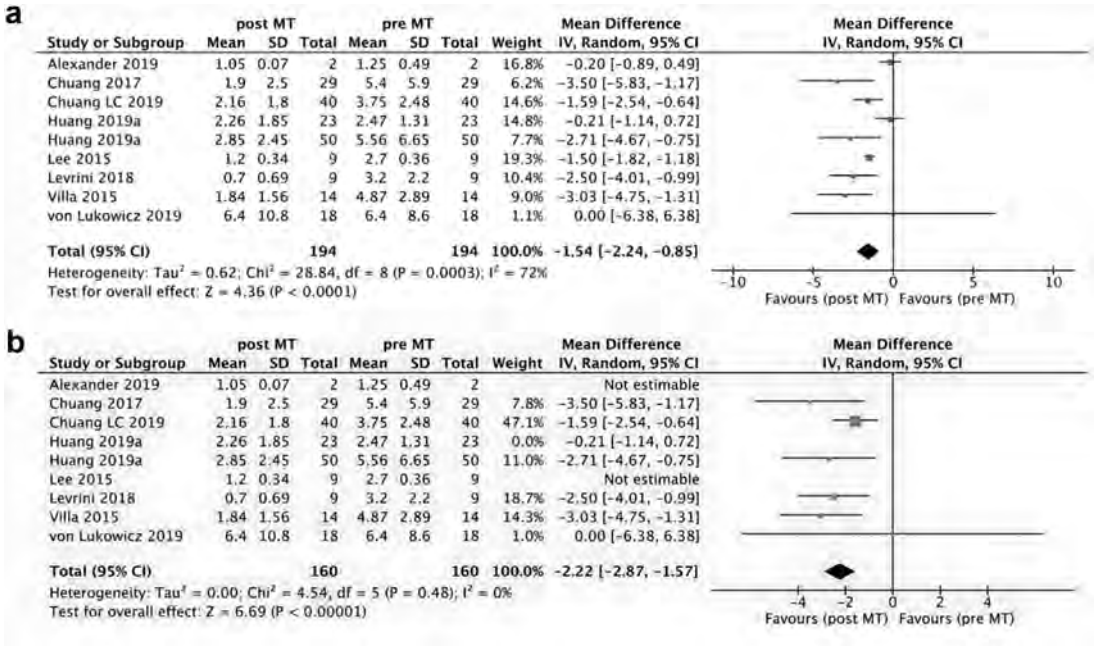

Fig. 2. **a**: Forest plot of Effect of myofunctional therapy on AHI in children. **b**: Forest plot of Effect of myofunctional therapy on AHI in children (removing studies for heterogeneity).

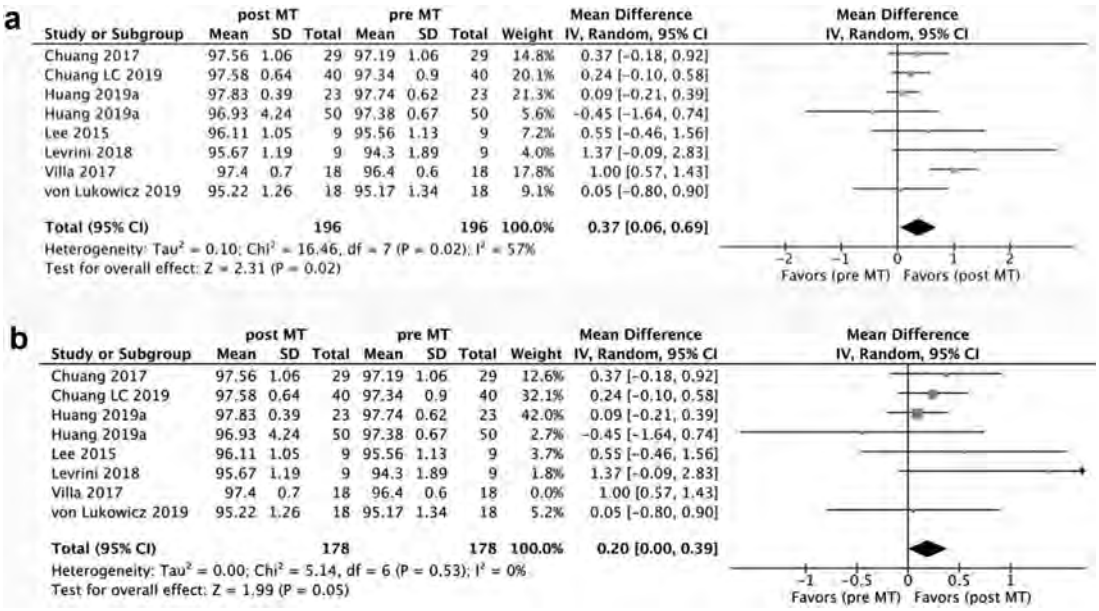

Fig. 3. **a**: Forest plot of Effect of myofunctional therapy on mean oxygen saturations in children. **b**: Forest plot of Effect of myofunctional therapy on mean oxygen saturations in children (removing studies for heterogeneity).

wide variation in the type of myofunctional exercises and duration of therapy. Reported compliance for active myofunctional therapy was lower than passive myofunctional therapy. Active exercises involved soft palate, tongue, labial seal and lip tone exercises. Passive myofunctional therapy included an oral device for advancing mandible with bead mounted on lower frame for the tip of the tongue to roll on. Frequency of therapy ranged from 20 min/day to three 45 min sessions per day. Duration of therapy ranged from one week to 50 months. One of the studies had an active and passive myofunctional therapy arm compared to a control arm [27]. The study did not find a significant difference in AHI in the active myofunctional therapy group, however, there was a high rate of drop out in the active myofunctional therapy group. Our study found a small yet significant decrease in AHI in children with residual OSA as well as children with OSA without adenotonsillar hypertrophy.

Our study showed a small but significant increase in mean oxygen saturations in the children who received myofunctional therapy. There was no significant difference in nadir oxygen saturations. This is different compared to adult literature. While it may be argued that myofunctional therapy does not result in a drastic difference in polysomnographic parameters, it should also be remembered that there is a significant difference in the sleep and respiratory physiology of children and adults [32]. The small

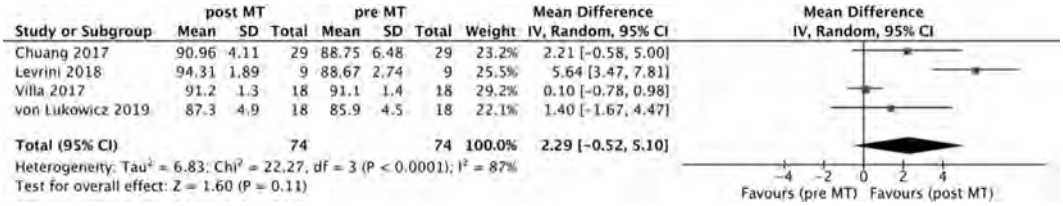

Fig. 4. Forest plot of Effect of myofunctional therapy on nadir oxygen saturations in children.

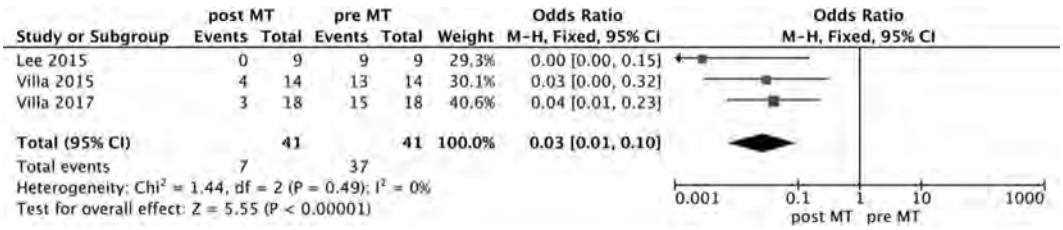

Fig. 5. Forest plot of Effect of myofunctional therapy on mouth breathing in children.

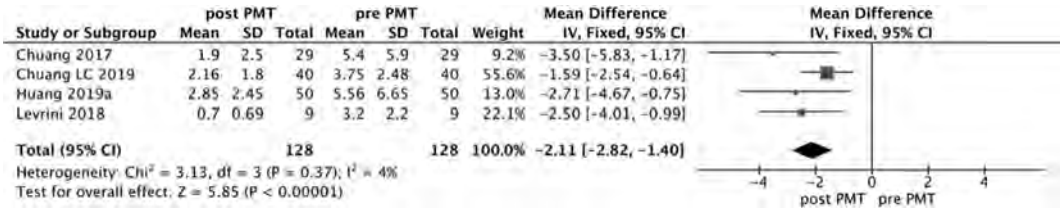

Fig. 6. Forest plot of Effect of passive myofunctional therapy on AHI in children.

difference in mean saturations holds promise and needs further investigation.

Our study reports significant improvement in mouth breathing after myofunctional therapy. Mouth breathing is fairly common in children with OSA and has been shown to be persistent despite adenotonsillectomy. Mouth breathing can lead to changes in proprioception, posture and loss of usage of nose. There is a growing body of literature which states that nasal breathing is of critical developmental importance for normal oropharyngeal development. Myofunctional treatments encourage normal orofacial muscle tone associated with normal nasal breathing through daily exercise involving orofacial muscles and stimulation of sensory pathways.

While polysomnographic data is important to determine improvement in OSA, few studies have evaluated other outcome measures. Due to inconsistency in reporting other outcome measures, we were unable to include them in our study. Cephalometric films [26,27], Iowa Oral Performance Instrument (IOPI) [30] and quality of life assessed with OSA-18[26] have been utilized by various studies. Night time symptoms like snoring and daytime symptoms like sleepiness or hyperactivity have not been consistently studied. There is a need to assess these symptoms to ascertain the clinical effectiveness of myofunctional therapy in children with OSA.

4.1. Limitations

Our study is the first to focus on the effect of myofunctional therapy in children with OSA. However, there were a few limitations. There were only three randomized controlled studies. However, due to the nature of the therapy, these studies had a high risk of bias. Risk of bias was due to paucity of random sequence generation, allocation concealment and blinding. Data on co-interventions has not been consistently reported so there is a risk for unclear bias. Another limitation is that there was no long term follow up of studies. Thus, it is difficult to infer whether the difference in AHI, mean oxygen saturations or mouth breathing were sustained or not. The heterogeneity of the frequency, duration and type of myofunctional exercises is another limitation. Moreover, most of the studies did not report compliance of the prescribed myofunctional therapy. Finally, there is a lack of studies focusing on effect of myofunctional therapy on night/daytime symptoms and quality of life [26].

5. Conclusion

Despite heterogeneity in exercises, myofunctional therapy can decrease AHI and increase mean oxygen saturations in children with mild to moderate residual OSA as well as children without adenotonsillar hypertrophy and serve as an adjunct treatment. Future studies should focus on ascertaining the sustainability of the effects of myofunctional therapy and interpreting a dose response relationship.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2020.08.003.

Conflict of interest

None.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2020.08.003.

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

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Aims: Review of evidence in support of an oral-facial growth impairment in the development of pediatric sleep apnea in non-obese children. **Method:** Review of experimental data from infant monkeys with experimentally induced nasal resistance. Review of early historical data in the orthodontic literature indicating the abnormal oral-facial development associated with mouth breathing and nasal resistance. Review of the progressive demonstration of sleep-disordered-breathing (SDB) in children who underwent incomplete treatment of OSA with adenotonsillectomy, and demonstration of abnormal oral-facial anatomy that must often be treated in order for the resolution of OSA. Review of data of long-term recurrence of OSA and indication of oral-facial myofunctional dysfunction in association with the recurrence of OSA. **Results:** Presentation of prospective data on premature infants and SDB-treated children, supporting the concept of oral-facial hypotonia. Presentation of evidence supporting hypotonia as a primary element in the development of oral-facial anatomic abnormalities leading to abnormal breathing during sleep. Continuous interaction between oral-facial muscle tone, maxillary-mandibular growth and development of SDB. Role of myofunctional reeducation with orthodontics and elimination of upper airway soft tissue in the treatment of non-obese SDB children. **Conclusion:** Pediatric OSA in non-obese children is a disorder of oral-facial growth.

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 anatomical 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

(PSG) 3 months post-operatively, an observation confirmed in later studies (Tauman et al., 2006; Guilleminault et al., 2007). In a more recent multi-center study (Bhattacharjee et al., 2010) with 500 subjects, half of whom were obese, adenotonsillectomy again led to improved clinical symptoms and PSG results but was not curative in 70% of the cases. Chen et al. (2012) conducted a prospective study of prepubertal children treated with adenotonsillectomy with subsequent normal PSG testing as defined by AASM 2007 scoring criteria (Iber et al., 2007). The prospective 5-year follow-up study included systematic PSG testing, clinical evaluations, attentional neurocognitive testing, and 3D-CT of the upper airway. The follow-up evaluations performed at 3 and 6 months showed normal PSG and neurocognitive scores. However, further follow-up once again demonstrated the simultaneous presence of abnormal breathing during sleep (AASM criteria) and abnormal neurocognitive test results in 40% of the subjects. Moreover, 3D-CT analysis showed abnormal oral-facial development in these children.

Kim and Guilleminault (2011) looked at the presentation of anatomical oropharyngeal abnormalities in 400 prepubertal children diagnosed with OSA who had enlarged adenotonsillectomy before otolaryngological treatment (Friedman et al., 1999). Nearly all of the children with OSA had at least one type of oropharyngeal abnormality from a list of pre-defined potential problems. Consistent with prior studies, clinical symptoms of OSA and abnormal PSG results persisted in some children at 3-month post-operative follow-up. However, presence of a pre-defined oropharyngeal abnormality was scored and was insufficient to predict post-surgical outcome on OSA.

Further analyses defined more specific clinical examination findings that better predicted persistence of abnormal post-adenotonsillectomy PSG results. These included the presence of a Mallampati scale score of 3 or 4 (Mallampati et al., 1985; Guilleminault et al., 2007), the presence of a deviated nasal septum, and the presence of a small mandible. The Mallampati scale does not identify one particular anatomical abnormality, but rather it represents a combination of deficiencies involving both the nasomaxillary complex and the position of the mandible. These findings suggest the need to assess anatomic elements of the upper airway in terms of oral-facial growth and impairment of general oropharyngeal growth rather than merely tallying the quantity of anatomic abnormalities.

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 associated 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; Löfstrand-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 silicone 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). The blockade of the nasal passage led to narrowing of dental arches, decrease 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 subjects. 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 maxillomandibular skeleton, halting growth (Harvold et al., 1981), and bringing about adaptive changes in the soft tissues that are associated 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 monkeys, 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 firing 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 adenotonsillectomy

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 subjection to repetitive abnormal stimulations resulting from mouth breathing causes an inflammatory reaction in the tonsils (Zettergreen et al., 2002). The resulting tonsilar 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

have high and narrow hard palates (with palatal width smaller than 24 mm at 6 months post delivery). Infants born at 37 weeks had palates whose widths measured between 27 and 31 mm, while in 35% of infants born at 36 weeks and in all infants born sooner, they measured less than 27 mm. The measurements correlated directly with gestational age.

Problems with feeding behavior were present in infants born at 36 weeks and younger. All infants with extended in-hospital stays due to premature birth were bottle fed, while term infants were breast fed. All infants held in the hospital postnatally were separated from their mothers and bottle fed either with formula or expressed breast milk.

Currently 82% of the studied infants ($n = 207/252$) have presented with a high and narrow hard palate, as well as apnea and/or hypopnea during sleep. Mouth breathing has been noted in these children and has become more apparent with age, as noted during the first follow-up visit at 3 months post-partum.

All children born at 35 weeks or earlier exhibited limb hypotonia during the general neurological evaluation. Some older infants also demonstrated hypotonia, but the frequency of this was inversely proportional to pregnancy duration. Hypotonia was defined by the persistence of a positive "scarf" sign (i.e., position of elbow, crossing the midline, when arm is pulled toward opposite side), which was noted in infants born as late as 37 weeks (Korobkin and Guilleminault, 1979). At 6 months old, the 207 subjects without history of intubation showed no signs of abnormally enlarged tonsils, but all of them presented with a high and narrow hard palate.

Enlarged tonsils when present were only noted in later examinations in children who exhibited mouth breathing, high and narrow hard palates, and mouth breathing during sleep. The hypothesis that the enlargement of tonsils occurs as a result of mouth breathing and the presence of a high and narrow hard palate is supported here. The effect on adenoids was not observed in this study, since otoscopy of the back of the nose was not performed. Nevertheless, documentation of a high and narrow hard palate at birth predicts the presence of abnormal oral-facial features existing from birth in most cases.

DEVELOPMENT OF ABNORMAL HARD PALATE AFTER BIRTH

The most interesting cases are the small fraction of subjects (9%, $n = 23$), that had a normal hard palate at birth, but then developed an abnormal hard palate by the 6-month-old follow-up visit. 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. Also, all of these children were bottle fed due to difficulties with breast feeding. At the 6-month evaluation, 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 demonstrated 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; Behlfelt 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 myofonctional 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 31/2 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 abnormal 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

may lead to normal development and absence of SDB at follow-up. As suggested by Swedish investigators, tonsillar enlargement appears to be a secondary phenomenon that further impacts nasal resistance. No information on adenoids had been collected in our infant studies, but was obtained in the long-term follow-up of older children with 3D-CT scans. Adenotonsillectomy often is insufficient to achieve complete and lasting resolution of breathing problems.

Understanding the continuous interaction between muscle activity of the tongue and other oral-facial muscles, as well as the development of normal anatomic structures supporting the upper airway may lead to expansion of myofunctional reeducation as a therapeutic tool. We still do not know when the interaction between the potential airway-limiting oral-facial anatomic structures and its musculature begins. Interruption of normal development with premature birth may explain the frequency of sleep-related breathing problems in premature infants. However, these events also can be seen in full-term infants, leading to negative consequences (Rambaud and Guilleminault, 2012). It is possible that the abnormality leading to oral-facial hypotonia begins *in utero*. Investigation of facial expression and movements shows that beginning in early pregnancy, the fetus exhibits regular movements of the mouth and face. For example, the most frequent movement seen during the second trimester is sucking (Kurjak et al., 2005). Abnormal pregnancy and/or impairment of these movements may impede normal muscle activity at birth.

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Original Article

Teenage sleep-disordered breathing: Recurrence of syndrome

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ABSTRACT

Objectives: The study aims to better understand the reappearance of sleep apnoea in adolescents considered cured of obstructive sleep apnoea (OSA) following adenotonsillectomy and orthodontic treatment.
Study design: The study employs a retrospective analysis of 29 adolescents (nine girls and 20 boys) with OSA previously treated with adenotonsillectomy and orthodontia at a mean age of 7.5 years. During follow-up at 11 and 14 years of age, patients were clinically evaluated, filled the Pediatric Sleep Questionnaire (PSQ) and had systematic cephalometric X-rays performed by orthodontists. Polysomnographic (PSG) data were compared at the time of OSA diagnosis, following surgical and orthodontic treatment and during pubertal follow-up evaluation.
Results: Following the diagnosis of OSA and treatment with adenotonsillectomy and rapid maxillary expansion (Apnea–Hypopnea Index (AHI) 0.4 ± 0.4), children were re-evaluated at a mean age of 11 years. During follow-up at 14 years, all children had normal body mass indices (BMIs). Teenagers were subdivided into two groups based on complaints: Nine asymptomatic subjects (seven girls and two boys) and 20 subjects with decline in school performance, presence of fatigue, indicators of sleep-phase delays and, less frequently, specific symptoms of daytime sleepiness and snoring. Presence of mouth breathing, abnormal AHI and RDI and significant reduction of posterior airway space (PAS) was demonstrated during repeat polysomnography and cephalometry. Compared to cephalometry obtained at a mean of 11 years of age, there was a significant reduction of PAS of 2.3 ± 0.4 mm at a mean age of 14 years.
Conclusion: Previously suggested recurrence of OSA during teenage years has again been demonstrated in this small group of subjects. Prospective investigations are needed to establish frequency of risk, especially in non-orthodontically treated children.

1. Introduction

Obstructive sleep apnoea syndrome (OSAS) in adults is an important public health problem that can lead to behavioural and cognitive dysfunction, cardiovascular risk and negatively impact quality of life. Adult OSAS is related to a dyscoordination of upper airway dilator muscles and inspiratory muscles during sleep. This dyscoordination can be explained in part by local neuropathy in sleep apnoea [1,2]. Nasal continuous positive airway pressure (CPAP) treatment appears to be the only treatment capable of completely controlling the problem in these cases. However, many adult patients fail to achieve complete control of their OSAS due to non-compliance with CPAP, particularly in older teenagers and young adults.

Significant efforts have been made to recognise the presence of abnormal breathing during sleep at an early age in hopes of preventing the progression of the complete syndrome. OSA can be recognised and treated during childhood. Nevertheless, even with early childhood intervention, long-term treatment may be required. In some cases, children deemed cured of OSA after adenotonsillectomy during prepubertal years relapse in their late teens [3,4]. With this in mind, we have made efforts to better understand the reappearance of sleep apnoea during teenage years. Normally, once a child's symptoms of sleep-disordered breathing (SDB) resolve in the setting of a normal postoperative polysomnogram (PSG), no long-term follow-up testing is performed. There is little information available regarding the course of breathing beyond the immediate postoperative period. In fact, the only published series of children with long-term follow up after OSA treatment involves orthodontic treatment of 10 prepubertal children with 3-year follow-up [5].

Parents of pubertal teenagers reported return of symptoms despite treatment with adenotonsillectomy and/or orthodontia at an

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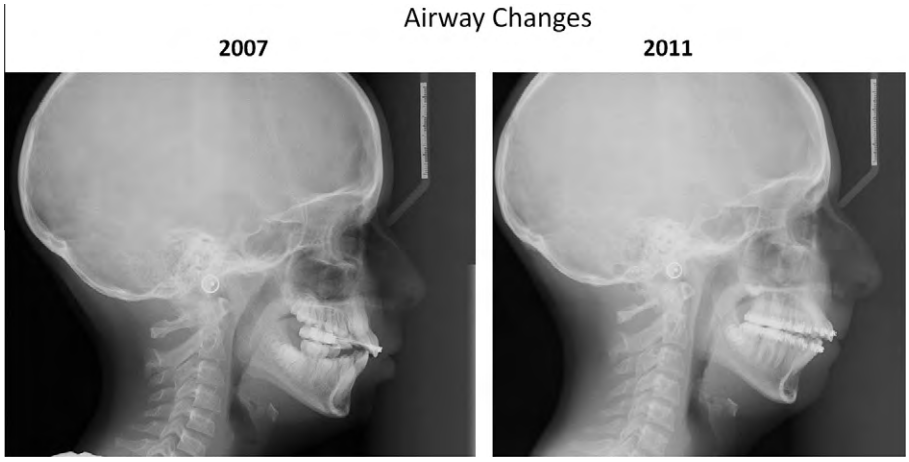

Fig. 1. Subjects involved in the study. Graph of the retrospective chart investigation to find the candidates for the retrospective study.

earlier age. We queried how many of such cases we could identify and what interval history could be documented. A systematic search involving three different sleep clinics revealed that such an investigation was difficult due to absence of systematic follow-up information in many cases (see Fig. 1). This report presents limited findings obtained during a retrospective study of children diagnosed with SDB and treated with adenotonsillectomy and orthodontics during their prepubertal years, then later evaluated and treated by orthodontists for dental and/or facial aesthetic indications. The primary goal of this retrospective report was to understand the characteristics of children diagnosed and successfully treated for OSA following adenotonsillectomy and orthodontia during prepubertal years who later presented for orthodontics with recurrence of symptoms and/or signs associated with SDB after the onset of puberty.

2. Methods

2.1. Sources of clinical information

Due to long-term collaborations between three sleep clinics, private and university orthodontic clinics and a craniofacial department, specialists in these clinics have been keenly aware of the presence of SDB and OSA in young individuals. Therefore, as part of a routine clinical evaluation of pediatric patients, the Pediatric Sleep Questionnaire (PSQ) or its validated translation in Chinese [6,7] is given to all children who present for orthodontic evaluation in both the private orthodontic clinic and university-based orthodontic clinics. If the questionnaire suggests a sleep problem, the child is referred to pediatric sleep clinics based upon insurance criteria. Information obtained from these sleep clinic referrals is then sent back to the orthodontic practice.

We used the following inclusion criteria: (1) diagnosis of OSA based on the presence of clinical symptoms investigated by a paediatric sleep medicine specialist and results of an in-laboratory PSG, (2) referral for treatment for OSA as outlined by an expert specialised team (in the the locations, the diagnostic and treatment recommendation involved the combined expertise of otolaryngologist, orthodontist and sleep medicine specialist), (3) having had post-treatment follow-up with clinical evaluation by the clinical team and PSG and (4) having been considered as exempt from SDB at the end of treatment based on parent reports, clinical evaluation and findings and nocturnal PSG. Syndromic and obese children with OSA were excluded from this review. Obesity was an uncommon observation at the time in the three practices.

Unidentified information collected in the universities and private practices was reviewed, including results of the PSQ, results of the orthodontic and sleep medicine evaluations at each available visit, cephalometric radiograph readings and PSG test results.

2.1.1. Chart review

An initial review showed that there was no systematic long-term follow-up schedule through sleep medicine services, as these services were referral clinics. There was also no long-term follow-up in the otolaryngology clinics. The only long-term clinical follow-up available was through the orthodontic clinics (see Fig. 1).

Chart records at the orthodontic–craniofacial clinics were reviewed to identify pubertal individuals (age 12–16 years) who were diagnosed with SDB and appropriately treated with adenotonsillectomy usually followed by rapid-maxillary-expansion (RME) treatment during their prepubertal years [5,8]. There were a total of 35 pubertal individuals seen in an orthodontic clinic who met this requirement. All unidentified information on these individuals was included for analysis.

There were Institutional Review Board (IRB) approvals for evaluation of the previously obtained clinical and PSG data rendered anonymous for research purposes.

2.2. Data collection

In reviewing the retrospective data for potential subjects, we developed three sets of data, described below. To be presented in this retrospective review, subjects must have data available at three different times:

(1) Time of initial diagnosis of SDB as a young child with objective demonstration of resolution of the SDB problem;
(2) Intermediate evaluation at some point after initial diagnosis and treatment period at a mean age of 11 years; this age was selected based on the relationship between age and facial growth;
(3) Facial presentation and breathing evaluation as a pubertal teenager.

As shown in Fig. 1, despite a large review of children, a low number of cases could be extracted. Orthodontic clinics had follow-up for dental, facial aesthetics or routine yearly post-procedural follow-up for rapid maxillary or bimaxillary expansion [8]. The extracted data were as follows:

2.2.2. +Data set 'Prepubertal and young age – (time 1-T1-)'

The data included: initial clinical complaints and symptoms, pediatric, otolaryngological and sleep evaluations and polysomnographic results. Surgical intervention follow up information and follow-up polysomnography were also collected. Age at time of referral to the sleep clinic, gender, height and weight (to derive BMI), reason for the referral, clinical upper airway evaluation, results of initial cephalometric X-ray at time of referral, results of the PSQ, results of sleep clinic evaluation and sleep tests were retrieved.

2.2.3. +Data set 'older-prepubertal children – (time2-T2-)': (mean age 11 years)

Age, BMI, clinical complaints, clinical examination, results of PSQ and cephalometric data were also retrieved.

2.2.4. Data set 'pubertal teenagers – (time 3-T3-)'

These data included results of orthodontic and sleep clinics' re-evaluation covering PSQ results, new clinical evaluation of upper airway anatomy, cephalometric X-rays results and results of a new PSG or polygraphy.

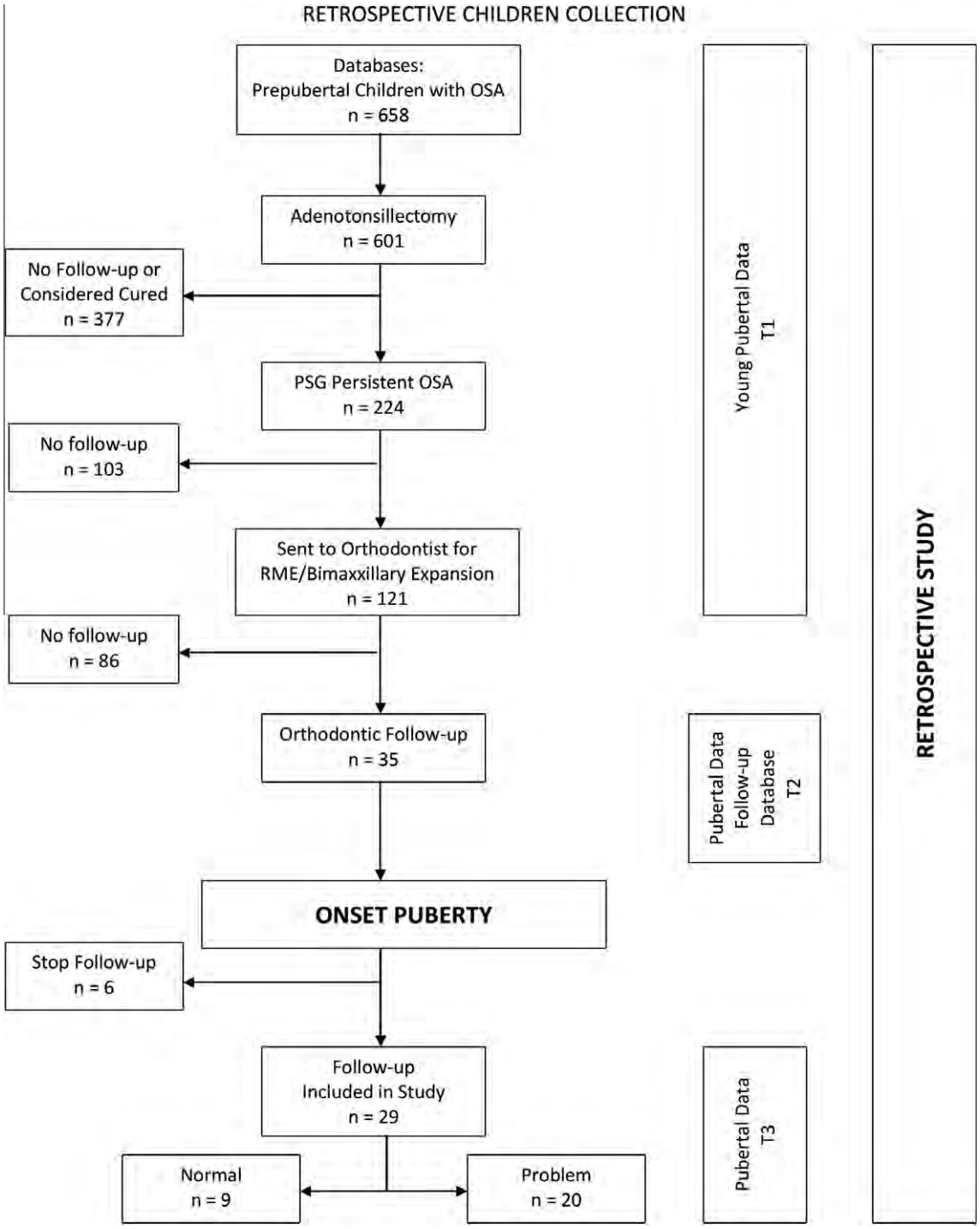

Fig. 2. Cephalometrics at 9.8 and 13.8 years in a boy. Example of the changes noted in the posterior-airway size between pre-pubertal and pubertal.

The clinical new upper airway evaluation included presence of mouth breathing at rest when distracted or performing intellectual tasks; indication of narrow maxilla or mandible, evidence of bruxism. Particularly if partial tonsillectomy had been performed, there was a grading of tonsils based on the Friedman et al. scale [9], grading of upper airway space using the Friedman-modified Mallampati scale with 4 scores [10] and determination of presence of septum deviation and of nasal inferior turbinate hypertrophy based on the mention of "abnormally enlarged" or "hypertrophic" in the chart.

Once all data were collected, results were placed in a spreadsheet for analyses.

To unify PSG information and avoid inter-scorer variability, all polygraphic recordings performed during the pubertal period were obtained and rescored anonymously by one individual for the purpose of the study. As recordings were obtained on different computerised sleep systems, PSG data collected on systems other than Sandman™ were transformed into European Data Format (EDF). All cephalometric X-rays were also reviewed blindly by one individual for consistency of measurements.

During the review, we found that we had 35 cases that had been seen at T1 and T2, but only 29 individuals had data collected at the three required time-points. These 29 subjects represent the 'reviewed group' (Fig. 1).

2.3. Analyses

Sleep scoring was performed using the international manual from Rechtschaffen and Kales [11]. This scoring manual had been used previously to score PSG at any age. It was based on a sleep montage that always included: 4-EEG (electroencephalography) channels, one-chin electromyograph (EMG) and two-leg EMGs; two electrooculography (EOG) leads, one electrocardiograph (ECG) derivation and a position sensor.

Respiratory variables had been measured using similar technology overtime and location with systematic monitoring of the nasal cannula-pressure transducer, mouth thermistor thoracic and abdominal belts, either piezo-electric (mostly in the recordings obtained at a young prepubertal age) or inductive plethysmography (older prepubertal and in all cases during pubertal recordings), diaphragmatic-intercostal EMG, neck microphone and pulse oximetry from which oxygen saturation and finger plethysmography tracings were derived. Depending on age and location, end-tidal or transcutaneous CO_2 was also monitored. Respiratory variables had been scored using the international recommendations defining apnoea and hypopnoea similar to those outlined in the AASM "recommended" criteria [12,13] and the AHI was calculated. A respiratory-disturbance index was also calculated scoring respiratory event related arousals, RERAs, defined as events in which there is a drop in the amplitude of the nasal cannula tracing curve by at least 30% compared to prior normal tracing. Presence of snoring or heavy breathing and increase in snoring signal from beginning to the end of an evening that is associated with the presence of an increase in respiratory efforts was seen on the thoracic and abdominal tracing curves, with termination by an EEG arousal and return to normal amplitude of the nasal cannula curve [14]. EEG arousal was based on the international recommendation [15]. The duration of all events (apnoea, hypopnoea and RERA) was a minimum of 10 s. The apnoeas were further subdivided into obstructive, mixed or central sub-types following the international definitions. Mouth breathing during sleep was documented by the mouth thermistor. The time spent with 'flow limitation' based on the curve obtained from the nasal cannula was calculated at T3. The definition of flow limitation was based on the Hosselet et al. report [16] and a percentage of time spent presenting flow limitation was calculated following prior report [17].

Such montages and monitoring were used in all reported cases except for nine pubertal teenagers seen at T3. These nine teenagers presented with absence of clinical symptoms, normal PSQ responses, normal clinical and orthodontic evaluation and cephalometric X-rays considered as normal for age and had an ambulatory study performed with a cardio-respiratory monitor (Ambletta™) with oxymetry and peripheral arterial tonometry-(PAT) measuring apnoea and hypopnoeas and "RERAs Embletta". The "RERA Embletta" was based on nasal flow and thoraco-abdominal efforts, with a decrease in nasal flow by at least 30% and an increase in respiratory efforts shown by thoraco-abdominal curves, terminated by evidence of a sympathetic activation indicated by change in the PAT curve. Mouth breathing was monitored with a thermistor.

Cephalometric X-rays were taken in a neutral head position seated with a cephalostat. Cephalometric assessments were performed according to Ricketts parameters [18]. Lateral and frontal cephalometrics were analysed by the orthodontist–craniofacial specialists. For calculation, correction using the Frankfort plane was done. From the many measurements that can be extracted from cephalometric X-rays, several measurements were pre-selected as 'variables of interest' for this retrospective study. They included the measured angles sella-nasion-supradentale or point A (SNA), sella-nasion-infradentale (or pogonion-point B) (SNB), the difference between the two angles: that is, the angle formed by point A-nasion-point B (ANB), the distance mandibular plane-hyoid bone (MP-H), the length of the mandibular ramus (BL) and the posterior airway space (PAS) – defined as the narrowest point

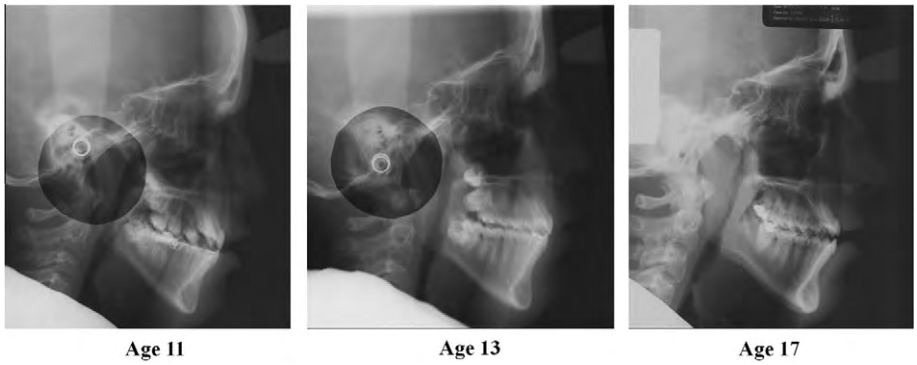

Fig. 3. Cephalometrics changes with age. Another example of the changes in the upper airway anatomy with aging; the teen-ager was treated with nasal CPAP after recurrence of OSA with planning for maxilla-mandibular advancement at late teen-age. Despite presence of symptoms, compliance with nasal CPAP was poor and there was progressive worsening of clinical symptoms and oral-facial presentation.

behind the base of tongue [19]. It was calculated from the anterior point of the velum to the pharyngeal wall (see Figs. 2 and 3).

2.4. Statistical analysis

T-tests for repeated measures were used when comparing two measurements at different ages, and the non-parametric Wilcoxon sign rank test was used for all other comparisons.

3. Results

All children were either Asian or Caucasian. During the survey period of these retrospective evaluations, only 29 children were seen at the three time points and formed the primary study group (see flow chart, Fig. 1). There were nine girls and 20 boys. When seen at the orthodontic clinic at the pubertal time point (T3), nine adolescents had no clinical complaints. Parents reported that they intermittently looked "tired" during the week and three of them had some indication of mild sleep-phase delays with long sleep on weekends; these teenagers had normal responses at PSQ and had normal orthodontic evaluation. The 20 other children had changes on orthodontic imaging and underwent in-laboratory PSG.

The retrospective findings at three different time points from time of diagnosis as a young prepubertal child (T1) till the pubertal evaluation period (T3) for these 29 teenagers are outlined below and in Tables 1–3:

3.1. +Pre-pubertal initial data (T1): (see Table 1)

All 29 children had clinical symptoms and presentation supporting the diagnosis of SDB at the time, and adenotonsillectomy was recommended and performed in all cases following the diagnosis of OSA as confirmed by PSG.

The PSG results before and after adenotonsillectomy are outlined in Table 1.

Following the surgical treatment, clinical evaluation and post-operative PSG, it was felt that these subjects would benefit from RME or bi-maxillary treatments [8]. All children were followed up for about 12 months by orthodontists. They had a PSG performed at the beginning of orthodontic treatment, and again at approximately 1 year (range 10–13 months) after termination of all upper airway treatments (see Table 1). At this time, there were no further recommendations for treatment of SDB in any of the children undergoing orthodontic treatment. However, it was recommended that all children follow-up with their orthodontists to evaluate their bite.

3.2. +Pre-pubertal-orthodontic clinics data (T2)

Orthodontic charts indicate the follow-up of these 29 children between 10 and 11 years of age. At this time point, all 29 children completed the PSQ and had cephalometric radiographs. All were still prepubertal. PSQ showed no indication of sleep-related problems, parents had no complaint and cephalometric radiographs were reported as normal for age. Selected measures from cephalometric X-rays were calculated at the time of the retrospective analysis by a single specialist and were considered to show normal growth and development (see Table 3).

Table 1

	Initial diagnosis	Post-treatment T and A	Post-treatment orthodontics+	Post treatment final evaluation
Number of subjects	29	29	29	29
Number of boys	20	20	8	20
Age (y) mean ± SD	7.6 ± 1.7	7.8 ± 1.8	7.10 ± 2.0	8.6 ± 2.8
AHI mean ± SD	9 ± 5	3 ± 4	0.5 ± 0.2	0.4 ± 0.4
RDI mean ± SD	15 ± 6.4	7 ± 6	0.8 ± 0.2	0.6 ± 0.5
Lowest SaO2-% mean ± SD	91 ± 2.5	94 ± 3	97 ± 1	98 ± 1.5

Table 2
Recording results in mean age 14 years teen-agers.

Pubertal teen-agers $N = 29$	No clinical complaints	With clinical complaints
Number of subjects	9	20
Number of boys	2	18
BMI (kg/m^2)	15.9 ± 1.9	15.7 ± 2.1
Age (y) mean ± SD	13.8 ± .9	14.2 ± 1
AHI** mean ± SD	0.5 ± 0.2*	3.1 ± 1.0
RDI** mean ± SD	1.5 ± 1.2*	7 ± 1.2
Lowest** SaO2-% mean ± SD	97 ± 1%*	92.5 ± 1.5

* Polygraphic recording with "Embletta-PAT".
** Significantly different between group (Wilcoxon test $p = 0.05$).

Table 3
Selected measures from cephalometrics, before puberty and at investigation during puberty.

Cephalometrics	Mean age 11 years	Mean age 14 years
SNA	84.7(1.7)	85.1(2.4)
SNB	79.4(2.65)	79.85(2.65)
H-MP	10.1(3.75)	11.8(9.25)
PAS*	9.0(1.85)	6.6(1.85)*
BL	76.4 (5.5)	83.2 (5.1)*

S = sella.
N = nason.
A, point A: the most posterior midsagittal point on anterior maxillary surface.
B, point B: the most posterior midsagittal point on anterior mandibular surface.
PAS: posterior-airway-space.
H-MP: distance from mandibular plane to hyoid bone.
BL: length of the mandibular ramus.
* Wilcoxon test (two tailed) $p = 0.05$.

3.3. +Pubertal (teenagers) data (T3)

When seen at that age, due to the concerns about the past medical history, and also due to the medical-orthodontic environment and collaborative work between the sleep and orthodontic offices, these teenagers were again questioned about any sleep problems, filled out the SDQ and had repeat cephalometric X-rays performed. It was recommended that these patients also consult the associated sleep clinic. As mentioned, these 29 teenagers were the only ones that followed the suggestion.

3.4. Sleep clinic follow-up for 29 teenagers

3.4.1. Clinical symptoms

The sleep clinic follow-up occurred at a mean age of 14.4 ± 0.9 years. Charts indicated that the Tanner stages [20] were stage 2 in one case, stage 3 in 18 cases and stage 4 in 10 cases; none of the teenagers were post-pubertal. The PSQ indicated that teenagers were sleeping in their own bedroom in all cases [21].

Nine teenagers (seven girls and two boys) had no indication of a sleep problem on SDQ, though there was a tendency to go to bed late in all cases without mention of morning or daytime consequences. Parents reported shortened sleep duration during school days and some late to very late awakenings on weekends,

particularly in three of them. There was no clear clinical concern and these teenagers adjusted without problem to sleep schedule changes particularly between school and vacation schedules.

In 20 cases, there were more concerns expressed by parents and in 10 of them parents had specifically raised the issue with their orthodontist. Symptoms were reported on PSQ. Sixteen of these teenagers had difficulties getting up in the morning and 12 showed some degree of symptoms consistent with sleep-phase delay with consequences on weekdays, including napping on the way home from school (eight cases). Interestingly, the complaint of 'sleepiness' was never mentioned, but report of daytime 'fatigue' was mentioned in 11 cases. Poor sleep with nocturnal awakenings was reported in two cases and snoring sufficiently loudly to be noted by family members was present in five cases. Parents expressed their concern about school performance and difficulty to perform in 15 cases. The same 15 teenagers reported difficulty in concentrating.

Clinical examination of upper airway showed absence of tonsils and adenoids in all cases, but six teenagers (two girls, four boys) had deviated septum and five of them had enlargement of inferior nasal inferior turbinates occupying more than 50% of the nasal passage. At examination, all these teenagers ($n = 20$) had a Friedman 'modified Mallampati' [10] scale score above 2, (while in the nine other teenagers presenting without complaint, sign or symptom of sleep-related problems only one had a score above 2 (=3). Twelve of the 20 teenagers with sleep-related-complaints had the same Friedman scale score of 4, 16 had high and narrow hard palates, 14 had an overjet of more than 2.5 mm and five had an abnormal overbite.

3.4.2. Myofunctional evaluation

Awake myofacial evaluation [22] of the oral–facial region showed that subjects had an abnormally low tongue position in the mouth, 18 were unable to perform appropriately 'clicking' sounds with tongue, 15 were unable to protrude their tongue upwards when asked to try touching their nose with the tip of the tongue; six had difficulties holding a button between their lips and two had difficulties swallowing when drinking fast. At the end of the evaluation by all subjects were scored with abnormal oral–facial muscle tone during wakefulness. All subjects without complaints had been scored as normal at myofunctional testing [22].

3.4.3. Polygraphic and polysomnographic results

Results of nocturnal polygraphy, performed on the nine teenagers without signs or symptoms, and nocturnal polysomnography performed on the last 20 teenagers, are shown in Table 2. This last group of teenagers had a mean time spent in flow limitation of 65 ± 12%, compared to 21 ± 6% in the non-complaining group (See Fig. 4). This measurement was the most abnormal finding at this test performed at the teenage.

3.4.4. Cephalometric-selected-variable evaluation

We evaluated the cephalometric- selected variables at T2 (mean age of 11 years) and no significant difference could be found between the 29 subjects. Results were considered normal for age and growth. There was, however, a change at a mean of 14 years of age. When comparing the measurements obtained on the 20 children with clinical symptoms and SDB by polysomnography at a mean age of 14 years at T2 versus those obtained at T3, a significant decrease in the width of the PAS [19], from 9.15 ± 1.85 to 6.6 ± 1.85 mm was noted (two-tailed $p = 0.05$) (see Table 3 and Figs. 2 and 3). This finding was in contrast with the comparison performed in the nine other children, where no significant change was observed.

The other measurements performed showed no other change (see Table 3). The measurement of the mandibular ramus indicated that all children had growth of the mandible with significant

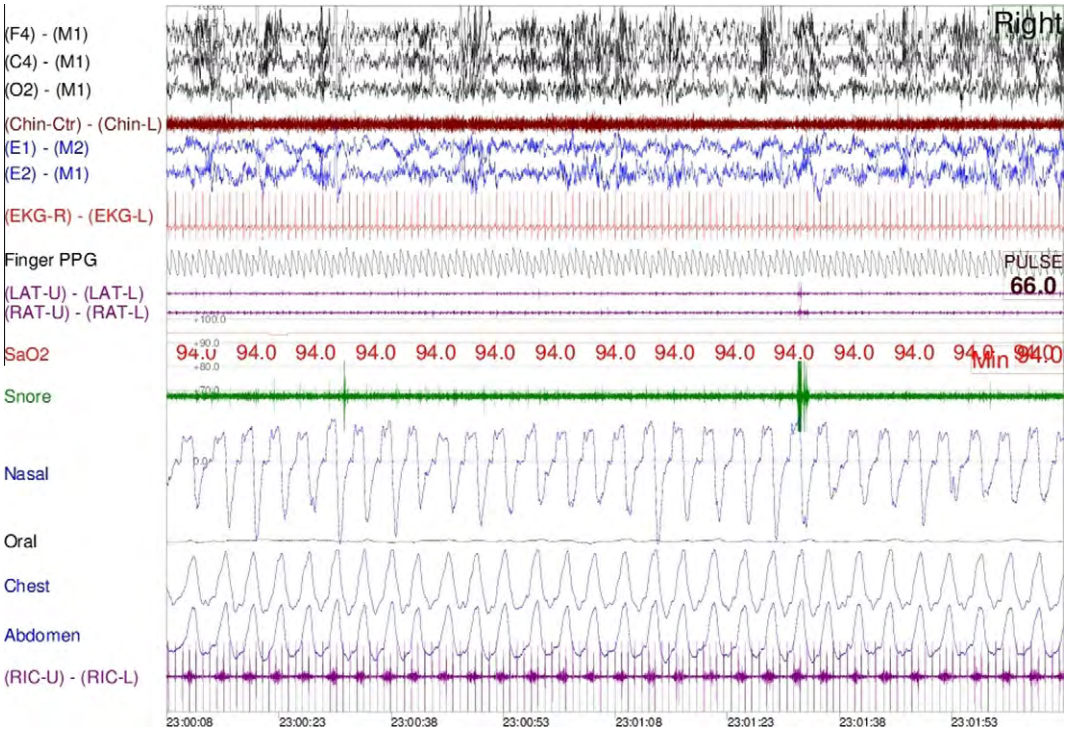

Fig. 4. Flow limitation. Example of 2 min polysomnographic recording with flow limitation in a pubertal teen-ager with clinical symptoms. Note the repetitive high amplitude EEG discharge part of the phaseA of the cyclic alternating system on the EEG leads (1–3 from the top), note the abnormal curve of nasal cannula-pressure-transducer recording on tracing #13 from the top (''nasal''). This tracing is characteristics of '':flow limitation'' tracing. Note that oxygen saturation tracing (# 11 from the top) do not change.

change between the mean of 11 years and mean of 14 years of age, and there was no significant difference between the two subgroups of teenagers at a mean of 14 years of age.

In summary, a group of teenagers considered as cured of SDB since their treatment in early childhood and with no clinical complaint and normal clinical oral–facial evaluation had reoccurrence of clinical complaints and presented with abnormal clinical oral–facial and myofunctional examinations [22] and changes in measurement of the PAS [19] at cephalometric X-rays (and to a lesser degree, a lengthening of the MP-H distance [19]. In one case, symptoms and cephalometric changes were documented 1 year apart. The most abnormal polysomnographic findings involved the amount of flow limitation and mouth breathing during sleep. This was associated with an increase in RERAs and to a lesser degree with an increase in AHI. SDB complaints had reoccurred between a mean age of 11 and 14 years.

4. Discussion

This is the first study that illustrates the very long-term evolution of OSA in children after report of adequate treatment of SDB. It suggests that the reappearance of SDB can occur several years following adequate surgical and orthodontic treatment, and that the presence of flow limitation on PSG may be an early indicator of this recurrence in adolescents. Anecdotally, many adult patients with OSA in our clinic report a history of snoring during childhood that resolved or improved after adenotonsillectomy, only to return in their late teens or early twenties. This study provides possible insights that may help to explain this report. In our small study, recurrence of OSA was seen more frequently in boys than in girls and involved a clear decrease in PAS on cephalometrics X-rays (see Figs. 2 and 3). Several studies have shown that children may still present with OSA after adenotonsillectomy, and even after orthodontic treatment, when evaluated with polysomnography [23]. However, the children in our retrospective studies had normal PSGs after performing both treatments. With such results, paediatricians will consider the health problem as resolved, as did sleep specialists at the time.

Our study has all the problems associated with retrospective studies: A large number of children had no follow-up. Unfortunately, this is the reality of clinical practice. This study faced other limitations typically associated with retrospective studies: a small sample size due to inadequate medical records and non-compliant follow-up. In addition, our study gives no indication of the frequency of the recurrence of OSA in individuals considered as "cured" after adenotonsillectomy alone during early childhood, despite the fact that the two prior publications indicate that similar recurrence rates were also noted in pubertal teenagers. The children presented here were followed up by orthodontists, and this may indicate that their anatomy may have been different from other children. A prior systematic evaluation of children using clinical anatomic scales has shown that one mild anatomic oral–facial considered as abnormal was very common in children with OSA, and the involvement of each of these independent anatomic factors in occurrence of OSA was difficult to assess as a single of these abnormal findings was noted in subjects with both normal and abnormal PSG results post-adenotonsillectomy [21], rendering their predictive value very questionable. Only three factors were significantly associated with the need for further treatment including a 3 or 3–4 Friedman-modified-Mallampati score [10], presence of a deviated septum and presence of a small mandible [21]. The children presented here were recommended to have orthodontics post-adenotonsillectomy based on their thorough evaluation and follow-up PSG, indicating the importance of such follow-up test not necessarily performed at many other laboratories. However, once these two treatments had been performed, our children had normal PSGs. With such results, paediatricians will consider the health problem as resolved, as did sleep specialists at the time.

Consistency of PSG and cephalometric measurement analyses over the years was difficult to determine, though the clinics involved in the study had been in collaboration for years.

In addition, despite the fact that the investigation was performed in clinics accustomed to collaborating, one cannot affirm that recordings were analysed similarly, despite the fact that all evaluations and scoring followed international criteria.

One may have wanted several scorers, particularly for cephalometric analyses, with comparison of obtained results between two or more specialists. The protocol called upon only one blinded reader, based on the belief that any bias presented when performing analyses would be systematic and reflected in all results.

In the teenagers with no complaints and symptoms, normal evaluation and normal cephalometry, a simple home study was judged as clinically justified. However, once again one may argue that tests were not exactly similar (ambulatory vs. laboratory study), a problem linked to the retrospective aspect of the study.

Children evaluated at orthodontic and sleep clinics covered by national health insurance were more likely to have follow-up with referral recommendations as compared to those evaluated in locations where such coverage, particularly orthodontics, was handled by private insurances with separate medical and dental insurance plans.

Finally, no child with adenotonsillectomy alone presented data at the three pre-established time points; follow-up and data in these children were very meagre in the consulted databases as shown in Fig. 1.

Despite the above limitations, this is the first study that addresses the long-term evolution of children with early-in-life OSA and recurrence of SDB. We found documentation of normal PAS [20] at a mean of 11 years with absence of complaints, and presence of complaints and small PAS at a mean age of 14 years. Our study also indicates the presence of flow limitation (see Fig. 4) as an important PSG marker of early recognition of reoccurring SDB; flow limitation was associated with mouth breathing and these two polygraphic patterns were observed in large amounts and showed the largest difference compared to the PSG patterns recorded in the nine other non-complaining subjects with normal PAS at cephalometrics.

Our study indicates that the complaint recurrence was not immediate, it occurred during the pubertal period and after a mean age (11 years) where the oral–facial development has usually reached about 90% of its adult final growth. Our study also shows an important amount of flow limitation in association with recurrence of complaints, previously shown to be associated with abnormal sleep and clinical complaints, and large amount of mouth breathing [24,25]. Orthodontists have long associated mouth breathing with oral–facial hypotonia [22,26]. This was affirmed by the abnormal myofunctional evaluations in our SDB teenagers [22]. Muscle hypotonicity is considered to be somewhat responsible for maxillary and mandibular deficiencies noted in many OSA children [27].

5. Conclusion

Resolution of OSA by PSG and disappearance of clinical symptoms during the prepubertal years after adenotonsillectomy with or without [28] rapid maxillary or bi-mandibular expansion does not necessarily indicate complete resolution of the factors responsible for SDB at later age. Recurrence of clinical complaints and SDB is seen with polysomnographic finding of flow limitation in teenagers. Considering knowledge accumulated since the 1970s on risk

of abnormal maxilla and mandibular growth with abnormal breathing, regular follow-up of children with positive history of SDB should be performed particularly during oral–facial growth.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2012.08.010.

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Towards Restoration of Continuous Nasal Breathing as the Ultimate Treatment Goal in Pediatric Obstructive Sleep Apnea

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Abstract

The interaction between oral-facial structural growth and muscle activity starts early in development and continues through childhood. Chronic oral breathing is an important clinical marker of orofacial muscle dysfunction, which may be associated with palatal growth restriction, nasal obstruction, and/ or a primary disorder of muscular or connective tissue dysfunction. It is easily documented objectively during sleep.

Treatment of pediatric obstructive-sleep-apnea (OSA) and sleep-disordered-breathing (SBD) means restoration of continuous nasal breathing during wakefulness and sleep; if nasal breathing is not restored, despite short-term improvements after adenotonsillectomy (T&A), continued use of the oral breathing route may be associated with abnormal impacts on airway growth and possibly blunted neuromuscular responsiveness of airway tissues.

Elimination of oral breathing, i.e., restoration of nasal breathing during wake and sleep, may be the only valid end point when treating OSA. Preventive measures in at-risk groups, such as premature infants, and usage of myofunctional therapy as part of the treatment of OSA are proposed to be important approaches to treat appropriately SDB and its multiple co-morbidities.

Keywords

Obstructive sleep apnea; Pediatrics; Oral-facial muscles; Nasal-oral functions; Myofunctional-therapy

Pediatric sleep disordered breathing (SDB) is seen in children along the entire spectrum of body mass index (BMI). Whether underweight, overweight, or within normal BMI limits, when pediatric SDB is present, there is abnormal collapsibility of the upper airway leading to abnormal breathing during sleep. This abnormal breathing is commonly associated with snoring, and severity of the upper airway collapse has been polygraphically defined. Importantly, such definitions rely in part on the type of recording performed during sleep, the sophistication of the sensors used to investigate abnormal breathing, and the experience of the interpreter; abnormalities from primary snoring and "nasal flow limitation" to complete "obstructive sleep apnea" (OSA) have been defined [1-3].

Remarkably, studies have shown that independent of the type of abnormal breathing during sleep noted on polysomnography (PSG), negative daytime consequences of pediatric SDB have been observed that may be sub-classified as neuro-behavioral, cardiovascular, and/or inflammatory [4-6]. However, not all children with abnormal sleep suffer from each of these consequences. Considering the above comorbidities, phenotyping of pediatric SDB patients has been suggested, with an overweight/obese subgroup of children, who may tend to have more nocturnal desaturation, and possibly cardiovascular and metabolic comorbidities; and a normal weight subgroup of children who may tend to present with neurobehavioral complaints, including problems with focus and concentration, hyperactivity, non-REM sleep parasomnias, learning problems, headache, mood disturbances, for example [7-12].

First Line Treatment with Adenotonsillectomy and Decreased in Benefits Over Time

Whether overweight or not, often the tonsils and adenoids in children with SDB are found to be enlarged. Clinically, it is recognized that enlargement of these tissues is often associated with frequent oral breathing. Historically, adentonsillectomy (T&A) has been performed to treat obstructive sleep apnea in children since the late 1970s [13], though it was certainly used before this in the setting of enlarged tonsils and adenoids. T&A came to be considered the first-line of therapy for pediatric SDB, and earlier studies, usually with short follow-up durations and with a variety of endpoints, suggested that T&A was highly successful for SDB in children, in both normal weight and overweight subgroups.

Over the years, systematic follow-up studies have revealed that T&A may not be as successful as once thought. [14-21] For years, routinepost-operative PSG recordings were deemed unnecessary and expensive; so when subjective clinical report of improvement was observed post operatively, no further PSG testing was performed. However, increasingly there have been reports indicating that T&A may not be a reliable cure for SDB [16-21]. Of particular interest is how SDB fares in children in the long run, whether treated or not. Most research on natural history of treated and/or untreated pediatric OSA are biased towards the short-term, towards relatively younger children, and may not involve objective PSG measures. Reports on very long term follow-up (for example, 3 years or greater) of children with SDB, after T&A or not, are still rare, but suggest that sleep disordered breathing (AHI or symptoms) cannot be expected to remain resolved or significantly improved in the longer run [22-25]. The reports that do exist typically involve children who have presented again due to appearance of further clinical SDB-related symptoms, with OSA detected upon repeat testing. Intriguingly, snoring itself, even without hypoxia and frequent arousals, is associated with day time cognitive and behavioral morbidity similar to that seen with more pronounced nocturnal breathing abnormalities, which may suggest the importance of anatomy in the long run. One early article to attract attention focused on the orofacial structures as the predisposing factor involved in SDB "recurrence" [14]; however, until recently the substantial body of knowledge regarding the continuous interaction between normal breathing, particularly during sleep, and normal orofacial growth was not integrated into the sleep medicine field, despite longstanding and accepted understanding of such mechanisms in the dental and orthodontic fields [26-29].

A solid understanding of the factors that influence normal growth of the upper airway is critical to providing appropriate, long-sighted treatment to children with SDB. Based on important recent findings, it appears that complete SDB treatment may mean normalization of nasal breathing during sleep. Unfortunately, this outcome – continuous nasal breathing during sleep – is almost always ignored in pediatric PSG interpretation, even though the data is collected and available to analyze.

At this time, we are aware of only one study has reported systematic clinical, psychometric, and PSG follow-up evaluation of prepubertal children with SDB, who were enrolled at baseline and followed prospectively. This Taiwanese study involved 2 groups of children aged 6 to 12 years; and 4 to 6 years [25]. After T&A for SDB, follow-up occurred over 3 years, with systematic evaluation at 6, 12, 24, and 36 months post-surgically. Results at each time point were compared to pre-surgery findings. Independent of age group, this study demonstrated retention of about 70% of the initial group. There was substantial improvement of symptoms and PSG findings at 6 months post-T&A, with about 50% of children having a normal apnea-hypopnea index (AHI). However, a progressive recurrence of clinical complaints and reemergence of abnormal PSG findings during the following 2.5 occurred, affecting both incompletely resolved SDB at 6 months, as well as those children with normal test results at 6 month post T&A. About 25% of the children with normal PSG results at 6 months still normal findings at the end of the study. (Bonuck and colleagues found in a large, longitudinal study of symptoms associated with SDB that adenoidectomy lowered the risk of future SDB symptoms by about 40-50%). [24] An interesting finding in the Taiwanese study came from comparison of the 2 age groups over time: the younger group had less "recurrence", and when recurrence was present, it took longer to reappear and was less severe. The investigators concluded that: 1) It is important to recognize the SDB syndrome early; 2) It is important to perform T&A at an early age if SDB is present; and 3) even with early intervention, a large portion of children with SDB will redevelop SDB overtime.

We propose that one reason for high rates of re-emergence of SDB in susceptible children is that normal nasal breathing has not been completely or lastingly reestablished after T&A, contributing to facial growth alterations and/or orofacial muscle tone deficits that predispose to further SDB over time. The importance of adequate nasal airway development and patency, the absence of which is clinically seen as mouth breathing, is suggested by both experimental findings and in a variety of clinical scenarios, described below.

Mouth breathing is common [24] – reported in 10-25% of children [30] – but as a marker or contributor to sleep disordered breathing, its role is largely unstudied. Intriguing associations exist, and are provided in detail below.

Interactions Between Orofacial Function and Growth: Experimental Data Involving Nasal Obstruction

The observation that increased nasal resistance and its companion, chronic oral breathing, alter facial growth is by no means new in medicine – Meyer described "adenoidal facies" in 1868, in which nasal obstruction from adenoidal hypertrophy led to what he termed "long face syndrome". Other have also commented on the apparent relationship between function and form [28]-i.e., obstruction and "deviant facial growth."

The craniofacial growth consequences of frequent mouth breathing may predispose to SDB. Mouth breathing has been demonstrated to lead to changes in muscle recruitment in the upper airway, which then alter craniofacial growth [27,31]. Small studies have evaluated the influence of oral breathing due to nasal obstruction on dento-facial development [32-34]. Over thirty years ago, a series of experiments in which nasal obstruction was induced in Rhesus monkeys for the first six months of life demonstrated that blockage of the nasal passages led to narrowing of dental arches, decreased maxillary arch length, and increased anterior facial height, as well as anterior cross-bite and maxillary overjet. [35-37] In these studies, EMG activity of oral facial muscles, including the geniohyoid and genioglossal muscles of the tongue, the suprahyoid dorsal tongue fibers, the upper lip elevators, and the digastric muscles, was shown to be abnormal in the monkeys with nasal obstruction. These experiments related morphometric skeletal changes to changes in muscle tone, which were present in the setting of continuous mouth breathing.

In humans, abnormal masseteric contractions have also be demonstrated in the presence of mouth breathing [38], suggesting that abnormal orofacial muscle activity links nasal obstruction to deficits in structural airway growth. Secondary posture changes associated with chronic mouth breathing have also been identified [30,39,40]. Interestingly, in the Rhesus monkey model, removal of nasal obstruction at 6 months led to return of normal nasal breathing and yielded improved morphometric development, whereas continued impairment of normal nasal breathing led to continued mouth breathing and abnormal oral-facial growth and development.

Interactions Between Orofacial Function and Growth: Observations in Disorders Involving Upper Airway Muscle Dysfunction

Increased nasal resistance is unlikely to be the sole avenue to chronic oral breathing and subsequent craniofacial growth alterations. In humans, neuromuscular disorders provide further insight about the relationship between altered muscle tone and changes in craniofacial development. [41-43] for example, in the myotonic dystrophies and some congenital myopathies, abnormal orofacial muscle tone leads to impaired development of craniofacial structures. Presentation includes increased vertical facial growth, a narrower maxillary arch, and deeper palatal depths. In these disorders, abnormal orofacial muscle tone has consequences for the growth of upper airway structures, in association with early and chronic mouth breathing and frequent development of obstructive SDB, with rates reported to be 43-69%.

Ehlers-Danlos Syndrome (EDS), on the other hand, is an inherited connective tissue disorder involving abnormal collagen. The collagen-vascular mutations seen in Ehlers-Danlos syndrome lead to abnormal facial growth. These changes lead to narrow nasal passages, forcing mouth breathing, particularly during sleep [44]. Clinical evaluation demonstrates abnormally long facial shape, narrow and/or high maxillary hard palate, often with crossbite. While initially only abnormalities of the naso-maxillary complex maybe seen, as patients get older, defects of the mandibular condyle may become evident, which we hypothesizeis promoted by the presence of chronic oral breathing. A similar pattern of facial growth abnormality is noted with dental agenesis: Mutations in homeobox genes including those involved in normal tooth development (including those with ectodysplasin A -EDA- and WNT 10A genes as noted in our patients) lead to narrow facial skeleton, mouth breathing and, in our study, to SDB [45-48].

History of prematurity is another circumstance associated with higher likelihood of sleep disordered breathing in childhood, and is therefore another interesting example of the interplay between muscle tone, craniofacial growth, and nasal versus oral breathing route. Recently a large convenience cohort of 300 premature infants (36 to 27 weeks gestational age) was followed for 3 years after birth with clinical evaluation, psychometric testing, facial and oral dimension assessment, and PSGs at birth, 12, 24 and 36 months of age. [49-50] as expected, the infants had a variable degree of hypotonia, with severity generally related to degree of prematurity. High and narrow hard palate (HNP) was noted at birth in many premature infants and was more common with younger gestational age; HNP infants were more likely to exhibit mouth breathing; and their mean apnea-hypopnea index (AHI) was significantly higher compared to the non-high/narrow palate group; and the HNP infants were also found to have significantly more feeding difficulties. While many infants with feeding difficulties did not receive early feeding/orofacial education services, including sensory stimulation training and oral-facial exercises, 42infants did receive these services and rather remarkably, demonstrated improvements in palatal dimensions at 36 months relative to those without orofacial training. We hypothesizethat orofacial muscle development played a role in normalization of palatal structures at 36 months. There were also 23 infants who had a normal palate at birth, but evolved toward HNP, mouth breathing and SDB, suggesting that postnatal developmental factors also alter palatal growth [49].

In summary, whether experimentally induced or developmentally provoked, science and nature have provided with examples of the interplay between increased nasal resistance and/or poor muscle tone leading to chronic oral breathing, and subsequent altered craniofacial dimensions. We believe that the presence of chronic oral breathing is both a marker of an inadequate or obstructed nasal-pharyngeal airway, and a marker of persisting abnormalities in the developmental interplay between muscular control, breathing route, and structural growth of the upper airway.

Applications in the Treatment of Pediatric Sleep-Disordered Breathing

While the above considerations are suggestive, much more work is needed to understand chronic mouth breathing as a marker of, and possible precipitator of, SDB in pediatrics. To further understand the proposed detrimental role of abnormal orofacial tone and mouth breathing during sleep, PSGs of 64 non-obese children aged 3 to 9 years (with mean AHI=8.5 events/hour and mean flow limitation= 76%), and who had PSGs pre- and post- treatment for SDB, were assessed [51]. In our lab, an oral-only sensor (utilizing an oral scoop) is used toaccurately and simply monitors mouth breathing [52]. In all of the baseline PSGs of the 64 children with SDB, there was evidence of excessive mouth breathing (defined as at least one third of total sleep time) on baseline diagnostic PSG. After adenotonsillectomy, 26 children had an AHI equal or higher than 1.5 events/hour. These children continued to have evidence of significant oral breathing. An additional 9 children whose AHI was under 1.5 events per hour also continued to have oral breathing - this is a very interesting group deserving further study. Clinically, children with SDB and persistent chronic mouth breathing after T&A may be referred for myofunctional therapy [53] in addition to usual therapies (e.g., consideration of anti-inflammatory medications, rapid maxillary expansion, CPAP). Eighteen children returned for 12 month follow-up, with only 9 having completed 6 months of myofunctional therapy. Though the numbers are very small, those who completed myofunctional therapy in addition to usual therapies were observed to have had improvements in nasal breathing as well as sleep, as measured by AHI and nasal flow limitation, beyond improvements seen in children without myofunctional therapy [51]. This suggests that even after nasal obstruction has been alleviated, improving muscle function of certain airway muscles, including the tongue, may improve function and/or growth of the upper airway, with resultant consequences for nasal breathing during sleep [51-55].

Observations and Conclusions: The Interplay Between Muscle Activity, Structural Growth, and Breathing During Wake and Sleep

The interaction between orofacial structural growth and muscle activity starts early in development, and the physiologic functions of suction, mastication, swallowing and nasal breathing in infancy play an important role in stimulating subsequent growth [55-58]. In the service of these functions, orofacial muscle use serves to help stimulate the direction and degree of growth. Mouth breathing is associated with altered oral-facial muscle activity and oral-facial growth. As such, its persistence is never normal. In fact, oral breathing has been termed "the most obvious manifestation of a syndromic pattern" involving a circuit of frequent infections, development of malocclusion, incorrect phonation, abnormalities of body posture, and changes in sleep. [30] Fortunately, oral breathing as a clinical sign has the advantage that its presence can be detected by simple direct observation, and its severity during sleep can be quantified with PSG.

During the past several decades, efforts have been undertaken to develop programs that will foster normal development of orofacial functions in at-risk children, including appliances as well as speech therapy, even, it could be argued, without recognition of all of the many benefits of doing so. Reeducation programs targeting normal orofacial muscle function have been developed in many countries, particularly among the orthodontic field, where oral-facial growth problems are often first identified [30,55,59-60]. Variants of myofunctional therapy have also been used in muscular dystrophies to delay secondary impacts on craniofacial bone growth and maxilla-mandibular impairment, and in young children to correct speech abnormalities, another common consequence of improper orofacial/ genioglossal tone, coordination, and/or structure. Despite these many applications, it is only in the recent past that myofunctional therapy has been proposed to make an impact in the treatment of SDB [30,53-54]. This is somewhat surprising, since muscle retraining has been used in adults with OSA with reduction of AHI, even without a proposed impact on the facial skeleton. Timing is likely to be important, since the gains from therapy are proposed to be via a mechanism of improved nasal breathing and improved craniofacial growth. Unfortunately, except for very limited reports, usage of myofunctional therapy very early in the course of SDB in pediatrics is limited, despite the fact that these therapies have existed for a long time. Thinking broadly, it could be argued that all of the accepted therapies for pediatric SDB may target improved nasal airflow one way or another; adding muscle strengthening might be an additional tool towards encouraging optimal craniofacial growth and perhaps long term improved outcomes in those at risk for SDB.

We conclude that oral breathing is an important clinical marker of orofacial muscle dysfunction, which may be associated with palatal growth restriction, nasal obstruction, and/or disorders of musculoskeletal dysfunction. Framing full treatment of pediatric SBD as restoration of continuous nasal breathing during wakefulness and sleep ought not to be considered. Our view based on the collected data is that if nasal breathing is not restored, despite short-term improvements after T&A, continued use of the oral breathing route will be associated with abnormal impacts on airway growth and possibly blunted neuromuscular responsiveness of airway tissues, both of which may predispose to the eventual return of upper airway collapse in later childhood, or in the full blown syndrome of OSA in adulthood. We believe elimination of oral breathing, i.e., restoration of nasal breathing during wake and sleep, may be the only valid "finish line" in pediatric sleep disordered breathing.

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Effects of Oropharyngeal Exercises on Patients with Moderate Obstructive Sleep Apnea Syndrome

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Rationale: **Upper airway muscle function plays a major role in maintenance of the upper airway patency and contributes to the genesis of obstructive sleep apnea syndrome (OSAS). Preliminary results suggested that oropharyngeal exercises derived from speech therapy may be an effective treatment option for patients with moderate OSAS.**

Objectives: **To determine the impact of oropharyngeal exercises in patients with moderate OSAS.**

Methods: **Thirty-one patients with moderate OSAS were randomized to 3 months of daily (~30 min) sham therapy (n = 15, control) or a set of oropharyngeal exercises (n = 16), consisting of exercises involving the tongue, soft palate, and lateral pharyngeal wall.**

Measurements and Main Results: **Anthropometric measurements, snoring frequency (range 0–4), intensity (1–3), Epworth daytime sleepiness (0–24) and Pittsburgh sleep quality (0–21) questionnaires, and full polysomnography were performed at baseline and at study conclusion. Body mass index and abdominal circumference of the entire group were 30.3 ± 3.4 kg/m^2 and 101.4 ± 9.0 cm, respectively, and did not change significantly over the study period. No significant change occurred in the control group in all variables. In contrast, patients randomized to oropharyngeal exercises had a significant decrease ($P < 0.05$) in neck circumference (39.6 ± 3.6 vs. 38.5 ± 4.0 cm), snoring frequency (4 [4–4] vs. 3 [1.5–3.5]), snoring intensity (3 [3–4] vs. 1 [1–2]), daytime sleepiness (14 ± 5 vs. 8 ± 6), sleep quality score (10.2 ± 3.7 vs. 6.9 ± 2.5), and OSAS severity (apnea-hypopnea index, 22.4 ± 4.8 vs. 13.7 ± 8.5 events/h). Changes in neck circumference correlated inversely with changes in apnea-hypopnea index ($r = 0.59$; $P < 0.001$).**

Conclusions: **Oropharyngeal exercises significantly reduce OSAS severity and symptoms and represent a promising treatment for moderate OSAS.**

Clinical trial registered with www.clinicaltrials.gov (NCT 00660777).

Keywords: obstructive sleep apnea; treatment; oropharyngeal exercises

Obstructive sleep apnea syndrome (OSAS) is a significant public health problem characterized by repetitive episodes of upper airway occlusion during sleep associated with sleep fragmentation, daytime hypersomnolence, and increased cardiovascular risk (1, 2). It is well established that the most effective treatment for OSAS is continuous positive airway pressure (CPAP) (3). CPAP virtually eliminates OSAS in conjunction with elimination of snoring, reduction of daytime sleepiness, and improvement in subjective sleep quality (3, 4). The improvement is especially true for patients with severe OSAS, in whom the apnea-hypopnea index (AHI) is greater than 30 events/hour. However, for moderately affected patients (AHI between 15 and 29.9 events/h), CPAP therapy may not be suitable for a significant proportion of patients. Alternative treatments for moderate OSAS include mandibular advancement, weight loss, and surgery; these treatments have variable results (5). Therefore, it is necessary to test the efficacy of other modalities of treatment for moderate OSAS, particularly considering that this subset of patients makes up a significant percentage of the OSAS population.

The genesis of OSAS is multifactorial and includes anatomical and physiological factors. Upper airway dilator muscles are crucial to the maintenance of pharyngeal patency and may contribute to the genesis of OSAS (6, 7). A recent study showed that upper airway muscle training while awake with the use of didgeridoo playing significantly ameliorated OSAS severity and associated symptoms (8). A set of oropharyngeal exercises, cited hereafter as "oropharyngeal exercises" for the sake of simplicity, is derived from speech therapy and consists of isometric and isotonic exercises involving the tongue, soft palate, and lateral pharyngeal wall, including functions of suction, swallowing, chewing, breathing, and speech. Oropharyngeal exercises have been previously shown to be effective in small and noncontrolled studies (9). In the present study, recently presented in the form of an abstract (10), we tested in a randomized controlled trial the effects of oropharyngeal exercises in patients with moderate OSAS on objective measurement of severity derived from polysomnography as well as subjective sleep symptoms, including snoring, daytime sleepiness, and sleep quality.

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Continuous positive airway pressure is the treatment of choice for obstructive sleep apnea syndrome (OSAS) but is not suitable for a large proportion of patients. Alternative treatments for OSAS have shown variable results.

What This Study Adds to the Field

This randomized controlled trial showed that oropharyngeal exercises developed for the treatment of OSAS significantly reduced OSAS severity and symptoms. This novel modality of OSAS treatment represents a promising approach for moderate OSAS.

METHODS

Patients

We considered eligible patients between 25 and 65 years of age with a recent diagnosis of moderate OSAS evaluated in the sleep laboratory, Pulmonary Division, Heart Institute (InCor), University of São Paulo Medical School. We excluded patients with one or more of the following conditions: body mass index (BMI) 40 kg/m^2 or greater,

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craniofacial malformations, regular use of hypnotic medications, hypothyroidism, previous stroke, neuromuscular disease, heart failure, coronary disease, or severe obstructive nasal disease. The local ethics committee approved the study, and all patients gave written informed consent.

Polysomnography

All patients were evaluated by full polysomnography using the following electrophysiological parameters: EEG (C3-A2, C4-A1, O1-A2, O2-A1), electrooculogram (two channels), submentonian and anterior tibial EMG, snoring sensor, air flow (two channels) measured with oronasal thermistor and nasal pressure cannula, thoracic and abdominal belts, ECG, position detector, oxygen saturation, and heart pulse, as previously described (11). Moderate OSAS was defined by an AHI between 15 and 29.9 events per hour of sleep (1). The person who analyzed the sleep study was blinded to the group allocation.

Questionnaire

Snoring frequency, ranging from 0 (never) to 4 (every day) and intensity 1 (similar to breathing) to 3 (very loud) were derived from the Berlin questionnaire (12, 13). Subjective daytime sleepiness was evaluated with the Epworth questionnaire that evaluates the propensity to sleep from no (0) to intense (3) in eight different situations. Total score greater than 10 is considered excessive daytime sleepiness (14). Quality of sleep was evaluated with the Pittsburgh sleep quality questionnaire that evaluates seven sleep components on a scale of 0 to 3, 0 indicating no difficulty and 3 indicating severe difficulty. The results are expressed as a global score (ranging from 0–21). Values greater than 5 are consistent with poor sleep quality (15).

Control Group

Sham therapy consisted of a weekly, supervised session (~30 min) of deep breathing through the nose while sitting. The patients were also instructed to perform the same procedure at home once a day (30 min), plus nasal lavage with application of 10 ml of saline in each nostril three times a day. At study entry bilateral chewing was recommended when eating meals.

Study Group

The same schedule and set of instructions applied to the control group were given to these patients with the substitution of deep breathing by effective therapy. Oropharyngeal exercises are derived from speech–language pathology and include soft palate, tongue, and facial muscle exercises as well as stomatognathic function exercises. The patients were instructed by one single speech pathologist (K.C.G.) to perform the following tasks (*see* online supplement, which includes a film of the exercises).

Soft palate. Pronounce an oral vowel intermittently (isotonic exercise) and continuously (isometric exercise). The palatopharyngeus, palatoglossus, uvula, tensor veli palatini, and levator veli palatini muscles are recruited in this exercise. The isotonic exercise also recruits pharyngeus lateral wall. These exercises had to be repeated daily for 3 minutes and were performed once a week under supervision to ensure adequate effort.

Tongue. (*1*) Brushing the superior and lateral surfaces of the tongue while the tongue is positioned in the floor of the mouth (five times each movement, three times a day); (*2*) placing the tip of the tongue against the front of the palate and sliding the tongue backward (a total of 3 min throughout the day); (*3*) forced tongue sucking upward against the palate, pressing the entire tongue against the palate (a total of 3 min throughout the day); (*4*) forcing the back of the tongue against the floor of the mouth while keeping the tip of the tongue in contact with the inferior incisive teeth (a total of 3 min throughout the day).

Facial. The exercises of the facial musculature use facial mimicking to recruit the orbicularis oris, buccinator, major zygomaticus, minor zygomaticus, levator labii superioris, levator anguli oris, lateral pterygoid, and medial pterygoid muscles. The exercises include: (*1*) Orbicularis oris muscle pressure with mouth closed (isometric exercise). Recruited to close with pressure for 30 seconds, and right after, requested to realize the posterior exercise. (*2*) Suction movements contracting only the buccinator. These exercises were performed with repetitions (isotonic) and holding position (isometric). (*3*) Recruitment of the buccinator muscle against the finger that is introduced in the oral cavity, pressing the buccinator muscle outward. (*4*) Alternated elevation of the mouth angle muscle (isometric exercise) and after, with repetitions (isotonic exercise). Patients were requested to complete 10 intermittent elevations three times. (*5*) Lateral jaw movements with alternating elevation of the mouth angle muscle (isometric exercise).

Stomatognathics functions.

1. Breathing and Speech: (*1*) Forced nasal inspiration and oral expiration in conjunction with phonation of open vowels, while sitting; (*2*) Balloon inflation with prolonged nasal inspiration and then forced blowing, repeated five times without taking the balloon out of the mouth.
2. Swallowing and Chewing: Alternate bilateral chewing and deglutition, using the tongue in the palate, closed teeth, without perioral contraction, whenever feeding. The supervised exercise consisted of alternate bread mastication. This exercise aims for the correct position of the tongue while eating and targets the appropriate functionality and movement of the tongue and jaw. The patients were instructed to incorporate this mastication pattern whenever they were eating.

Experimental Design

After fulfilling entry criteria, the patients were randomized for 3 months into either the control or treatment group, with oropharyngeal exercises. All patients were evaluated by the speech–language pathologist once a week for 30 minutes. All patients had to fill a diary recording compliance to exercises (yes or no). The query was subdivided in three distinct domains: tongue, palate, and face. Overall, adequate compliance was evaluated on a weekly basis and defined by the performance of 85% or more of the exercises proposed in all domains. Patients who failed to return for three consecutive weeks or failed to comply with the exercises at home (performing <85% of the exercises) were excluded from the study. Polysomnography and questionnaires were performed at the beginning and end of the study. The primary outcome was AHI. Secondary outcomes included lowest oxygen saturation and sleep-related questionnaires.

Statistical Analysis

Data were analyzed with STATISTICA 5.0 software. Baseline characteristics of patients with OSAS according to the group assigned were compared by two-tailed unpaired *t* tests for continuous variables and Fisher exact test for nominal variables. For variables with skewed distribution, we performed Mann-Whitney test. Two-way repeated-measures analysis of variance and Tukey test were used to compare differences within and between groups in variables measured at baseline and after 3 months. In addition, we performed Pearson correlations between changes in AHI with changes in possible explanatory variables, including BMI, abdominal circumference, and neck circumference. A value of $P < 0.05$ was considered significant.

RESULTS

We screened more than 50 patients in whom moderate OSAS had been recently diagnosed in our sleep laboratory. Because of our exclusion criteria, we recruited 39 patients. Eight patients (3 in the active treatment arm) were excluded due to low adherence as defined in the METHODS section. The 31 patients included in the final analysis were predominantly middle-aged males, overweight or obese. The demographic and sleep characteristics and symptoms of the population, according to the group assigned, are presented in Table 1. Patients assigned to control and therapy groups had similar baseline characteristics (Table 1). No changes in weight or abdominal circumference during the study period were observed in either group (Table 2). After 3 months, no significant changes were observed in the control group (Table 2). In contrast, patients randomized to

TABLE 1. BASELINE DEMOGRAPHIC AND SLEEP CHARACTERISTICS OF THE PATIENTS ASSIGNED TO CONTROL OR OROPHARYNGEAL THERAPY

	Control (*N = 15*)	Therapy (*N = 16*)	*P* Value
Age, years	47.7 ± 9.8	51.5 ± 6.8	0.23
Males, %	73	63	1.0
Whites, %	71	60	0.97
BMI, kg/m^2	31.0 ± 2.8	29.6 ± 3.8	0.24
Neck circumference, cm	40.9 ± 3.5	39.6 ± 3.7	0.30
Abdominal circumference, cm	103 ± 7	100 ± 10	0.37
Smoking, %	20	6.3	0.33
Hypertension, %	33.3	18.8	0.43
Diabetes, %	6.7	6.3	1.0
Epworth Sleepiness Scale	14 ± 7	14 ± 5	0.83
Snoring frequency	4 (3.3–4)	4 (4–4)	0.21
Snoring intensity	3 (2.3–4)	3 (3–4)	0.33
Sleep quality, Pittsburgh	11 ± 4	10 ± 4	0.69
Sleep efficiency	86 ± 10	87 ± 8	0.72
Arousals	148 (73–173)	140 (102–236)	0.26
AHI (events/hour)	22.4 ± 5.4	22.4 ± 4.8	0.98
Apnea index (events/hour)	9.1 ± 6.6	6.6 ± 4.7	0.35
Hypopnea index (events/hour)	14.8 ± 8.4	14.7 ± 6.6	0.20
Lowest Sa_{O_2}, %	82 ± 4	83 ± 6	0.56

Definition of abbreviations: AHI = apnea-hypopnea index; BMI = body mass index.

Plus-minus values are mean ± SD. Snoring frequency, snoring intensity, and arousals were presented as median (25–75%) because of skewed distribution.

therapy had significantly decreased neck circumference, snoring symptoms, subjective sleepiness, and quality of sleep score (Table 2). In addition, patients assigned to oropharyngeal exercises experienced a significant decrease in AHI compared with control subjects (Figure 1). There was a small but significant decrease in minimal oxygen saturation in the control group and a significant increase in minimal oxygen saturation in the treatment group (Figure 2). In the treatment group, 10 patients (62.5%) shifted from moderate to mild (n = 8) or no (n = 2) OSAS. Considering the entire group, changes in AHI did not correlate significantly with changes in anthropometric measurements except with changes in neck circumference (Figure 3).

DISCUSSION

This randomized controlled study is the first to investigate the effects of upper airway muscle training by a series of oropharyngeal exercises in patients with moderate OSAS. Three months of exercise training reduced by 39% the severity of OSAS evaluated by the AHI and lowest oxygen saturation determined by polysomnography. The significant OSAS improvement in the patients randomized to muscle training occurred in conjunction with a reduction in snoring, daytime sleepiness, and quality of sleep score. Despite no significant changes in body habitus, patients randomized to oropharyngeal therapy had a significant reduction in neck circumference, suggesting that the exercises induced upper airway remodeling. Changes in AHI correlated negatively with changes in cervical circumference.

The set of oropharyngeal exercise used in the current study was developed over the last 8 years and has previously been shown to be effective in uncontrolled studies (9). There is proof of the concept that muscle training while awake will reduce upper airway collapsibility during sleep in patients with OSAS. Tongue muscle training during the daytime for 20 minutes twice a day for 8 weeks reduced snoring, but did not change AHI significantly in a randomized controlled study (16). A recent trial found that in patients with moderate OSAS 4 months of training of the upper airways by didgeridoo playing reduced daytime sleepiness, snoring, and AHI (8). However, in contrast to our study, the study was not a fully controlled group (control group consisted of subjects on the waiting list for didgeridoo playing), sleep was not monitored (cardiorespiratory studies), the primary outcome was subjective sleepiness, and the reduction of AHI was marginal ($P = 0.05$) (8). In our study, the oropharyngeal exercises were developed with the primary objective of reducing OSAS severity (9). The reduction in the AHI observed in patients with moderate OSAS was remarkable and in the same order of magnitude as that previously reported by a review of randomized studies that used a mandibular advancement appliance for OSAS (17) (39 vs. 42%, respectively) (17, 18). The effects of oropharyngeal exercises were observed not only in the AHI and lowest oxygen saturation, but also in the symptoms associated with OSAS. In the control group no significant changes were reported in all parameters. The effect of oropharyngeal exercises on daytime somnolence was quite effective, reducing the Epworth sleepiness scale an average of 6 units (Table 2). For severely affected patients, the minimum significant difference on this scale was suggested to be around 4 units (19). Oropharyngeal exercises also induced significant improvements in several subjective sleep scales, including Pittsburgh and snoring symptoms.

TABLE 2. ANTHROPOMETRIC, SYMPTOM, AND SLEEP CHARACTERISTICS AT BASELINE AND AFTER 3 MONTHS OF RANDOMIZATION

	Control (*N = 15*)			Therapy (*N = 16*)		
Variables	Baseline	3 mo	*P* Value	Baseline	3 mo	*P* Value
BMI, kg/m^2	31.0 ± 2.8	30.8 ± 3.0	0.34	29.6 ± 3.8	29.5 ± 4.3	0.65
Neck circumference, cm	40.9 ± 3.5	40.7 ± 3.7	0.53	39.6 ± 3.6	38.5 ± 4.0	0.01*
Abdominal circumference, cm	102.9 ± 7.3	102.3 ± 7.4	0.26	100.0 ± 10.4	98.9 ± 12.1	0.33
Epworth Sleepiness Scale	14 ± 7	12 ± 6	0.35	14 ± 5	8 ± 6	0.006*
Snoring frequency	4 (3.3–4)	4 (3–4)	0.79	4 (4–4)	3 (1.5–3.5)	0.001†
Snoring intensity	3 (2.3–4)	3 (2–3)	0.30	3 (3–4)	1 (1–2)	0.001*
Sleep quality, Pittsburgh	10.7 ± 3.7	10.8 ± 4.1	0.88	10.2 ± 3.7	6.9 ± 2.5	0.001†
Sleep efficiency, %	86 ± 10	87 ± 11	0.79	87 ± 8	86 ± 9	0.58
Apnea index, events/hour	9.1 ± 6.6	9.6 ± 6.0	0.94	6.6 ± 4.7	3.3 ± 3.2	0.009†
Hypopnea index, events/hour	14.8 ± 8.4	14.7 ± 6.6	0.90	14.7 ± 6.6	9.5 ± 5.8	0.07
AHI REM, events/hour	29.9 ± 11.6	39.3 ± 21.0	0.06	29.8 ± 12.7	17.4 ± 15.9	0.007†
AHI NREM, events/hour	20.3 ± 9.6	23.7 ± 8.8	0.75	19.8 ± 7.0	15.2 ± 10.3	0.13

Definition of abbreviations: AHI = apnea-hypopnea index; BMI = body mass index; NREM = non–rapid eye movement; REM = rapid eye movement.

Plus-minus values are mean ± SD. Snoring frequency and snoring intensity were presented as median (25–75%) because of skewed distribution.

* $P < 0.05$ for the comparisons between the groups.

† $P < 0.01$ for the comparisons between the groups.

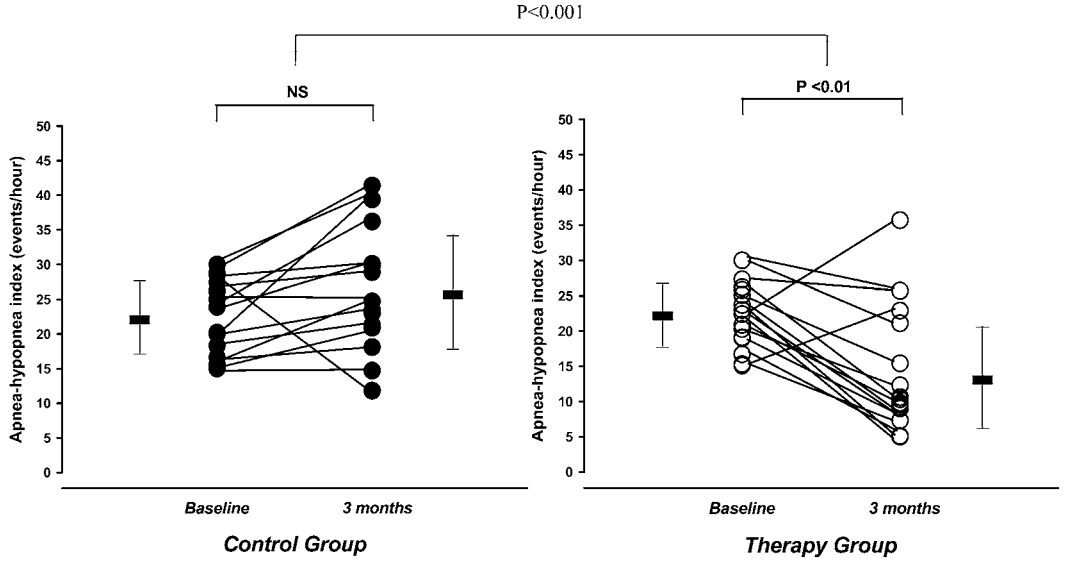

Figure 1. Individual values for apnea-hypopnea index (AHI). In the control group, the AHI from baseline to 3 months (from 22.4 ± 5.4 to 25.9 ± 8.5 events/h) was similar. In contrast, the AHI significantly decreased in the group randomized to oropharyngeal exercises (from 22.4 ± 4.8 to 13.7 ± 8.5 events/h; $P < 0.01$). The differences between groups remained significant ($P < 0.001$). Short horizontal lines and bars are mean ± SD. NS = not significant.

This study describes a new method of upper airway exercise training for which there is no comparable study available to date. The series of exercises was primarily developed to increase upper airway patency and is based on the concept that the functions of sucking, swallowing, chewing, breathing, and speech are closely related and are part of the stomatognathic system (20). The exercises were developed based on this integrated concept of overlapping functions of the upper airways as well as on the clinical observation of patients with OSAS. Patients with OSAS typically had elongated and floppy soft palate and uvula, enlarged tongue, and inferior displacement of the hyoid bone (21–23). The exercises targeting soft palate elevation use speech exercises that recruit several upper airway muscles. In addition to the recruitment of the tensor and levator veli palatine, these exercises also recruit muscle fibers of the palatopharyngeal and palatoglossus muscle. Based on the evidence that tongue posture appears to have a substantial effect on upper airway structures (16, 24), specific exercises were developed targeting tongue repositioning. The facial muscles are also recruited during chewing and were also trained with the intention of training muscles that promote mandibular elevation, avoiding mouth opening. We speculate that this treatment modality may affect the propensity to upper airway edema and collapsibility (25). It must be stressed that this study was not designed to explore the exact mechanisms by which this set of oropharyngeal exercises improves OSAS severity and symptoms. However, the observation of a moderate association between changes in neck circumference with changes in AHI (Figure 3) suggests that the exercises induce upper airway remodeling that in turn correlates with airway patency during sleep (26).

Our study has limitations. First, the therapy is based on an integrative approach and therefore does not allow determining the effects of each specific exercise on the overall result. Moreover, these exercises are derived from oral motor techniques to improve speech and/or swallowing activity, an area that lacks the empirical support necessary for evidence-based practices (27). On the other hand, this approach allowed us to select an appropriate sham intervention, wherein patients were given breathing exercises and nasal lavage. Second, the generalization of oropharyngeal exercises for moderate OSAS must be viewed with caution, because it will depend on the training speech

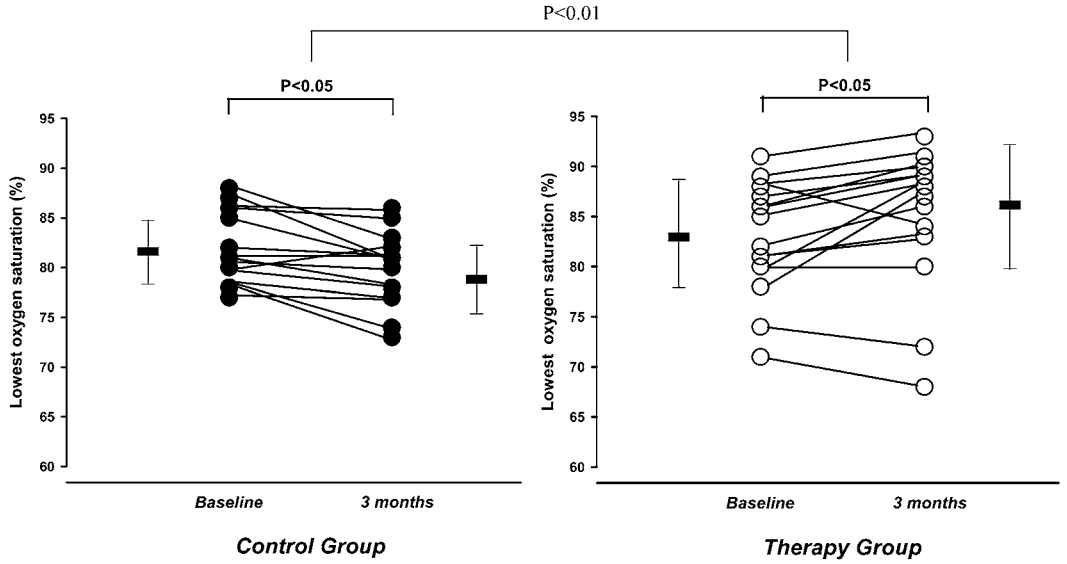

Figure 2. Individual values for lowest oxygen saturation. In the control group, the lowest oxygen saturation significantly decreased from baseline to 3 months (from 82 ± 4 to 80 ± 4%). In the group randomized to oropharyngeal exercises, the lowest oxygen saturation significantly increased (from 83 ± 6 to 85 ± 7%). The differences between groups remained significant ($P < 0.01$). Short horizontal lines and bars are mean ± SD.

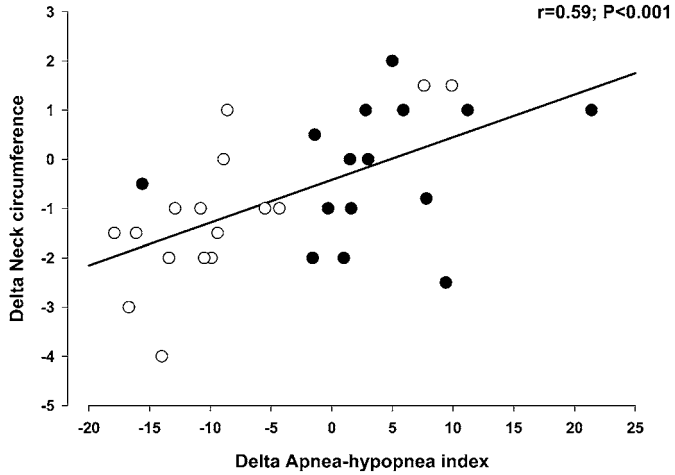

Figure 3. Correlations between apnea-hypopnea index with neck circumference. *Solid circles,* control group; *open circles,* therapy group.

pathologists. Based on our experience over the last 8 years (9), these patients will need to continuously exercise the upper airway muscles, which will raise an important issue related to treatment compliance. Finally, we observed that the overall effects of oropharyngeal exercises were present both in rapid eye movement (REM) and non-REM sleep, reaching statistical significance in REM sleep but not in non-REM sleep. We believe that this result may be justified by the relatively small sample size involved in this randomized study. However, we would like to stress that this study was designed to test the hypothesis that a set of oropharyngeal exercises is effective in reducing the severity of OSAS, as measured by the overall AHI across the night.

In conclusion, in patients with moderate OSAS, oropharyngeal exercises improved objective measurements of OSAS severity and subjective measurements of snoring, daytime sleepiness, and sleep quality. Our results suggest that this set of oropharyngeal exercises is a promising alternative for the treatment of moderate OSAS.

Conflict of Interest Statement: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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Effects of Oropharyngeal Exercises on Snoring
A Randomized Trial

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BACKGROUND: Snoring is extremely common in the general population and may indicate OSA. However, snoring is not objectively measured during polysomnography, and no standard treatment is available for primary snoring or when snoring is associated with mild forms of OSA. This study determined the effects of oropharyngeal exercises on snoring in minimally symptomatic patients with a primary complaint of snoring and diagnosis of primary snoring or mild to moderate OSA.

METHODS: Patients were randomized for 3 months of treatment with nasal dilator strips plus respiratory exercises (control) or daily oropharyngeal exercises (therapy). Patients were evaluated at study entry and end by sleep questionnaires (Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index) and full polysomnography with objective measurements of snoring.

RESULTS: We studied 39 patients (age, 46 ± 13 years; BMI, 28.2 ± 3.1 kg/m^2; apnea-hypopnea index (AHI), 15.3 ± 9.3 events/h; Epworth Sleepiness Scale, 9.2 ± 4.9; Pittsburgh Sleep Quality Index, 6.4 ± 3.3). Control (n = 20) and therapy (n = 19) groups were similar at study entry. One patient from each group dropped out. Intention-to-treat analysis was used. No significant changes occurred in the control group. In contrast, patients randomized to therapy experienced a significant decrease in the snore index (snores > 36 dB/h), 99.5 (49.6-221.3) vs 48.2 (25.5-219.2); $P = .017$ and total snore index (total power of snore/h), 60.4 (21.8-220.6) vs 31.0 (10.1-146.5); $P = .033$.

CONCLUSIONS: Oropharyngeal exercises are effective in reducing objectively measured snoring and are a possible treatment of a large population suffering from snoring.

TRIAL REGISTRY: ClinicalTrials.gov; No.: NCT01636856; URL: www.clinicaltrials.gov

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ABBREVIATIONS: AHI = apnea-hypopnea index

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OSA is a common condition characterized by recurrent upper airway obstruction during sleep.[1,2] Snoring is one of the most common symptoms associated with OSA and is caused by vibration of soft tissues obstructing the pharynx during sleep.[3,4] Among patients with OSA, snoring is common (70%-95%), and there is an association between snoring intensity and OSA.[5,6] On the other hand, subjects who suffer from snoring do not necessarily have OSA. The prevalence of snoring in the general population varies widely (from 15% to 54%), mainly because most studies rely on subjective reports.[7-10] Self-perception of snoring is imprecise[11] and is largely dependent on subjective reports from bed partners.[12] The social problems caused by snoring are most likely underestimated. Snoring is frequently denied, because it is a stigmatizing symptom that is poorly perceived by the beholder. In addition to the social problems caused by snoring, the vibration of the upper airway associated with snoring may contribute to pharyngeal neurogenic lesion,[13] progression of carotid artery atherosclerosis due to vibration transmitted locally,[7] as well as sleep disruption when associated with respiratory event-related arousal.[14] Despite the evidence that snoring is a major burden to our society, the management of patients with primary snoring or patients with mild forms of OSA has been poorly investigated.

The treatment of primary snoring varies widely and includes general measurements, such as avoiding alcohol and sedatives, avoiding the supine position, weight reduction, treatment of nasal problems, palate and upper airway surgeries, and use of a mandibular advancement device.[15,16] However, the majority of the studies have not objectively measured snoring, and results are based on subjective questionnaires.[17] Therefore, new forms of treatment of snoring are necessary. Studies show that training the upper airway muscles either by playing a wind instrument (didgeridoo)[18] or oropharyngeal exercises[19] can ameliorate moderate OSA. A recent meta-analysis demonstrated that oropharyngeal exercises provides a reduction in apnea-hypopnea index (AHI) of 50% in adults and decreases snoring.[20] Oropharyngeal exercises are, therefore, an attractive possibility to treat patients suffering from snoring. In the present randomized controlled study, we tested the effects of oropharyngeal exercises on the snoring of minimally symptomatic patients with primary snoring and mild to moderate OSA. In contrast to most studies on this subject, snoring was measured objectively.

Materials and Methods

Patients

We considered eligible patients between 20 and 65 years of age referred to the Sleep Laboratory InCor-HCFMUSP, with a primary complaint of snoring and a recent diagnosis of primary snoring or mild to moderate OSA. Patients with BMI $\geq$ 40 kg/m^2, smokers, history of alcohol abuse, edentulous, severe nasal obstruction, hypertrophic tonsils grade 3 or 4, craniofacial malformations, regular use of hypnotic medications, and severe comorbidities were excluded. The local ethics committee approved the study, and all patients gave written informed consent (CAPPESQ 0140/11).

Polysomnography

All patients were evaluated by full polysomnography as previously described,[21] with the inclusion of a snore recording. Snore sound was captured by microphone, located at 1 m from the surface of the bed, of a digital audio recorder, ZoomH4n. The clocks of the snoring recorder and the polysomnography computer were synchronized. Since snoring is a predominantly low-frequency sound, a bandpass filter between 80 and 300 Hz was used. Snoring was automatically detected by using an algorithm with an intensity threshold cutoff of 36 dB. The World Health Organization guidelines indicate that indoor continuous sound pressure level above 30 dB should be avoided during sleep.[22] Our threshold was based on pilot studies in our sleep laboratory that evaluated the best threshold to discriminate between snoring and ambient sounds. In addition, all automatically detected snoring sounds were listened to and validated by one single researcher in a blinded fashion (V. I.). Results are expressed as snore index (total number of snores/total sleep time) and total snore index (sound intensity power generated by all snoring episodes/total sleep time, expressed in arbitrary units/10^7). Primary snoring, mild OSA, and moderate OSA were defined as an AHI $<$ 5, $\geq$ 5 and $<$ 15, and $\geq$ 15 and $\leq$ 30 events/h, respectively. The investigator who scored the sleep study was blinded to the group allocation. Apnea was defined as the complete cessation of airflow for at least 10 s; hypopnea was defined as a significant reduction ($>$ 30%) in respiratory signals for at least 10 s associated with an oxygen desaturation $\geq$ 3%.[23]

Questionnaires

Snoring of the patient was evaluated by the patient as well as by the bed partner (whenever present) using questions derived from the Berlin questionnaire: snoring frequency (ranging from 0: never, to 4: every day) and snoring intensity (1: similar to breathing, to 4: very loud).[24] Subjective daytime sleepiness and quality of sleep were evaluated with the Epworth Sleepiness Scale questionnaire[25] and Pittsburgh Sleep Quality Index questionnaire,[26] respectively.

Control Group and Therapy Group

Patients in the control group were instructed to use nasal dilator strips during sleep, to perform nasal lavage with saline solution tid, and to perform deep breathing exercises through the nose while sitting. Patients in the therapy group were instructed to perform nasal lavage three times a day followed by oropharyngeal exercises for approximately 8 min. The oropharyngeal exercises from our previous study[19] were simplified and included the following: (1) push the tip of the tongue against the hard palate and slide the tongue backward (20 times); (2) suck the tongue upward against the palate, pressing the entire tongue against the palate (20 times); (3) force the back of the tongue against the floor of the mouth while keeping the tip of the tongue in contact with the inferior incisive teeth (20 times); (4) elevation of the soft palate and uvula while intermittently saying the vowel "A" (20 times). After gaining control and coordination of movement (typically after 3-5 weeks), elevation of the soft palate and uvula was performed without vocalization for 5 s; (5) recruitment of the buccinator muscle against the finger that is introduced in the oral cavity, pressing the buccinator muscle outward

(10 times each side); and (6) alternate bilateral chewing and deglutition using the tongue in the palate, without perioral contraction, whenever feeding. The patients were instructed to incorporate this mastication pattern whenever they were eating.

Experimental Design

After fulfilling entry criteria, patients were randomized for 3 months to either control or therapy group. The two groups attended weekly visits. The therapy group performed oropharyngeal exercises under supervision. The control group performed exercises of deep breathing through the nose under supervision. The control group received nasal dilators once a week, and the number of units used in the previous week was counted. All patients were also asked to keep a diary to record compliance to the 8-min set of exercises prescribed three times a day of either oropharyngeal exercises (therapy) or deep breathing exercises (control) The patient had to mark with a pen whether the assigned exercise section for that period of the day was performed ("yes") or not. The diary was returned to the investigator once a week and provided information about patient compliance in the previous week. Compliance was expressed as a percentage and calculated as the number of sections answered with "yes" divided by the total number of sections in the week. Anthropometric measures, questionnaires, and polysomnography with recording of snoring were performed at the beginning and end of the study. The primary outcome was snoring analysis as expressed by the snore index and the total snore index.

Statistical Analysis

Statistical analysis was performed using SPSS 20.0 (IBM Corporation) and R statistic software. Normality was assessed using the Kolmogorov-Smirnov test. We anticipated a 50% reduction in objective snoring in patients randomized to oropharyngeal exercises based on our previous research.[19] We included 38 patients ($\beta = 80\%$, $\alpha = 95\%$). Data are presented as mean and SD or median (25%-75%) percentile when appropriate. Baseline characteristics were compared using two-tailed unpaired *t* tests or Mann-Whitney test when appropriate. Paired *t* test or Wilcoxon test was performed to evaluate within-group changes over the study period. Repeated measures analysis of variance was used to compare the interaction between the two groups (control and therapy) and the two moments (baseline and after 3 months). In addition, we used the generalized estimation equation to determine the influence of the time in a supine position on the results. Comparisons were performed by intention-to-treat analysis. Missing data at study termination were repeated from baseline according to last observation carried forward methods.[27] A value of $P < .05$ was considered significant.

Results

We recruited 156 patients and 117 were excluded, leaving 39 patients in the final analysis. The reasons for exclusion were described in Figure 1. One patient in each group withdrew from the study after randomization. The demographic and sleep characteristics and symptoms of the population, according to the group assigned, are presented in Table 1. Patients assigned to control and therapy groups had similar baseline characteristics (Table 1). The demographic characteristics, questionnaires, and polysomnographic and snore characteristics of the patients assigned to control or oropharyngeal exercises at baseline and after 3 months are presented in Table 2. The percentage of adherence to the exercises according to the weekly diaries was $> 75\%$ for all patients and was on average $85\% \pm 8\%$. No changes occurred in the control group in all variables during the study period, except on the subjective frequency of snoring reported by the patient. No changes in BMI or abdominal circumference during the study period were observed in patients randomized to oropharyngeal exercises (Table 2). In contrast, patients treated with oropharyngeal exercises had a small but significant decrease in neck circumference after 3 months (Table 2). Snoring

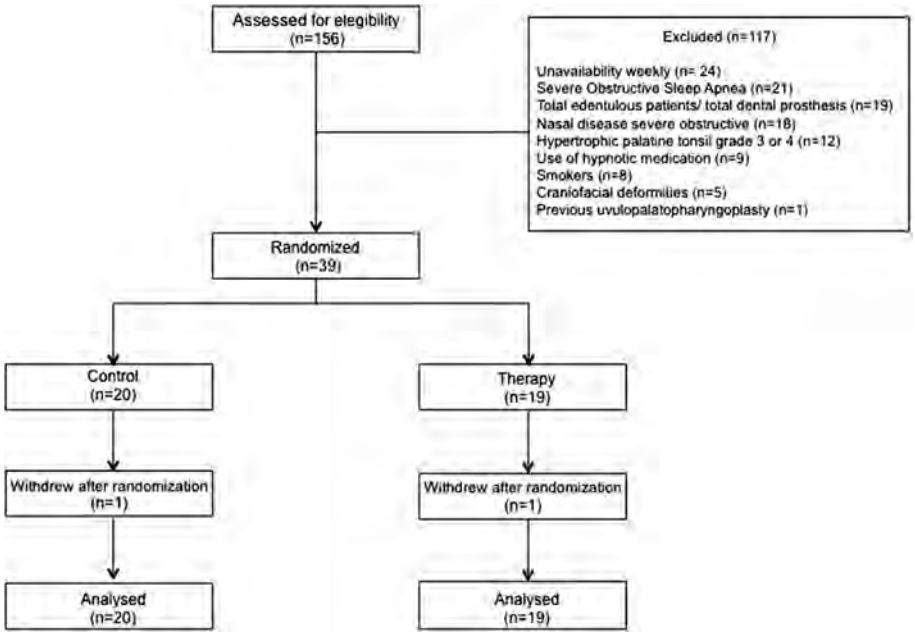

Figure 1 – *Flow diagram of the progress through the phases.*

TABLE 1] Baseline Demographic Characteristics, Questionnaires, and Polysomnographic and Snore Characteristics of the Patients Assigned to Control or Oropharyngeal Therapy

Measure	Control Group (n = 20)	Therapy Group (n = 19)	*P* Value
Demographic characteristics			
Male, No. (%)	11 (55)	11 (57.9)	1.000
Age, y	45 ± 13	48 ± 14	.458
BMI, kg/m^2	28.3 ± 2.5	28.1 ± 2.7	.818
Neck circumference, cm	38.0 ± 3.5	38.0 ± 2.6	.994
Abdominal circumference, cm	94.3 ± 10.2	93.9 ± 5.7	.872
Polysomnography			
TST, h	6.2 ± 0.6	6.1 ± 0.8	.755
Sleep efficiency, %	84.4 ± 7.5	86.0 ± 9.7	.565
Arousal index, events/h	15.3 ± 5.4	20.0 ± 10.2	.080
AHI, events/h	15.1 ± 9.5	15.6 ± 9.3	.875
Spo_2 min	85.1 ± 5.8	85.5 ± 7.5	.844
Desaturation index, events/h	12.3 ± 8.7	10.8 ± 8.8	.600
Snoring measures			
Snore index, events/h	180.6 ± 203.1	156.1 ± 164.4	.682
Total snore index, events/h	54.4 (3.5-386.6)	60.4 (21.8-220.6)	.613
Questionnaires			
Patient			
Pittsburgh Sleep Quality Index	6.9 ± 3.4	6.0 ± 3.2	.427
Epworth Sleepiness Scale	9.0 (7.0-13.5)	7.0 (3.0-11.0)	.154
Subjective snore intensity	3.0 ± 1.0	2.3 ± 1.1	.037
Subjective snore frequency	4.0 (3.0-4.0)	3.0 (2.0-4.0)	.070
Bed partner (control group [n = 12], therapy group [n = 13])			
Subjective snore intensity	3.5 (2.3-4.0)	4.0 (2.5-4.0)	.858
Subjective snore frequency	4.0 (3.0-4.0)	4.0 (3.0-4.0)	.698

Data are presented as mean ± SD. Epworth Sleepiness Scale, subjective snore frequency, subjective snore intensity, and total snore index are presented as median (25%-75%) because of skewed distribution. AHI = apnea-hypopnea index; Spo_2 min = lowest oxygen saturation; TST = total sleep time.

perception as reported by the bed partner also decreased (Table 2). Objectively measured snore index (Fig 2) and total snore index (Fig 3) did not change in the control group and decreased significantly in the patients assigned to oropharyngeal exercises. The mean AHI of the population studied was relatively low at study entry (15.3 ± 9.3 events/h) and did not change significantly in either group. However, in the subgroup of patients with moderate OSA at study entry, AHI decreased significantly in the patients assigned to oropharyngeal exercises (n = 8; AHI, 25.4 [22.1-28.7] vs 18.1 [15.4-24.1], $P = .017$, baseline and study termination, respectively) (Fig 4).

Discussion

This randomized controlled study was designed to objectively measure the effects of oropharyngeal exercises on snoring in patients with primary snoring and mild to moderate OSA. We showed that 3 months of oropharyngeal exercises significantly reduced both the frequency of snoring by 36% and the total power of snoring by 59%. The objective decrease in snoring was associated with a decrease in the perception of snoring by the bed partner but not by the patient.

This study shows the beneficial effects of oropharyngeal exercises in a population that is poorly evaluated by the scientific community. The population studied was composed of middle-aged and overweight patients who were disturbed by snoring, were on average not sleepy (Epworth Sleepiness Scale = 9.2 ± 4.9), and did not present severe OSA (AHI = 15.3 ± 9.3 events/h). This group of patients benefit from a sleep study because severe OSA is ruled out. However, they typically do not receive

TABLE 2] Demographic Characteristics, Questionnaires, and Polysomnographic and Snore Characteristics of the Patients Assigned to Control or Oropharyngeal Therapy on Basal and After 3 Mo

Measure	Control Group (n = 20)			Therapy Group (n = 19)		
	Baseline	3 mo	*P* Value	Baseline	3 mo	*P* Value
Demographic characteristics						
BMI, kg/m^2	28.3 ± 2.5	28.2 ± 3.5	.453	28.1 ± 2.7	28.2 ± 2.8	.469
Neck circumference, cm	38.0 ± 3.5	37.9 ± 3.4	.628	37.9 ± 2.5	37.5 ± 2.4	.000[a]
Abdominal circumference, cm	94.3 ± 10.2	94.6 ± 10.4	.673	93.9 ± 5.7	93.7 ± 4.5	.687
Polysomnography						
TST, h	6.2 ± 0.6	6.2 ± 1.1	.894	6.1 ± 0.8	6.5 ± 0.9	.079
Sleep efficiency, %	84.4 ± 7.5	85.0 ± 11.1	.776	86.0 ± 9.7	86.3 ± 8.6	.825
Arousal index	15.3 ± 5.4	16.9 ± 5.2	.239	20.0 ± 10.2	6.2 ± 1.4	.077
Spo_2 min	85.1 ± 5.8	84.0 ± 7.6	.325	85.5 ± 7.5	83.8 ± 8.9	.120
Desaturation index	12.3 ± 8.7	12.1 ± 6.9	.881	10.8 ± 8.8	9.7 ± 6.0	.437
Questionnaires						
Patient						
Pittsburgh Sleep Quality Index	6.9 ± 3.4	6.4 ± 3.9	.459	6.0 ± 3.2	4.0 ± 2.6	.004
Epworth Sleepiness Scale	9.0 (7.0-13.5)	8.0 (3.5-12.5)	.190	7.0 (3.0-11.0)	7.0 (4.0-10.0)	.084
Subjective snore intensity	3.0 (2.0-4.0)	3.0 (2.0-3.0)	.083	2.0 (2.0-3.0)	2.0 (1.0-2.0)	.155
Subjective snore frequency	4.0 (3.0-4.0)	3.5 (2.0-4.0)	.010[a]	3.0 (2.0-4.0)	2.0 (1.0-4.0)	.030
Bed partner (control group [n = 12], therapy group [n = 13])						
Subjective snore intensity	3.5 (2.3-4.0)	3.0 (2.0-4.0)	.194	4.0 (2.5-4.0)	1.0 (1.0-2.0)	.003[a]
Subjective snore frequency	4.0 (3.0-4.0)	3.5 (3.0-4.0)	.180	4.0 (3.0-4.0)	2.0 (1.5-3.0)	.004[a]

Data are presented as mean ± SD or median (25%-75%). See Table 1 legend for expansion of abbreviations.

[a]$P < .05$ for the comparisons using repeated measures analysis of variance: compare the interaction between the two groups (control and therapy) and the two moments (baseline and after 3 mo).

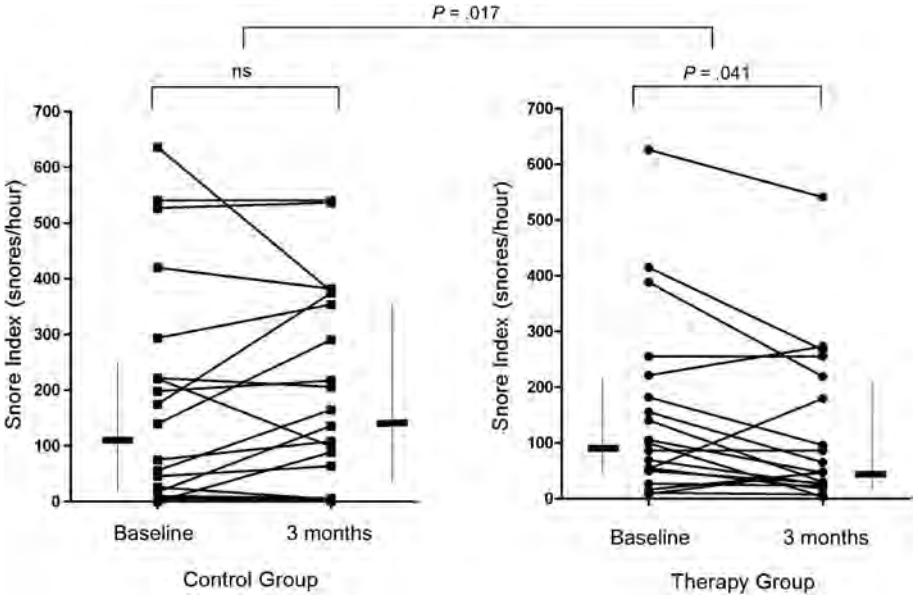

Figure 2 – *Individual values for snore index. In the control group, the snore index from baseline to 3 mo was similar. In contrast, the snore index significantly declined in the group randomized to oropharyngeal exercises. There were group × time interaction effects (*P = .017*). Short horizontal lines and bars are mean ± SD. ns = not significant.*

standardized medical follow-up. The prevalence and significance of snoring in the general population varies widely in epidemiologic studies (from 15% to 54%).[7-10] It is plausible, although not proven, that every night vibration of the palate caused by snoring may contribute to upper airway neurogenic lesion[13] and progression of mild forms of OSA.[28] In addition, primary snoring (ie, AHI < 5 events/h) may be associated with disrupted sleep due to respiratory events, related arousals,[14,29] or progression of carotid atherosclerosis due to vibration.[7] Independent of the possible health problems aggravated by snoring, most patients with mild forms of OSA must have some degree of social burden generated by snoring.[30,31] For instance, a Google search using the key words "snoring" and "treatment" showed > 5 million results, indicating that snoring is a major burden to the society.

In contrast to well-established metrics like the AHI, snoring is not a standard measurement during full polysomnography.[32] In a previous study, our group proposed a simple and accurate method to identify OSA based on time intervals between snoring events.[33] In this study, we objectively quantified the frequency and

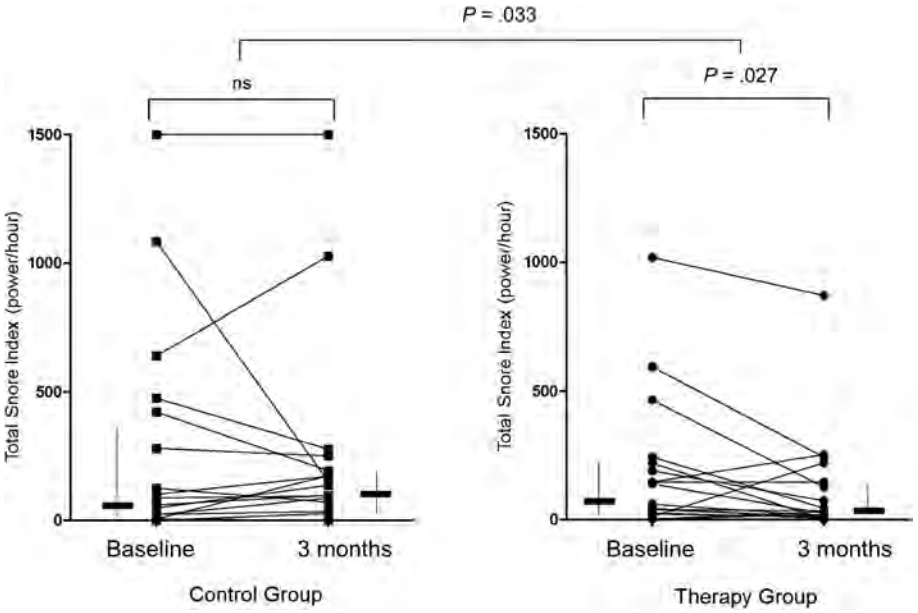

Figure 3 – *Individual values for total snore index. In the control group, the total snore index from baseline to 3 mo was similar. In contrast, the total snore index significantly declined in the group randomized to oropharyngeal exercises. There were group × time interaction effects (*P = .033*). Short horizontal lines and bars are mean ± SD. See Figure 2 legend for expansion of abbreviation.*

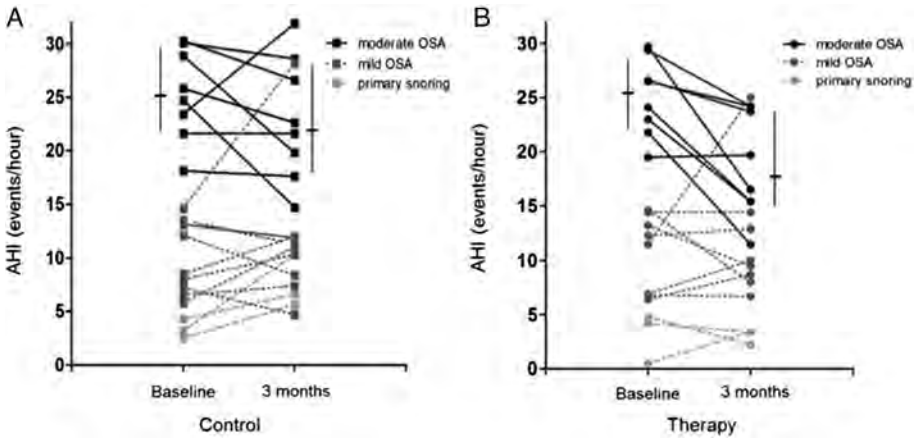

Figure 4 – *A, B, Individual values for AHI at baseline and after 3 mo. There were no statistical differences on AHI in either group. However, the subgroup of patients with moderate OSA (15 ≤ AHI ≤ 30) randomized to oropharyngeal exercises had a significantly decreased AHI. In the control group, the AHI from baseline to 3 mo (from 25.3 [22.1-29.8] to 22.1 [18.2-28.1] events/h) was similar. In contrast, the AHI significantly declined in the group randomized to oropharyngeal exercises (from 25.4 [22.1-28.7] to 18.1 [15.4-24.1] events/h; P = .017). Short horizontal lines and bars are medians (25%-75%), because of skewed distribution. AHI = apnea-hypopnea index.*

intensity of snoring. We used a similar distance of the microphone to the patient (1 m)[34,35] and adopted the snore index to express our results as previously reported.[34,36-38] In addition, we used the total snore index to represent the total snore intensity power generated during sleep. The objective reduction in snore indexes among patients randomized to oropharyngeal exercises occurred in conjunction with an improvement in the perceived snoring evaluated by the bed partner. Our study is in-line with previous studies that showed the beneficial effects of different forms of oropharyngeal exercises, such as didgeridoo playing,[18] singing,[39,40] and specific oropharyngeal exercises,[19] on upper airway physiology during sleep. Upper airway exercises have been also used to treat children and teenagers with promising results.[41-43] Our study was based on exercises previously reported by our group. We extended our previous study by reducing the number of exercises by 50% that were applied for 3 months.

Our study has strengths and limitations. First, the oropharyngeal exercises are based on an integrative approach and, therefore, do not allow determining the effects of each specific exercise on the overall result. Moreover, these exercises are derived from oral motor techniques to improve speech activity, swallowing activity, or both, an area that lacks the empirical support necessary for evidence-based practices.[44] As compared with our previous study that evaluated the effects of oropharyngeal exercises on moderate OSA, the number of exercises proposed in the present study was reduced by 50%. In contrast to the original study, we found no overall significant reduction in AHI after oropharyngeal exercises, which could be due to a reduction in the exercises protocol.[19] However, our clinical experience accumulated over the last 5 years has shown that reducing the number of exercises does not affect the effectiveness of therapy. Moreover, there was a significant reduction in AHI of patients with moderate OSA at study entry randomized to oropharyngeal exercises. The most likely explanation is that a "floor effect" in the AHI prevented the observation of any effect on this metric among patients with mild or no OSA at study entry. Our results point out that snoring rather than AHI is probably the best metric to follow patients with mild forms of OSA in whom the most significant complaint is snoring. On the other hand, we acknowledge that there are no standard methods to measure snore, and the field needs to be developed. Finally, there is a perceived concept that exercises are difficult to incorporate. To this end, the simplified protocol is a feasible series of 8 min (tid) that could be more easily incorporated into daily activities, such as immediately after tooth brushing or commuting to work.

In conclusion, oropharyngeal exercises can reduce the objective measurements of frequency and intensity of snoring. This set of oropharyngeal exercises is a promising treatment of large populations suffering from snoring who are currently largely ignored by the medical community.

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CLINICAL REVIEW

Pediatric sleep-disordered breathing: New evidence on its development

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SUMMARY

Sleep-disordered breathing (SDB) in children could be resolved by adenotonsillectomy (T&A). However, incomplete results are often noted post-surgery. Because of this partial resolution, long-term follow-up is needed to monitor for reoccurrence of SDB, which may be diagnosed years later through reoccurrence of complaints or in some cases, through systematic investigations. Children undergoing T&A often have small upper airways. Genetics play a role in the fetal development of the skull, the skull base, and subsequently, the size of the upper airway. In non-syndromic children, specific genetic mutations are often unrecognized early in life and affect the craniofacial growth, altering functions such as suction, mastication, swallowing, and nasal breathing. These developmental and functional changes are associated with the development of SDB. Children without genetic mutations but with impairment of the above said functions also develop SDB. When applied early in life, techniques involved in the reeducation of these functions, such as myofunctional therapy, alter the craniofacial growth and the associated SDB. This occurs as a result of the continuous interaction between cartilages, bones and muscles involved in the growth of the base of the skull and the face. Recently collected data show the impact of the early changes in craniofacial growth patterns and how these changes lead to an impairment of the developmental functions and consequent persistence of SDB. The presence of nasal disuse and mouth breathing are abnormal functions that are easily amenable to treatment. Understanding the dynamics leading to the development of SDB and recognizing factors affecting the craniofacial growth and the resulting functional impairments, allows appropriate treatment planning which may or may not include T&A. Enlargement of lymphoid tissue may actually be a consequence as opposed to a cause of these initial dysfunctions.

Introduction

Sleep-disordered breathing is related to upper airway collapse during sleep. In order to appreciate how this collapse occurs, it is important to have an understanding of the development and anatomy of the upper airway. The size of the upper airway and factors contributing to its narrowing can lead to increased risk of collapse and subsequent abnormal breathing during sleep. Because the upper airway is located below the skull and behind the face, any developmental changes in either of these two structures will impact the size of the upper airway. Facial growth is relatively rapid early in life. At birth, the face represents one-seventh of the craniofacial structures and 50% by 20 y of age. Eighty percent of this development is reached early in life, by the age of 5–6 y [1]. The two facial components that are key in determining the size of the upper airway are the naso-maxillary complex and the mandible.

The development of the craniofacial structures

The naso-maxillary complex is located at the anterior part of the skull, and its growth has been classified by Bjork [2] according to age. From infancy until the toddler period, growth is 1 mm/y. During the prepubertal period (5–11 y), growth slows down to 0.25 mm/y and then accelerates again during the peripubertal period (12–17 y) to 1.5 mm/y. Maximal growth is thus seen early in life and during puberty.

Facial growth is influenced during the fetal period by the brain growth and in humans, particularly by the vast development of the

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Abbreviation

AASM	American Academy of Sleep Medicine
AHI	apnea–hypopnea index
Ba–S–N angle	basion-sella-nasion angle (also called "spenoidal angle")
BAT	brown adipose tissue
Ba	basion
BMP4	bone morphogenic protein-4
EDS	Ehlers Danlos syndrome
EEG	electro-encephalogram
FGF8	functional growth factor-8
GA	gestational age
Msx1	muscle segment homeobox-1 (gene)
N	nasion
OSA	obstructive sleep apnea
PSG	polysomnogram
SDB	sleep-disordered breathing
S	sella turcica
T&A	adenotonsillectomy
WAT	white adipose tissue

frontal lobe. The growth of the brain is critical in the development of the face. As indicated by Enlow and Poston [3], there is a distinct angle between the vertical axis of the brainstem and the spinal cord, known as the nevrax, and the cortical regions. This angle is more or less obtuse and impacts the development of the face and features distinct to the ethnic differences seen between Caucasians and Far-East Asians [4]. Genetics also play a role in the growth of the brain and thereby the skull and its base which then impact the size of the upper airway. This association is clearly demonstrated in that the posterior width of the middle fossa of the skull is the exact lateral size of the erect and awake adult pharynx. The development of these structures further defines the relationship between the maxilla and the mandible, categorizing subjects either as "Class II" or "Class III", based on their relative position to each other in addition to the upper and lower teeth. A Class II malocclusion refers to a retrognathic abnormal posterior positioning of the maxilla or mandible, particularly the mandible, relative to the facial and soft tissue structures. The mesiobuccal cusp of the upper first molar is not aligned with the mesiobuccal groove of the lower first molar and instead sits anterior to it. Conversely, a Class III malocclusion is prognathic with the upper molars posterior to the mesiobuccal groove of the mandibular first molar.

The interaction between the development of the naso-maxillary complex and support of the head in an individual with vertical posture is a critical adjustment. The extremity superior and posterior of the odontoid must be aligned, and this involves exact placement of the spheno-palatine suture, the anterior part of atlas, and the superior limit of the odontoid. The spheno-palatine suture involves the "spenoidal angle" (Ba–S–Na) and the position of the naso-maxillary complex, i.e., the face. The sphenoidal angle can be easily traced on lateral cephalometry that is obtained in standardized conditions fixing the head in a defined position through usage of a cephalostat. Three structures easily recognizable on this form of imaging are the sella turcica (S), the nasion (N) and the posterior base of skull (basion-B). The Ba–S–N angle in a normal adult, is about 120°, although this measurement varies based on several factors including ethnicity. Delaire [5] defined a segment of this angle, the line from S to B, as C4. Calculation of the position of the superior and posterior part of the odontoid in relation to the two other landmarks in the occipital hole (anterior part of atlas and speno-palatine suture) allows to determine abnormal positioning of the odontoid. Any abnormalities in the development of this crucial junction may lead to well-known neurological syndromes such as hydrocephaly, Arnold-Chiari, Dandy-Walker and other conditions typically associated with abnormal breathing dominant during sleep. The placement of the face and the development and adjustment of the naso-maxillary complex is vital in maintaining the crucial protection of the neuro-vascular structures below the cerebellum. This complex interaction between growth of the face and the posterior skull-base is again a consequence of being erect and having a relatively large brain to support in this erect position Fig. 1.

The development of the face is thus a very closely regulated event, with continuous interaction between the development of the entire brain, the skull, and the skull-base.

The growth of the transversal portion of the naso-maxillary complex is influenced by three factors, the development of the nasal fossae during fetal life, the growth of the ocular cavities related to ocular development during fetal life, and the activity of the inter-maxillary suture that utilizes an enchondral mode of ossification and is active until about 16 y of age and undergoes complete synostose by the age of 25 y. The face is located at the anterior most point of the skull-base and is therefore especially dependent on the processes involved in its growth with maxilla and mandible been "pushed forward" by the development of the skull-base.

Development of skull-base and naso-maxillary complex

Genetic factors are critical in such development. Most of the growth of the skull-base is cartilaginous growth, and growth occurs in relation to "synchondroses" [6]. These serve as the site of bone growth in the skull-base and are located in the sutures between the

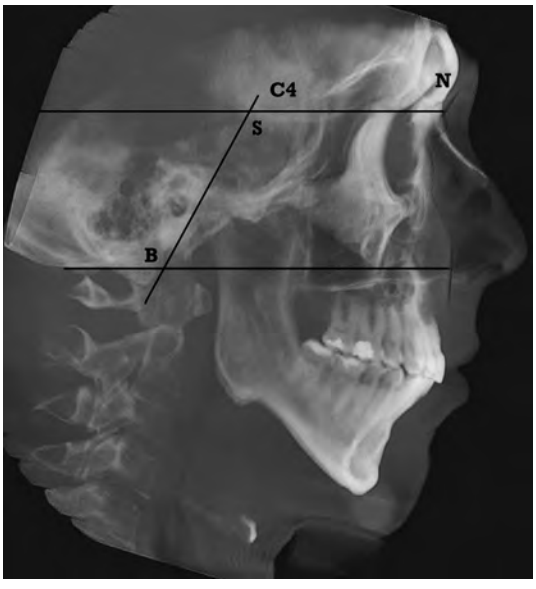

Fig. 1. Cephalometric X-ray with indication of basion-sella-nasion angle and "lines" investigated to evaluate position of odontoid and occipital hole. Basion-sella-nasion – Ba–S–Na-angle, also called sphenoidal angle is related to the vertical growth of the skull base and it is under the control of the spheno-occipital synchondrose. This suture brings the occipital hole in a lower position. The movements of the occipital and sphenoid bones are important as there must be an adjustment with a position tangent to the tip of the odontoid. The craniocervical junction and the hard palate orientations are dependent on the spheno-occipital synchondrose and on its flexion. Placement of the anterior spinal spine, of the hard palate, of the naso-maxillary complex and the skeletal class will have an impact on the width and placement of the hard palate and the size of the upper airway.

bones forming the skull and the skull-base. Synchondroses undergo three stages of growth and are particularly active during the "chondro-synostose" phase and early in life up to 5 y of age. If they are not stimulated, they may not induce growth. The spheno-sphenoidal chondrose is responsible for the vertical growth of the skull base. It has an oblique direction and lowers the location of the occipital lobe thereby affecting facial growth. The growth of the naso-maxillary complex is related not only to the sphenoido-occipital synchondrose but also to the activity of the synchondrose of the skull base and particularly the cleft at the following sutures: inter-malar, inter-maxillary, inter-palatine, maxillo-malar, and temporo-malar.

It is important to note that the inter-maxillary suture is active postnatilly as mentioned above, and is influenced by specific functions, such as suction, mastication, swallowing, and nasal breathing. These functions mobilize the facial muscles that play a clear role in facial growth.

The development of these functions is influenced by the quality of nasal respiratory roles, dental development which involves the position and height of alveoli and teeth position, and the activity and strength of the tongue and facial muscles. These facial muscles include the labial muscles, which influence not only the facial growth but also the position and height of the hard palate. As mentioned previously, the vertical growth of the naso-maxillary complex is related to the activity of the posterior skull base but also to that of the frontal-malar, frontal-maxillary, and maxillo-malar sutures. It is also related to the position of the hard palate and the alveolo-dental activity [6].

Mandibular development

While the mandible is also involved in the space controlling the size of the upper airway, it is independent of the base of skull and instead associated with the cervico-thoraco-digestive axis. This structure involves many muscle and ligament attachments and dictates head posture. It has both membranous and enchondral growth. The mandible is comprised of two parts, the condyle and the body. Although both these parts determine the upper airway size, the condyle plays a significantly more important role.

Genetic factors influence mandibular development in fetal life; other factors, however, are involved after birth. Trauma impacting the condyle's function as a joint can occur in a variety of ways, such as from a vaginal delivery using or even not using forceps, from a fall, or from inflammation due to disorders such as juvenile idiopathic arthritis [7]. This disorder impairs growth through rapid ossification of the joint. Any changes in the position of the condyle will cause the growth region to migrate. An example of this is apparent in cases in which chronic buccal (mouth) respiration develops. The position of the condyle in the articulation changes, and therefore the growth location also changes, transferring cartilaginous production more posteriorly. This will alter the incline at which bone grows causing a posterior mandibular rotation during youth development and leading to narrowing of the upper airway.

Three phases exist in the condylar growth and activity: *Phase 1*: fetal and early postnatal life where the suction function will be vital to the postnatal growth. *Phase 2:* 1–20 y of age where the mastication function influences growth and there is a progressive but clear decrease in growth role. *Phase 3:* the joint no longer has a growth role [6].

The role of two synchondroses active postnatally: the inter-maxillary and alveolo-dental synchondroses

Genetic abnormalities affecting membranous and cartilaginous craniofacial growth can lead to obvious malformation syndromes associated with sleep-disordered breathing (SDB) such as Appert, Crouzon or Traecher-Colin syndromes [8] In these disorders, abnormal breathing during sleep is recognized early in life.

However, in genetic impairments of endochondral growth leading to SDB, recognition is often delayed until after childhood. Ehlers Danlos syndrome (EDS) [9] is secondary to either an autosomal dominant, autosomal recessive, or X-linked mutation of genes located on proteins or enzymes, most commonly COL-1A1, COL 5A1, or 5A2. Several degrees of Ehlers Danlos syndrome have been described in humans, with one form not commonly recognized until adulthood as it manifests only with hyperextensibility of articulations and development of SDB. SDB may lead to complaints, but because the clinical symptoms are more of poor sleep, insomnia, daytime fatigue, rarely parasomnias, and attention difficulties in school or at work, they may not immediately be recognized as obstructive breathing during sleep. Regular evaluation of young family members of an adult case may uncover abnormal breathing during sleep when systematic polysomnography (PSG) is performed. In a report of our recently seen cases [9], clinical symptoms were as those mentioned above, with the most significant PSG finding being the degree of flow limitation [10,11] during total sleep time more so than the apnea–hypopnea index (AHI). Clinical evaluation again demonstrated the presence of an abnormally long face, narrow and high hard palate, and frequently associated cross-bite. While initially only abnormalities of the naso-maxillary complex may be seen, as patients enter adulthood and develop worsening SDB, defects of the condyle may also be found Fig. 2.

The syndromic EDS with cardiac or other systemic complication and more importantly, the often unrecognized non-syndromic cases with only hyperlaxity, demonstrate that impairment of the normal naso-maxillary complex and mandibular growth during fetal life leads to abnormal breathing during sleep in childhood.

The alveolo-dental synchondroses

When teeth are absent or are extracted in early life during their growth, this can lead to bone retraction and affect the facial growth. Over the past seven years, we have collected data on 257 individuals of age 14–30 y, who underwent extraction of wisdom teeth and had associated symptoms of obstructive breathing during sleep. These patients had documented flow limitation [10,11] between 50 and 90% of total sleep time and presence of obstructive sleep apnea (OSA) with a mean apnea–hypopnea index (AHI), as

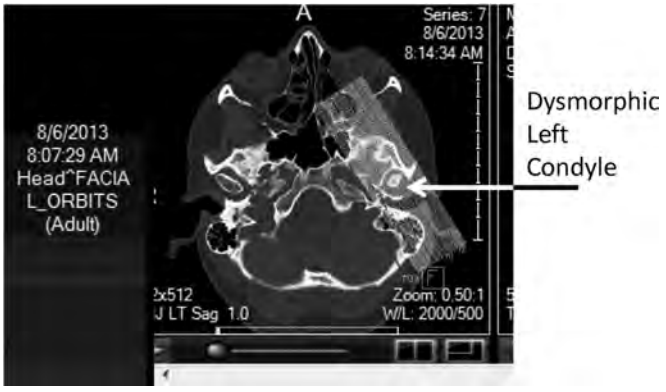

Fig. 2. Dysmorphia of the mandibular condyle in an 18 y old Ehlers Danlos Type III patient (a genetic cartilage impairment). This CT-scan allows studying the impairment of the mandibular condyle. Patient misdiagnosed for years: repetitive ankle luxations and temporo-mandibular pain with bruxism, presence of daytime fatigue, some degree of daytime sleepiness, difficulty to concentrate, and mandibular pain. Results of polysomnography: apnea–hypopnea index-AHI = 16.9 events/hour of sleep, lowest oxygen saturation: 89%, flow limitation: 85% of total sleep time.

defined by the American Academy of Sleep Medicine (AASM)-2013 [12], of 7.5 ± 2.3 events/h.

During this initial investigation, it was revealed that some of these patients had prior recognition of wisdom teeth agenesis. After this discovery, a systematic search was done to retrospectively analyze, through collaboration with an orthodontist, an association between teeth agenesis and presence of OSA in non-syndromic children seen during the prior five years. Forty-one cases were found. Dental agenesis is linked to genetic mutations with a dental homeo-code for agenesis of canine, incisive, and molar teeth. These mutations involve certain transcription factors as demonstrated in mice investigations [13]. We identified varying degrees of agenesis of the molar, incisive, and canine teeth. Independent of the degree of dental agenesis, all 41 subjects, aged 4–14 y, referred to an orthodontist office for their teeth agenesis and not for any symptom associated with sleep-disordered breathing, presented with abnormal breathing during sleep with associated flow limitation for more than 50% of total sleep time, a mean AHI of 7.3 ± 2, and a mean minimum oxygen saturation of 90 ± 1.5% Fig. 3.

Clinical history revealed the presence of daytime fatigue more so than daytime sleepiness, poor sleep, and difficulty in school due to poor concentration and attention span. Less frequently ($n = 18$), there was a positive history of parasomnias. On clinical evaluation, all cases had an abnormally "long face" with an elongated lower facial third in addition to an abnormally narrow hard palate. In some cases, parents were hesitant to consider the possibility of abnormal breathing during sleep. This is likely due to poor recognition of abnormal facial features associated with SDB in the dentist-orthodontist and pediatric communities. The association between congenitally missing teeth and facial skeletal changes with "straight to concave profile, pointed chin, reduced lower facial height and altered dental inclination" was already noted by Ben-Bassat and Brin (2009) [14] but these authors did not investigate breathing during sleep.

Genes, facial growth and alveolo-dental synchondroses (see Table 1)

Embryologic development and craniofacial studies have shown that at least one Homeobox gene [15], the muscle segment homeobox gene (Msx1), is involved in early embryological development of the facial aspects derived from the neuro-ectodermal stratus. While this gene is very active early in development, its expression becomes more limited in "progenetrical cells," controlling proliferation and differentiation of cells involved in formation of the craniofacial skeleton.

Fig. 3. Agenesis of teeth related to gene mutation in a child that developed SDB. This simple dental X-rays show the many absent teeth related to mutation. The child has an apnea–hypopnea-index (AHI) of 3.8 with a much higher AHI in rapid-eye-movement-REM-sleep. Flow limitation defined with nasal cannula – pressure transducer, leading to important daytime fatigue and large and abnormal amount of cyclic-alternating pattern with abnormal amount of phase A2 and A3 during non-rapid-eye-movement – NREM-sleep indicative of sleep-disruption, is present during 71% of total sleep time. SDB: sleep-disordered breathing.

Msx1 controls proteins diffusing outside the cell, such as growth factors, particularly the bone morphogenetic protein (BMP4) that also has an inductive role on Msx1 expression. Overexpression of Msx1 keeps bone and odontoblastic cells in an undifferentiated state. Msx1 controls specific cell populations, particularly the amount of mother cells involved in the formation of bones. Mutations of Msx1 are associated with presence of dys-genesis such as in Pierre Robin syndrome, a syndrome associated with SDB. The MSX1 and PAX9 proteins are highly correlated and the presence of mutations in these genes has been considered to lead to a haploinsufficiency (i.e., reduced amount of functional protein) allowing occurrence of abnormalities in odontogenesis [16]. The genes homeobox LHX 6/7 and Gsc are also involved in placement of the odontogenic cells and control the growth factor FGF8. This growth factor, through induction of a protein (Lf7), inhibits Gsc, and then the DLXs genes [13] induce odontogenesis, as do the genes LHX 6/7.

The DLX genes, as mentioned above, were well studied in mice [11] and shown to cause specific mutations altering dental development. In humans, the DLX genes are located on chromosome 7, showing a similar dental homeocode as that existing in mice. This dental homeocode, deciphered by Thomas and Sharpe [13], shows a link between specific dental agenesis and certain mutations of or elimination of one of these genes. For example, absence of DLX1 and DLX2 leads to absence of molars in the maxilla, and mutations of DLX 5 and 6 lead to absence of inferior molars. Other genes have been associated with dental agenesis and: Mutations on Pax 9 on chromosome 14 is associated with variable forms of oligodontia that mainly affect the molars and mutations involving AXIN2, WTA10, EDA genes have also been associated with hypodontia [8,14,17–25]. But potentially many other genes could be involved as several hundreds – up to 200-have been mentioned as directly or indirectly involved in the regulation of tooth development [14,23]. Table 1 indicates the major families of genes that may be associated with genetic mutations leading to abnormal ondotogenesis.

Dental research has shown that tooth agenesis is a common congenital disorder, it may be associated with syndromes but it is also often seen in non-syndromic children and its prevalence has been variable depending of authors but findings oscillate between 10 and 20% of the studied population [20]. Most commonly only one tooth is agenetic but in 10% of the agenetic cases two are involved with the 2nd premolar and the lateral incisive being considered as more frequent agenesis and 1–2% having oligodontia.

In our children recognized with SDB there were at least two agenetic teeth. The clinical presentation was not obvious as snoring was not a chief a symptom as the more regularly mentioned mouth breathing [26]. During infancy, they were crying infants labeled as having colic, sleep disruption, poor development of long sleep phase with circadian clues [27] and difficulty in feeding. When older, the children and their parents, complained of daytime fatigue, impaired attention and focus in school, and poor and disrupted sleep more so than daytime sleepiness [28]. Clinical evaluation outlined presence of a high and narrow hard palate and an asymmetrical development most often involving the lower third of the face and frequently associated with a counter-clockwise rotation of the mandible. Evaluation of the upper airway shows an abnormal Friedman–Mallampati scale score [29,30] of 3 or 4 and a high and narrow hard palate associated with a narrow maxilla with or without cross-bite. A deviated septum and mouth breathing are commonly found in association with a high and narrow hard palate, likely from hard palate elevation. The most significant PSG finding was the degree of flow limitation [10,11] during total sleep

Table 1
Missing teeth and genes identified with occurrence of small upper airway in syndromic and non-syndromic children.

Genes and teeth: Between 70 and 200 genes are involved in the development of normal teeth
Some specific genetic mutations have been identified leading to syndromic (at least 60 syndromes) and non-syndromic absence of permanent teeth
Two genes play a key role in odontogenesis and interact with many other genes: the muscle-segment-homeobox-1 (MSX1) gene and the paired-box-9 gene (PAX9). MSX1 is a regulatory gene and PAX9 is a developmental control gene. They have a very strong interaction between themselves, and interact with many other proteins
Mutations in these genes lead to both syndromic and non-syndromic presentations
Example: a mutation in MSX1 is present with Pierre-Robin syndrome, and in the Witkop tooth and nail syndrome
Examples of mutation without syndromic presentation: mutation in PAX9 leads to "*Hypodontia*" (more than 6 missing teeth); mutation in Arg-31-Pro [homeodomaine of MSX1] leads to absence of maxillary 1st premolar, maxillary and mandibular 2nd pre-molars and 3rd molars; mutation in the tumor necrotic factor of the homology domain of the Ectodysplasin A is associated with absence of maxillary incisors and canines
Other important genes involved in odontogenesis:
Signaling molecules: these molecules, binding to the cell-surface receptors, activate specific transcription factors. They direct expression or repression of specific sets of genes controlling cell behavior
And key-signaling molecules are often *growth factors*: four families of growth factors are highly involved in orofacial development
-Fibroblast growth factor (examples: mutations leading to Appert syndrome, Kallman syndrome, scraniosynostosis, all syndromes with small upper airway)
-Hedgehog and Sonic Hedgehog (SHH) (examples: mutations leading to Gorlin-Goltz Syndrome associating oligodontia, clefts and nevoid basal cell carcinoma)
-Wingless (WTT) (example: mutation leading to oligodontia and colo-rectal cancer, but also to non-syndromic lack of superior lateral incisors and small upper airway (particularly mutation on Axis-inhibition-protein-2 [AXIN2])
-Transforming-growth-factor-beta (TGF-beta) [examples: mutations of bone morphogenetic protein (BMP)] and activins (associated with orofacial-digital syndromes, orofacial clefting syndromes, and dental ageneses with, in decreasing frequency, 3rd molars, mandibular 2nd premolars, maxillary lower incisors, and lower central incisors agenesis.)
Mutations in genes of these different families may be associated with syndromic and non-syndromic (involving only teeth agenesis) orofacial development
Dental agenesis either part of a syndromic presentation or isolated and limited to dental agenesis, are associated with changes in maxillar and/or mandibular growth
This abnormal growth is a risk-factor for small upper airway and increased collapsibility during sleep

time more so than the AHI. There was a progressively increasing AHI with age, with this latest finding suggesting perpetual worsening after birth with age.

Our cases demonstrate the important role of abnormal craniofacial growth in the development of pediatric SDB and involvement of synchondroses particularly those still active during childhood.

Craniofacial muscle activity, genes and abnormal orofacial growth

There is an interaction between muscle activities, particularly those of the face, and growth and normal development of the upper airway. Genetic abnormalities impairing normal activity of striatal muscles, including facial muscles, lead to SDB. The most studied genetic disorder involving mutations and generalized muscle impairment is myotonic dystrophy, both type I and type II [31]. The impact of abnormal facial muscle contractions present in myotonic dystrophy on the development of SDB in children was investigated and demonstrated many years ago. The studies showed a progressive worsening in AHI from the teenage years to adulthood. There was also increased worsening of daytime sleepiness documented by a multiple nap test; clinical features included presence of a long face and a high and narrow hard palate. The deduction from these studies is that the abnormal activity of muscles controlling the craniofacial structures also has an impact on the development of the naso-maxillary complex and the mandible leading to a small upper airway. Myotonic dystrophy is again related to genetic mutations that are already present during fetal life. Other genetic mutations that diffusely impact all muscles in the body may also lead to SDB, again due to impairment of normal facial muscle functioning: in our own clinical pediatric cases, Duchenne dystrophy was also associated with high narrow hard palate and with a combination of obstructed breathing and respiratory problems related to muscle weakness during sleep. Training in breathing and facial muscle activity is present during fetal life as demonstrated by ultrasonography [32], so abnormalities of craniofacial growth related to muscle impairments due to genetic mutations may begin in-utero.

Environmental impairment of orofacial muscle activity

Experiment done by Harvold et al. involving monkeys [33], demonstrates that non-genetic postnatal impairment may also have a similar impact as genetically induced muscle impairment. Between 1980 and 1990, a number of ground-breaking experiments on newborn rhesus monkeys were performed, whereby a small silicone 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 six months of life [33–36]. The blockage of the nasal passages led to narrowing of dental arches, decrease in maxillary arch length, anterior cross-bite, maxillary overjet, and increase in anterior facial height [33–35]. Experimentally induced abnormal nasal resistance led to systematic changes in the orofacial muscles. The changes were noted in the 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 contrast to the nearly continuous and desynchronized discharges in most normal subjects. Tonic EMG discharges reverted back to the normal pattern when nasal breathing was restored at the end of the six-month experiment [34]. These experiments demonstrate that impairment of certain normal functions impact normal craniofacial growth. In this particular study, impaired nasal breathing had an impact on the inter-maxillary suture (as do mutations seen in Ehlers Danlos syndrome [9]), and secondary mouth breathing also had an immediate impact on the mandibular condyle position. This experimental manipulation impacting tongue and facial muscle activities consequently leads to craniofacial growth impairment and mouth breathing which narrows the size of the upper airway and further deteriorates normal nasal breathing, particularly during sleep.

The experimental data show presence of a continuous interaction between abnormal nasal resistance and orofacial growth through the intermediary of abnormal muscle tone and mouth breathing (with a change in the mandibular condyle position). The abnormal growth leads to further worsening of the nasal resistance. The consequence is a small upper airway.

In children, prematurity is often associated with generalized muscle hypotonia. Its severity is dependent on degree of prematurity. In our follow-up cohort of 400 premature infants born as early as 27 wk of gestational age, initial evaluations of 292 of these infants indicated progressive development of obstructive breathing during sleep. This was in spite of the disappearance of the

diaphragmatic apneas of prematurity [37]. This atypical breathing pattern was associated with the development of mouth breathing and a high and narrow hard palate. Early premature infants have often abnormalities involving feeding functions such as suction, mastication, and swallowing with weakness of orofacial muscles that negatively alter the craniofacial growth, and lead to small upper airway.

Full term children are also at risk due to abnormal functional behavior early in life. These infants have no identifiable genetic or neurological disorder and have a normal oto-laryngological evaluation but are found to have abnormal mouth breathing or mild feeding difficulty despite a normal growth curve. Subsequent PSG in this subset of infants has shown flow limitation and a low but abnormal AHI with disrupted nocturnal sleep during the first six weeks of life [37]. It is possible that these infants have an unrecognized genetic problem despite thorough clinical evaluation, but the abnormal functional behavior, including the presence of mouth breathing during sleep, was the only evidence of increased risk for SDB. This suspicion was confirmed by PSG done in the ensuing 10 mo that showed a slow but progressive increase in flow limitation and secondary development of snoring sounds.

Some muscle activity limitations are easily recognized at birth such as the presence of a short anterior frenulum leading to abnormal feeding behavior and speech development. All our children with short mandibular frenulum had an association with SDB when seen untreated between two and six years of age. They all had a narrow and high hard palate Fig. 4.

Environmental impairment of the alveolo-dental synchrosis

Dental agenesis may be related to infection (e.g., rubella), chemotherapy, radiation or toxic substances (Thalidomide) [38], Schalk-van der Weide et al. [39] reported impact of extraction of temporary teeth and secondary permanent dental agenesis. We have studied a small group of 11 children with permanent teeth extraction (mostly second molar or lateral incisive) between age 10 and 13 y who developed symptoms of SDB within five years associated with abnormal maxilla-mandibular growth and small upper airway.

Environmental impairment of the temporo-mandibular articulations and development of SDB

Chronic inflammatory diseases, such as rheumatoid juvenile arthritis, that lead to impairment of temporo-mandibular articulation leads to post-natal abnormal craniofacial growth with again progressive development of small oral cavity and presence of a high and narrow hard palate. In our children we observed presence of abnormal breathing during sleep as early as two-years of age associated with poor sleep [40]. Trauma on temporo-mandibular articulation has similar impact: in our own data-base we have three teen-agers with unilateral trauma that led to secondary impairment orofacial growth, narrow oral cavity, daytime fatigue and sleepiness and typical sleep-disordered breathing.

The above findings imply that there are pathways at play placing children at increased risk of development of SDB abnormal functional behavior during wake and sleep associated with craniofacial growth. There appears to be a continuous interaction between function and development involving the craniofacial region. Impairment of growth due to genetic mutations, environmental factors, and interaction between environmental factors and genes (epigenetics), leads to changes in facial growth patterns that influence facial tasks. These functional impairments have a negative feedback on orofacial growth, further impairing functions. The consequence is presence of a reduced upper airway size which in association with sleep leads to SDB.

Fig. 4. Frenulum. Example of a short frenulum in a child that presented with speech difficulties early in life and developed sleep-disordered breathing (SDB) associated with a narrow hard palate. The abnormally short structure limits normal movements of the tongue and keeps it in an abnormally low set position when at rest. While the child had orthodontic treatment for his abnormal maxillary growth, the presence of his short frenulum was not recognized. It impaired successful results of orthodontia due to its continued restriction of tongue movements as indicated by persistence of high AHI (apnea–hypopnea index) at PSG (polysomnogram).

Adenoids, tonsils, turbinates, and sleep-disordered breathing

Adenoids and tonsils are secondary or peripheral lymphoid organs that develop during fetal life with lymphoid tissues developing near the fifth week of fetal life [41]. They are the sites of lymphocyte activation by antigens. When activation occurs, there is a clonal expansion and affinity maturation. The mature lymphocytes recirculate between the blood and the peripheral lymphoid organs looking for the specific antigen that they have been matured to target. It is in these secondary lymphoid tissues, specifically the adenoids and tonsils, that the antigen (a foreign or altered native molecule) is placed in contact with the lymphocytes. The specific lymphocytes targeted are primarily in the follicles present in adenoids and tonsils. Reaction against foreign molecules may be related to genetic patrimony, exposure during fetal life, or even due to the temporary interaction between a mother's immune defense system and the infant's own genetic patrimony. An inflammatory reaction will be triggered by the interaction between an antibody and the foreign molecule. This reaction leads to subsequent enlargement of the organ. Viral infections, cysteinyl leukotrienes endogenous synthesis, history of wheezing and familial factors play also an important role in the pathogenesis of adenotonsillar hypertrophy. Nasal turbinates are not similar to adenoids and tonsils, but they are also a site of the allergen and antibody reaction and therefore also swell and enlarge as a result of this effect.

It has been assumed that the enlargement of lymphoid tissues (probably related to the underlying inflammatory reaction discussed above) was directly related to the development of SDB early in life. Systematic evaluation of palatine tonsils in 27–35 wk of age premature infants, however, indicates that tonsils are small early in life [37]. Adenoids could not be investigated in this study, and thus enlargement of adenoids could not be ruled out. It is important to note that children without tonsil and adenoid enlargement as documented by cephalometric X-rays but with dental agenesis also develop SDB in early childhood.

Based on these findings, it appears that adenotonsillectomy may not be the primary treatment modality in preventing the development of SDB. There is a balance between bone and tissue development. The importance of maintaining this relationship has been shown as discussed above, however, postnatally there is also interaction between specialized tissue size and function. Due to fetal processes, an individual may have a naso-maxillary build-up that does not allow a large pharyngeal space [3]. The pharynx relates specifically to the middle cranial fossa and the size of this specific fossa in humans determines the horizontal dimension of the pharyngeal space, and these spatial relationships are

established during fetal life. Any reduction in skeletal dimensions will influence the space allocated for soft tissues. Similarly, enlarged adenoids will lead to impaired nasal breathing depending on the degree of bone development. Inflammatory reactions also play a role in influencing nasal breathing depending on the fetal development of the skull base and craniofacial structures.

Adenoids and tonsils influence function not necessarily because of their absolute size but due to their relative size compared to the available space. Because of their entrapment in a relatively small space due to adeno-tonsil enlargement, soft tissues will also become functionally impaired. If this impairment is counteracted by an increase in tongue and facial muscle activity, there may be no functional deficits of the soft tissue. If, however, this does not occur, the result will be continuous mouth breathing and nasal disuse [26]. Despite this absence of functional deficit, these children will still be vulnerable to sleep disruptions as discussed below. If the compensation is insufficient, there will be progressive development of a complete disuse in nasal breathing, leading to long-term consequences.

In the former situation in which there is adequate compensation of the tongue and facial muscles to offset soft tissue defects, children will not develop mouth breathing; putting them at time at a disadvantage should there ever be abrupt worsening of nasal flow during sleep. In this situation, they will not have the adapted tool of mouth breathing to compensate. This is commonly seen in very young infants where there is an increased effort to breathe nasally and no appropriate mouth breathing. This increased inspiratory effort will lead to increasingly negative intra-thoracic pressures with induction of the Muller maneuver and associated autonomic nervous system changes. Progression of these movements against a partially closed glottis will lead to a significant decrease in the already small tidal volumes of these infants. There will be development of asphyxia and potentially even death as documented on autopsies of infants with abrupt and unexplained deaths during sleep [42,43]. In those with inadequate tongue and facial muscle strengthening to counteract soft tissue impairment, there will be absence of return to normal breathing during sleep post T&A, even with concurrent aggressive nasal allergy treatment. This lack of control of abnormal breathing during sleep post T&A has been well documented in numerous studies of older children [44–49]. Interestingly, long-term prospective follow-up of children who appeared to have significant initial improvement following T&A [50] has shown reoccurrence over time despite absence of abnormal soft tissue in the upper airway. This finding has been confirmed in two retrospective studies [44,45].

There are several reasons why abnormal breathing during sleep in these children post T&A goes unrecognized. Changes in skeletal growth may not be well investigated and at times difficult to recognize by non-specialists. Even if a diagnostic PSG is done, a poor understanding of abnormal breathing patterns during sleep in children may lead to underscoring of respiratory events. Inappropriate or limited usage of tools, such as the esophageal manometry and appropriately calibrated nasal cannula pressure transducers, also hinder appropriate detection of these events. There tends to be too much reliance on oxygen saturation recordings and lack of appropriate investigation of arousal patterns in the sleep electroencephalogram (EEG). Finally, no systematic effort is made to ensure that the functions altered by abnormal breathing during sleep are managed appropriately in order to restore nasal breathing during wake and sleep periods.

There are several questions regarding the development of enlarged tonsils and adenoids. As noted previously, enlarged tonsils in premature children were observed only after documentation of abnormal breathing during sleep and presence of an obstructive pattern on PSG. Questions then arise whether continuous mouth breathing secondary to impaired nasal breathing leads to lack of appropriate oral humidification and, as a result, a local inflammatory reaction. In addition to changes in humidification, temperature, and air turbulence, there is also micro-trauma related to the mouth breathing itself. Oral breathing also leads to functional changes, including abnormal swallowing, feeding, and occurrence of esophageal reflux. Increasing respiratory efforts affect the diaphragmatic movements causing augmented pressure on the stomach, particularly at feeding times. This may lead to recurrent micro-trauma of the oropharynx and the adenoids with secondary inflammatory reactions. Specialists trained in myofunctional reeducation of infants have documented the need to train young mothers on appropriate positions in which to breast or bottle-feed infants [51]. Finally, in some instances, food or other allergies documented early in life may be present concurrently with inflammatory reactions causing palatine tonsils, adenoids or nasal turbinate enlargement and thereby reducing the upper airway size. A negative cycle then ensues in which impairment of nasal breathing leads to functional impairment, affecting the skeletal growth. This is well documented in experiments done on Rhesus monkeys [33–36].

In summary, it had been previously assumed without complete rationale that enlarged palatine tonsils and adenoids were the major cause of SDB in early childhood. There is a dependent relationship between appropriate nasal breathing and skeletal and soft tissue growth and distribution. Any defect in nasal breathing will affect many fundamental functions during early development and would lead to SDB. To ignore such interactions and focus on what may be the most visually recognizable abnormality, leads to inadequate and limited treatment.

Altering functions to entrain craniofacial growth: role of myofunctional therapy

Problems associated with abnormal nasal breathing were recognized prior to recognition of incomplete treatment with T&A for SDB [52–54]. The understanding of the relationships between function and growth of the craniofacial structures led to experiments on how the honing of the use of these functions would impact the craniofacial growth. Myofunctional therapy done in association with orthodontia and craniofacial surgery has been shown to correct the deficits caused by abnormal growth patterns [55,56]. Myofunctional therapy was developed as a significant tool in Europe in the 1960s. Specialists of the craniofacial sphere recognized the continuous interaction between the facial muscle activity and orofacial development. Individuals such as Delaire in France and Planas in Spain created therapeutic protocols utilizing the stimulation of proprioception and motor activity in the orofacial region in children with craniofacial syndromic presentations and orthodontic problems [55,56]. The extension of these myofunctional therapy protocols to those with SDB is more recent and has been shown to have limited benefit in improving outcomes in some centers. These published trials have been on adults in Brazil [57] and children in France, Northern California, and Taiwan [42,43]. They suggest the possibility of strengthening in function and thus ensuing improvement in SDB. In children, improvement in SDB is accomplished through modification of craniofacial growth. In 2009, Guimares et al. [57] reported on the effects of tongue and facial muscle exercises in adults of age 25–65 y with OSA, with a mean AHI of 22.4 ± 6.48, i.e., moderate OSA. Outcome measures after three months of approximately 30 min of daily exercises showed not only improved PSG results (with an average AHI score of 13.7 ± 8.5), but also improved scores evaluating sleepiness, snoring, and sleep quality. Compared to the

control group, subjects had significant improvement in all outcome measures.

Huang and Guilleminault [37] studied five premature infants at approximately 36 wk gestational age (GA), including a pair of twins born at 34 wk GA. The patients underwent myofunctional therapy from birth on, and at six months of age, were documented to have normal breathing during wake and sleep verified by nocturnal PSG. They had a normal craniofacial anatomy, normal hard palate, and normal nasal breathing, findings very different from all other studied premature infants who went on to develop obstructive respiratory patterns during sleep. Myofunctional therapy encompassed usage of primitive tongue reflexes to entice the tongue into a specific position. The children sucked on specially designed hard toys and also used a hard rather than soft nipple to feed. In doing so, the premature infants were forced to develop normal suction and swallowing responses. Guilleminault et al. [58,59] reported on the role of myofunctional reeducation in the development of nasal breathing and normal craniofacial development post T&A. These subjects acquired a normal naso-maxillary complex and mandible compared to those non-compliant with the exercise program in the control group. Recent studies have emphasized the importance of normal nasal breathing during sleep, most commonly associated with appropriate craniofacial growth and development of a normal upper airway.

Myofunctional reeducation hones the development of a normal and strong suction, mastication employing both sides of the jaw, normal swallowing, normal tongue position at rest against the upper and posterior face of the upper teeth, and normal nasal breathing with the lips in contact when at rest. The goals of reeducation programs are to eliminate abnormal swallowing, chewing, and speech articulation. They also aim to strengthen the posture and employ continuous usage of the nose when breathing whether the patient is awake or asleep. Reeducation techniques will vary depending on the age of the subject. Myofunctional therapy is applicable to subjects of any age, including premature infants, in whom exercises engage primitive reflexes present at birth. This may include having the infant close their lips around a finger gently placed in their mouth or having them touch their lips at different points in order to draw the tip of their tongue towards the sensory stimulated region [60]. Other techniques include utilizing specific nipples to reproduce the consistency and efforts demanded to pull milk from a mother's breast [61,62] and special toys to aid infants and young children in exploring their tongue and mouth [51]. These modalities should be applied by the parents to their children daily or as often as possible [58–60]. Myofunctional therapy is more advantageous compared to orthodontics in that it can be applied much earlier in life.

The role of obesity in children with sleep-disordered breathing

SDB has been described as a cause of not only poor development but also of failure to thrive. Obesity was not initially a key feature in these first reported cases. With the obesity epidemic beginning in the mid-1990s, increasing number of children were reported to also present with SDB. Certain ethnicities, particularly African American children, have a stronger association between obesity and SDB [63]. Obesity is a complex disorder leading to worsening supine ventilation secondary to restrictive chest-bellows syndrome [63]. This syndrome also leads to progressive fatty infiltration of the neck and upper airway. MRI studies have shown that a progressive fatty infiltration of the genio-hyoid and genio-glossal muscles occurs along with dissociation of muscle fibers with fat cells [64]. These fat cells also infiltrate the lateral walls of the pharynx in addition to other muscles. Such fatty infiltration leads to enlargement of the soft tissues, reduction in the size of the upper airway, and enlargement of the lingual tonsils. The reduction in tidal volume due to chest restriction from abdominal obesity also leads to mechanical changes that pull the trachea during inspiration. This constant pulling of the hyoid bone during inspiration leads to increased upper airway collapsibility. Obesity can thus result in abnormal breathing during sleep. Obesity is associated with a progressive dysfunction of the adipocyte. Preadipocytes differentiate into mature adipocytes and form adipose tissue in response to a positive energy balance. Adipose tissue not only stores energy, but also acts as a dynamic endocrine organ, vital for hormone and cytokine (adipokine) secretion. White adipose tissue (WAT), located in abdominal and subcutaneous deposits in mammals, performs the majority of energy storage and adipokine secretion [65]. Brown adipose tissue (BAT) mediates the non-shivering thermogenesis, well known to protect infants from cold exposure. Genetics play a role in the control and development of WAT and BAT. Specific animal models of obesity (such as the ob–ob mouse) have been developed showing such genetic role. The differentiation and maintenance of the two types of adipose tissue is interrelated, involving multiple signaling pathways and transcription factors whose expression varies over time. This includes the major genes implicated in WAT and BAT adipogenesis, such as hormones, adipokines, enzymes, transcription factors (particularly PPAR gamma and the C/EBP family), and signal transduction ligands, which are essential in studying the complex interactions between WAT and BAT. Dysfunction of the adipocyte leads to stimulation of adipokines, particularly TNF-alpha and interleukins 6 and 1. These defects lead to pivotal inflammatory responses, both local and general, in addition to abnormal secretion of peptides found not only in the adipocyte but also in the gut and brain. Peptides such as leptin, adinopeptin, obesin etc., are involved, and dysfunction of the adipocyte leads to leptin resistance and ghrelin dysfunction. These two peptides are crucial in food intake, insulin resistance, and dysregulation of glucose and lipid control [66]. Overweight and obese individuals, with or without SDB, will develop these dysfunctions. The consequences of these abnormalities affect the cardiovascular, respiratory, metabolic, and cerebral systems.

It is clear that the size of the upper airway has an impact on how quick obesity may lead to upper airway impairment and SDB. Initially, a smaller upper airway will have a faster infiltration than larger ones as shown many years ago by Jamieson et al. [67]; but the initial problem is related to two very distinct causes, thus if acute treatment in both cases utilizes positive airway pressure (PAP) therapy, etiogenic treatment and prevention will be very different. Sleep itself may be involved in the development of obesity. Sleep restriction, a consequence of new age electronics in the lives of children, has been shown to have a clear association with the obesity epidemic in children.

Sleep fragmentation, which occurs with abnormal breathing, will cause changes in metabolic controls in part through the process of epigenetics, by which environmental events trigger a genetic cascade that would not have otherwise occurred. Obesity along with the fatty infiltration of upper airway will always lead to SDB from simple flow limitation to frank OSA.

Treatment and prevention of SDB secondary to obesity, however, is very different from the ones in SDB in non-overweight children with impairment of orofacial growth. It is unfortunate that both syndromes are not clearly delineated as the ultimate goal should be prevention of SDB, and this requires a distinct therapeutic approach (Table 2).

Table 2
Overview of factors altering upper airway size that are risk factors for sleep-disordered breathing.

Upper airway
- The nose, naso-pharynx, and oro-pharynx form the upper airway (UA). UA skeletal muscles and soft tissues support respiratory and non-respiratory functions such as sucking, swallowing, and vocalization/phonation.
- The UA can be modeled as a collapsible tube with maximum flow (V_{max}) which is determined by upstream nasal pressure (Pn) and resistance (Rn)
- Upper airway patency depends on the balance between intrinsic collapsibility (Pcrit) versus the level of pharyngeal muscle dilator activity
- Sleep reduces pharyngeal muscle tone and impairs reflex responses: genioglossus negative pressure reflex is reduced and inhibitory inputs to the genioglossus muscle increase. The change in posture from upright to supine during sleep promotes upper airway collapse.
- Factors that affect upper airway size include the following:
  - Body position: supine posture yields lower lung volumes which result in loss of caudal traction on the upper airway and increased airway collapsibility
  - State of alertness: wakefulness versus sleep (NREM sleep, REM sleep)
  - Respiratory cycle: UA size decreases with decreased lung volume during expiration
  - External factors that reduce UA: fat deposits, hypertrophied tissues, and abnormal craniofacial features.

Factors that affect craniofacial features
- Genetic activity during fetal life
- Persistence of postnatal genetic activity particularly at orofacial growth 'centers'
- External pathological processes disturbing orofacial growth 'centers"
- Orofacial functions

Genetic activity responsible for normal development of tissues supporting the upper airway
- Fetal life: genetic activity at synchondroses is important for normal orofacial development. Impaired craniofacial growth may result from mutations involving many genes that affect development of the brain, skull base, and cranial vault
- Post-natal: Genetic activity persists at the intermaxillary synchondrosis and alveolo-dental synchondrosis. Activity of muscles interacting with active synchondroses also affect normal development
- Genetic mutations may lead to either syndromic or non-syndromic mutations. These mutations may result in abnormal orofacial growth.

Environmental factors that act on orofacial growth centers
- Pathologic processes: inflammatory, traumatic, tumors
- Impairment of normal orofacial functions: sucking, swallowing, chewing, nasal breathing

Interactions of genetic and orofacial structures
- Cranial neural cell crest (CNC) migrates toward developing branchial arches and the subgroup migrates toward specific areas, mixing with mesodermal cells
- The mesodermal cells give rise to muscle cells while CNC cells give rise to nearly all the structures in the head including bones and teeth
- Specialized CNC cells and epithelium continuously interact to cover the face and oral cavity
- Genes acting through proteins control the evolution of different structures in the orofacial region.
  - Mutations in the sequence of one or a group of genes alter expression or function of encoded proteins
  - Environmental factors can also affect expression or normal functioning of protein products
  - Abnormalities lead to orofacial and dental disorders. The result may be either syndromic or non-syndromic

Summary
- **Genetic and environmental factors have similar impact on orofacial growth and size of the UA**
- **Genetic and environmental factors may jointly influence the size of the UA**
- **Environmental factors may mimic the effects of genetic factors on UA size**
- **Treatment of environmental factors can reduce/eliminate the negative impact of genetic factors**
- **Delayed recognition/treatment and further abnormal development of orofacial structures are key factors that reduce the upper airway size and promote secondary development of SDB**
- **Early recognition of risk factors for abnormal development of orofacial structures allows implementation of preventive measures/interventions**

CNC: cranial neural cell crest; NREM: non-rapid-eye-movement; Pn: nasal pressure; Rn: nasal resistance; REM: rapid-eye-movement; SDB: sleep-disordered breathing; UA: upper airway.

Conclusion

It is important to understand how SDB develops and to separate the SDB seen in obese children from the one observed in non-overweight individuals particularly in its most common presentation of obesity. Understanding the development of the craniofacial structures, their interaction in the growth of the face, and the interaction between specific functions early in life and maxilla-mandibular growth is critical if we wish to prevent development of OSA and eliminate risk of reoccurrence in adulthood. Ultimately, the goal is to provide normal and continuous normal nasal breathing during wake and asleep.

Conflicts of interest

The authors do not have any conflicts of interest to disclose.

Support

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Practice points

SDB in children persists and re-occurs after T&A.

Naso-maxillary and mandibular development has an important impact on the size of the upper airway, and any impairment in this development will consequently impact the size of the upper airway.

Development of the facial structure is under the control of genetic and environmental factors.

Two growth centers (synchodroses) are active postnatally (intermaxillary and alveolo-dental) and can be affected further by genetic defects and environment factors.

Treatment of certain environmental factors impacting on the two active synchondroses can avoid development of OSA and be involved in OSA treatment.

Research agenda

It is important to recognize infants at risk of developing OSA. They may be at risk due to genetic or environmental factors which lead to abnormal functioning of the orofacial muscles. Once identified, these infants should undergo myofunctional treatment as early as possible to retrain these muscles. Myofunctional therapy may be implemented by trained therapists, dentists, physicians, or parents taught in the correct techniques of how to administer. Further studies of children of OSA family members need to be done to search for potential mutations of genes involved in embryologic development of the naso-maxillary complex and mandible. These investigations could involve looking for concordant or discordant orofacial development and possibly OSA development in homozygote twins in families with OSA.

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Pediatric Sleep Disorders and Special Educational Need at 8 Years: A Population-Based Cohort Study

Karen Bonuck, Trupti Rao and Linzhi Xu

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Pediatric Sleep Disorders and Special Educational Need at 8 Years: A Population-Based Cohort Study

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KEY WORDS

sleep-disordered breathing, behavior sleep problem, longitudinal, special education

ABBREVIATIONS

ALSPAC—Avon Longitudinal Study of Parents and Children
BSP—behavioral sleep problem
CI—confidence interval
OR—odds ratio
SDB—sleep disordered breathing
SEN—special educational need
SES—socioeconomic status

All authors meet the criteria for authorship. Dr Bonuck conceptualized and designed the study, drafted the initial manuscript, reviewed and modified the analyses in collaboration with Dr Xu, and incorporated co-author feedback into the final manuscript. Dr Xu developed the methods, carried out all statistical analyses, and reviewed and revised the final manuscript. Dr Rao drafted sections of the manuscript and reviewed the final version.

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WHAT'S KNOWN ON THIS SUBJECT: Sleep disordered breathing (SDB) and behavioral sleep problems (BSPs) affect cognitive, behavioral, and language development. No studies have examined associations between SDB and BSPs across early childhood, and later special education need (SEN), on a population basis.

WHAT THIS STUDY ADDS: A history of SDB through 5 years of age was associated with ~40% increased odds of SEN at 8 years, among >11 000 children. BSPs were associated with 7% increased odds of SEN, for each additional ~12 months of reported BSPs.

abstract

OBJECTIVES: To examine associations between sleep-disordered breathing (SDB) and behavioral sleep problems (BSPs) through 5 years of age and special educational need (SEN) at 8 years.

METHODS: Parents in the Avon Longitudinal Study of Parents and Children reported on children's snoring, witnessed apnea, and mouth-breathing at 6, 18, 30, 42, and 57 months, from which SDB symptom trajectories, or clusters, were derived. BSPs were based on report of ≥5 of 7 sleep behaviors at each of the 18-, 30-, 42-, and 57-month questionnaires. Parent report of SEN (yes/no) at 8 years was available for 11 049 children with SDB data and 11 467 children with BSP data. Multivariable logistic regression models were used to predict SEN outcome by SDB cluster and by cumulative report of SEN.

RESULTS: Controlling for 16 putative confounders, previous history of SDB and BSPs was significantly associated with an SEN. BSPs were associated with a 7% increased odds of SEN (95% confidence interval [CI] 1.01–1.15), for each ~1-year interval at which a BSP was reported. SDB, overall, was associated with a near 40% increased odds of SEN (95% CI 1.18–1.62). Children in the worst symptom cluster were 60% more likely to have an SEN (95% CI 1.23–2.08).

CONCLUSIONS: In this population-based longitudinal study, history of either SDB or BSPs in the first 5 years of life was associated with increased likelihood of SEN at 8 years of age. Findings highlight the need for pediatric sleep disorder screening by early interventionists, early childhood educators, and health professionals. *Pediatrics* 2012;130:1–9

Pediatric sleep disorders result in disrupted, inefficient, and inadequate sleep.[1,2] The most prevalent and pernicious are behavioral sleep problems (BSPs) and sleep disordered breathing (SDB). Both may affect brain development and cause neuronal damage, particularly during critical early development periods.[1–3] Slow wave sleep, the most restorative form of sleep, is largely governed by the frontal cortex, which mediates higher functions, such as decision-making, ambition, and emotional regulation. Disrupting this restorative process via either sleep fragmentation or hypoxemia may affect frontal cortex functioning and lead to aspects of the behavioral phenotype seen with childhood obstructive sleep apnea.[1,2,4]

BSPs, characterized by inadequate and fragmented sleep, affects behavior[5,6] and cognition[5–7] and language development.[8] Similarly, SDB is linked to delayed development,[9] speech-language impairments,[10,11] and adverse behavioral[2,12] and cognitive[2,13,14] effects. Thus, both disorders can affect school functioning and educational need, in addition to being 2 to 3 times as prevalent among children with developmental delay or disability versus the typically developing child.[15] In the United States, 3 million 6- to 21-year-olds receive special education for conditions associated with sleep disorders (ie, developmental delay, learning disability, or autism); 40% to 80% also have attention-deficit disorder/attention-deficit hyperactivity disorder.[16]

While sleep disorders in early childhood may affect special educational needs, just a few studies have analyzed this association. Parents of children in Spain (mean age 11–12 years) in special versus mainstream schools reported significantly higher rates of both BSPs (32.3% vs 10.5%) and SDB (26.8% vs 5.7%),[17] affirming results of an earlier UK study of 4- to 12-year-olds from special versus mainstream educational venues for both BSP (23.8% vs 11.6%) and SDB (19.8% vs 9.0%).[18] An Australian study of 6- to 15-year-olds found similar results, although a low response rate, small sample size, and poor matching[19] limit generalizability.

This is the first prospective, population-based study of the associations between SDB and BSPs throughout early childhood and effect on later special education need (SEN). Given the dynamic, multisymptom expression of SDB's hallmark symptoms (snoring, apnea, and mouth-breathing) SDB was examined as a combined trajectory of these symptoms. This is a secondary analysis of observational data collected during the peak period in the development of SDB and BSPs, in a cohort of >11 000 children. The study had 2 specific research questions. Is cumulative report of BSP across 4 intervals of ~12 to 15 months from 18 to 57 months of age associated with an increased likelihood of an SEN determination at 8 years of age? Similarly, are SDB symptom trajectories, or clusters, from 6 to 57 months of age associated with a greater likelihood of SEN at 8 years of age?

METHODS

Population

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a geographically based cohort study of children. ALSPAC enrolled ~85% of pregnant women (N = 14 541) residing in a defined section of southwest England with an expected date of delivery between April 1991 and December 1992. This study uses data from ALSPAC because it is the only known longitudinal, population-based cohort with measures of SDB, non–respiratory-related sleep problems, and school outcomes in early childhood.

The cohort, described in detail elsewhere,[20] was generally representative of the UK population. Our analyses, which excluded twins and triplet and quadruplet births, children who did not survive to 1 year, and children with conditions such as major congenital disorders that are likely to affect SDB or SEN yielded an initial base sample of 13 467 infants.

Ethical approval for the ALSPAC study was obtained from the ALSPAC Law and Ethics Committee and the local research ethics committees. All participants provided informed consent. This secondary data analysis was considered exempt from the lead investigator's committee on human subjects.

Assessment of SEN

"SEN identified" is the primary outcome variable. Comparable to the US categories for special education, SEN categories include speech, language, and communication needs; specific learning difficulty; and behavioral, emotional, and social difficulties. In 1999–2000, when this study's SEN data were obtained, ~17% of children in England had an SEN identified.[21] Most such children have their needs met in mainstream schools with an individualized education plan. We did not use the legal "statement of SEN," a much higher level of need, obtained for just ~3% of children in England who usually attend specialized schools, as this would exclude the ~14% of children generally served in mainstream schools.[22] For comparison, during this same period, ~13% of children were classified under the US Individuals with Disabilities Education Act as having a disability entitling them to special education.[23]

Assessment of SDB and Sleep Problems

SDB Symptoms

Parents reported on their child's snoring, mouth-breathing, and apnea at 6, 18, 30, 42, and 57 months of age in response to ALSPAC's mail questionnaires. ALSPAC's Likert scaled items are similar to items validated

against polysomnography data; objective sleep evaluation measures were unavailable. Snoring was assessed with the question: "Does she snore for more than a few minutes at a time?" Mouth-breathing was assessed with the item: "Does she breathe through her mouth rather than her nose?" Witnessed apnea was assessed with the question: "When asleep, does she seem to stop breathing or hold breath for several seconds at a time?"

We derived a series of unique (ie, statistically distinct) patterns of these SDB symptoms across the 5 time points via a methodology reported elsewhere.[24] Clusters were derived for children with SDB measures at ≥2 of these 5 time points. Briefly, this process yielded 5 unique symptom patterns, or clusters (see Fig 1 A–E), depicting the prevalence of snoring, mouth-breathing, and apnea in SD or *z* scores, at 6, 18, 30, 42, and 57 months of age.

These 5 clusters classified children as (1) normals, asymptomatic throughout (37% of sample); (2) peak at 6 months, all 3 symptoms peak at 6 months but abate thereafter (19% of sample); (3) peak at 18 months, all 3 symptoms peak at 18 months but lessen thereafter (17% of sample); (4) worst, elevated symptom levels beginning at 18 months that remain high, with a 30-month peak (9% of sample); and (5) late symptom, modestly elevated symptoms first appear at 42 months (18% of sample).

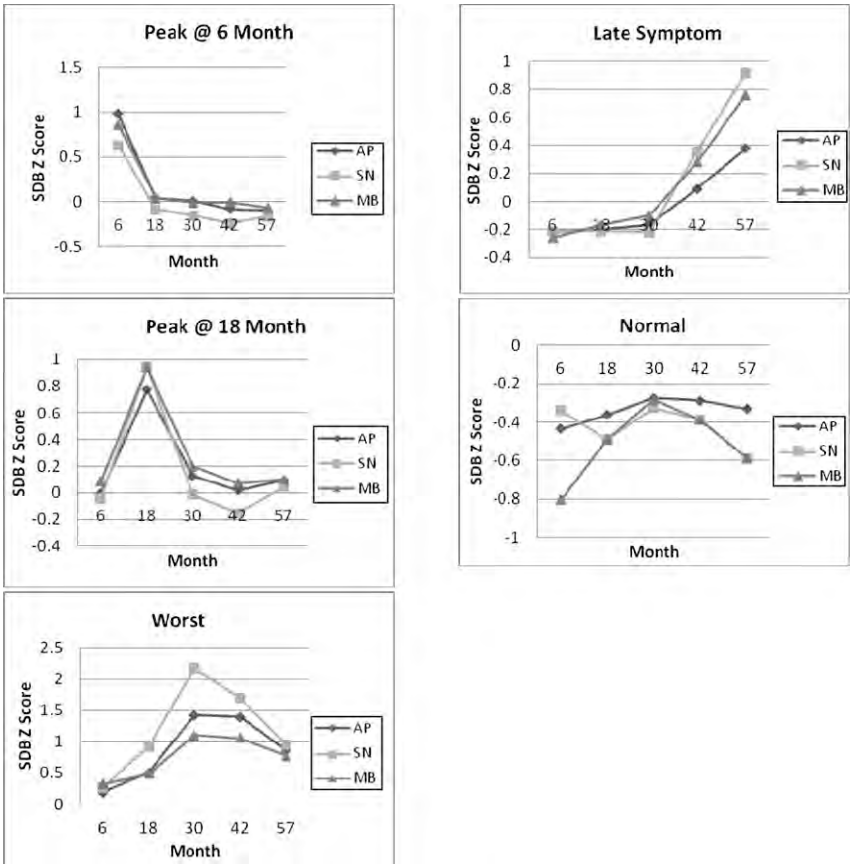

FIGURE 1
SDB clusters of combined apnea (AP), snoring (SN), and mouth-breathing (MB) in sample from 6 to 57 months of age.

BSPs

At the 18-, 30-, 42-, and 57-month questionnaires, parents were asked 7 items about their child's sleep. Most pertained to BSPs in the past year (except at 30 months when no recall period was given). Items included whether (yes/no) the child refused to go to bed, regularly woke early, regularly had difficulty sleeping, regularly had nightmares, regularly got up after being put to bed, regularly woke in the night, and regularly got up after a few hours. As in previous ALSPAC analyses,[25,26] we combined these into an index. We applied a cut-off score of ≥5 of these 7 items as a BSP, given that 15%, 27%, 24%, and 21% of the sample responded affirmatively to ≥5 of the 7 items at 18, 30, 42, and 57 months, respectively, consistent with previously published prevalence rates.[27,28] These items were, appropriately, not assessed at 6 months.

Descriptive Characteristics

The literature guided the selection of potential covariates and mediating variables. SDB is associated with multiple socioeconomic status (SES) variables, such as parental education and employment,[9,29,30] as well as maternal risk factors, such as maternal smoking,[9,30] race,[9,31] birth weight and gestational age,[32] and breastfeeding.[33,34] Optimal sleep hygiene reduces BSP risk[35] and is significantly related to race, SES, family structure, and household characteristics.[36] In several studies, child gender and race,[37,38] SES,[38,39] and parental education[40] moderated the effects of poor sleep on cognitive functioning and academic achievement. SDB is associated with reduced IQ, which may not resolve postadenotonsillectomy.[41]

Based on these associations, putative covariates included (1) maternal cigarette smoking: "ever" versus "never" before pregnancy; (2) ethnicity of child: white or nonwhite; (3) housing inadequacy: a composite variable for crowdedness (<1 room per person) and/or homelessness from birth to 4 years of age; (4) paternal social class: manual versus professional; (5) maternal education: low versus high, with "low" denoting the end of compulsory

education, resulting in a school leaving certificate at 16 in the United Kingdom; (6) family adversity index: 18 stressor items (eg, maternal psychopathology, crime, financial insecurity) used in other ALSPAC analyses[42]; (7) Home Observation for the Measurement of the Environment (HOME): an inventory[43] of the quality of parenting and home environment; (8) birth weight and gestational age: low birth weight was defined as <2500 g and premature as <37 weeks' gestation; (9) breastfeeding: whether the child was ever breastfed; (10) adenoidectomy/tonsillectomy: questionnaire at 57 months asked if child ever had tonsils or adenoids removed (exact age at surgery was not assessed); and (11) IQ: per the Wechsler Intelligence Scale for Children, Third Edition (WISC-III), administered at ~8 years of age. Consistent with other ALSPAC work, an IQ <80 was denoted as low.[44]

Statistical Analyses

We used χ^2 and analysis of variance tests for categorical covariates and *t* tests for continuous covariates to describe differences between or among: children with missing versus nonmissing data for the sleep or SEN variables, children with versus without an SEN, the SDB clusters, and children with BSPs at 0, 1, 2, 3, or 4 time points. Logistic regression was used to examine unadjusted relationships between BSP and SEN and between SDB and SEN. For BSP, the odds ratios (OR) and 95% confidence intervals (CIs) represent the odds of SEN associated with each additional time period of having a BSP (range 0–4). For SDB, ORs (95% CIs) were derived both for each of the 4 symptomatic clusters versus normals, as well as for all 4 symptomatic clusters combined versus normals.

Initial multivariate logistic regression models included all putative covariates, but only significant ($P < .05$) covariates were retained in final models. Models were run including and excluding IQ, as well as with IQ as an interaction term with SDB in the SDB model, and with race, gender, maternal education, and paternal employment with BSP in the BSP model. In addition, BSP models analyzed race, gender, maternal education, and paternal employment as interaction terms, based on earlier work. To address multicollinearity, variance inflation factors were derived to assess the effects of individual independent variables on variance. A conservative variance inflation factor threshold of 10 was used in model testing.[45] Analyses were conducted by using SAS version 9.1 (SAS Institute Inc, Cary, NC).

RESULTS

Sample Size

Excluding children of multiple births, children who did not survive to 1 year, and children with conditions related to sleep disorders or SEN, there were 13 024 children with either BSP or SDB (exposure variables) or with the SEN outcome measure. Of these, 11 026 children had SEN outcomes data, 11 049 children were reflected in the SDB clusters (ie, SDB measures for ≥2 of 5 time points), and 11 467 had BSP data (ie, ≥1 BSP measure at 18, 30, 42, or 57 months of age).

Sample Characteristics and Association With SEN

Table 1 presents the characteristics of the analytic sample of 13 024 children. Compared with the initial base sample of 13 467, the 443 children missing either sleep exposure variable and/or the SEN outcome variable had more adverse SES and family risk characteristics but did not differ by gestational age, birth weight, gender, or IQ (not shown). Among the 11 026 children with SEN outcomes, 16.6% (1825)

TABLE 1 Sample Demographics and Special Education Need

	Base Sample[a]	SEN Among Total Sample	
		Yes	No
N	13 024	1825	9201
Maternal characteristics			
Smoked during pregnancy, any, %***	24.8	33.7	24.3
Alcohol during pregnancy, any, %	54.8	53.6	54.3
Age at delivery, mean y (SD)***	28 (4.94)	27.91 (4.84)	26.78 (5.02)
Breastfed this child, ever, %***	75.6	66.0	74.6
Child characteristics			
Gender, male, %***	51.5	68.7	47.5
Race, white, %	97.6	97.3	98.0
Premature, <37 wk, %***	4.9	6.6	4.7
Low birth weight, <2500 g, %***	4.2	5.9	4.0
Adenoids removed, ever, %***	7.4	11.6	6.7
Tonsils removed, ever, %*	4.5	6.0	4.2
IQ, <80, %***	12.5	41.5	10.1
IQ, mean (SD)***	104.33 (16.42)	89.97 (16.68)	104.83 (15.32)
Socioeconomic/family characteristics			
Maternal education, lower, %***	64.7	78.4	67.3
Paternal employment, manual, %***	44.1	59.8	46.2
Housing, inadequate, %***	12.4	18.1	11.7
Family adversity index, range 0–18, mean (SD)***	1.80 (1.98)	2.17 (2.22)	1.72 (1.93)
HOME score, range 0–8, mean (SD)***	5.74 (1.66)	5.58 (1.75)	5.75 (1.64)
Parity, ≥1, %***	53.7	62.7	54.9
Sleep disorders			
SDB, symptomatic cluster, %[b]**	63.1	71.5	61.6
BSP, reported at >1 time point, %**	44.3	48.4	43.5

HOME, Home Observation for the Measurement of the Environment.

[a] These 13 024 constitute the base sample used to derive the SDB clusters, sleep problems score, and SEN outcomes presented.

[b] In any of the 4 symptomatic clusters versus the 1 asymptomatic cluster.

* $P < .05$; ** $P < .01$; *** $P < .001$.

had an SEN. Children who did not have an SEN (n = 9201) differed from those with an SEN on nearly every characteristic (Table 1).

SDB Cluster Association With Sample Characteristics

There were significant differences among the clusters for 16 of the 17 putative covariates (Table 2). Children in the symptomatic clusters had the most adverse risk profile, led by those in the "Worst" cluster, and followed by those in the "Late Symptoms" cluster. In contrast to SEN associations with sample characteristics, the normals were significantly less likely to be premature or low birth weight or to have had mothers who reported smoking or drinking alcohol in pregnancy. There was a 4-point IQ difference between the "Worst" (mean 102.4, SD 16.3) and normal (mean 106.4, SD 16.1) clusters.

Cumulative Sleep Problem Association With Sample Characteristics

Cumulative report of BSPs differed by maternal risk factors as well as SES and family characteristics (Table 3). A higher proportion of children with BSPs had disadvantaged profiles; for most significant variables, this association appeared to be linear. There was nearly a 4-point IQ difference between children with BSPs at all 4 time points (mean 101.80, SD 15.61) versus children with no reported BSPs (mean 105.76, SD 16.28) In contrast, to SDB, neither gender, race, prematurity, nor low birth weight was associated with duration of BSP.

BSP Associations With SEN

Table 4 presents crude and adjusted effects of each additional time point report of a BSP. In crude analyses, each additional time point with a BSP was associated with a 12% increased odds of SEN (95% CI 1.06–1.18). As neither the IQ × BSP nor the child race × BSP, gender × BSP, maternal education × BSP, or paternal employment × BSP interaction terms were significant, these variables were entered as covariates into logistic regression models. In adjusted analyses without IQ, BSP remained significant (OR 1.07, 95% CI 1.01–1.15). In analyses adjusted for IQ, BSP nearly attained significance (OR 1.08, 95% CI 1.00–1.17), even when controlling for the strong, significant effect of IQ (OR 6.17, 95% CI 5.10–7.48).

TABLE 2 SDB Cluster Associations With Sample Characteristics

	Peak at 6 mo	Peak at 18 mo	Worst	Late	Normal
N	2142	1830	934	2005	4138
Maternal					
Smoked during pregnancy, any, %***	24.6	26.6	30.0	23.8	17.5
Alcohol during pregnancy, any, %*	53.3	54.3	57.4	54.0	56.8
Age at delivery, mean y (SD)***	28.28 (4.73)	27.98 (4.90)	27.73 (5.03)	28.11 (4.79)	29.04 (4.64)
Breastfed this child, ever, %***	75.6	74.8	70.4	75.1	79.3
Child					
Gender, male, %***	54.0	53.5	55.9	49.6	49.2
Race, white, %**	98.2	96.7	97.7	98.1	98.2
Premature, <37 wk, %*	4.5	4.5	7.0	4.8	4.3
Low birth weight, <2500 g, %**	3.3	4.9	5.2	4.1	3.3
Adenoids removed, ever, %***	4.6	6.3	31.7	9.8	3.1
Tonsils removed, ever, %***	2.7	3.3	20.7	6.0	2.0
IQ, <80, %***	11.4	14.0	15.6	14.8	9.6
IQ, mean (SD)***	104.32 (16.14)	103.3 (17.05)	102.4 (16.25)	102.7 (16.28)	106.41 (16.07)
Socioeconomic and family					
Maternal education, lower, %***	65.3	66.0	68.3	66.4	56.9
Paternal employment, manual, %***	43.7	46.4	47.2	44.4	37.7
Housing, inadequate, %***	15.3	14.8	16.2	13.3	9.12
Family adversity index, range of 0–18, mean (SD)***	2.15 (2.11)	2.20 (2.09)	2.37 (2.19)	1.93 (2.00)	1.57 (1.81)
HOME score, range of 0–8, mean (SD)	5.7 (1.67)	5.73 (1.64)	5.70 (1.67)	5.78 (1.64)	5.79 (1.65)
Parity, ≥1, %**	54.7	54.1	54.1	51.6	56.6

HOME, Home Observation for the Measurement of the Environment.
* $P < .05$; ** $P < .01$; *** $P < .001$.

SDB Associations With SEN

The combined symptomatic clusters (Table 5) were associated with a 56% increased odds of SEN in unadjusted analyses (95% CI 1.37–1.77); children in the "Worst" cluster had the highest increased odds: 83% (OR 1.83, 95% CI 1.48–2.25). In adjusted analyses without IQ, the combined symptomatic cluster effect attenuated to 38% (95% CI 1.18–1.62). The "Worst" cluster continued to have the strongest effect: 60% (95% CI 1.23–2.08), while other cluster effects ranged from 30% to 40%. Adjusting for IQ only slightly attenuated the combined symptomatic cluster effect to 30% (95% CI 1.05–1.61), but the "Peak at 18" and "Late" cluster effects no longer reached significance. For streamlining purposes, significant covariates are not shown (table legend identifies which were significant).

DISCUSSION

This is the first population-based study of the association between respiratory-related (SDB) and behavioral (BSP) sleep

TABLE 3 BSP Association With Sample Characteristics, by Number of Time Points With Reported BSPs

	No. of Time Points With a BSP				
	0	1	2	3	4
N	6522	2527	1366	780	272
Maternal characteristics					
Smoked during pregnancy, any, %***	19.9	25.7	27.8	31.0	30.7
Alcohol during pregnancy, any, %*	54.3	54.6	58.5	58.4	53.2
Age at delivery, mean y (SD)***	28.61 (4.78)	28.09 (4.84)	27.94 (5.05)	27.6 (4.89)	27.96 (4.72)
Breastfed this child, ever, %	77.2	76.6	74.7	73.4	73.8
Child characteristics					
Gender, male, %	50.8	53.5	51.0	52.4	50
Race, white, %	98.0	97.7	97.5	97.1	98.5
Premature, <37 wk, %	4.6	4.3	6.2	5	3.3
Low birth weight, <2500 g, %*	3.6	3.9	4.7	5.7	3.7
Adenoids removed, ever, %**	6.7	7.2	9.6	9.9	7.0
Tonsils removed, ever, %	4.0	4.7	5.3	6.3	4.3
IQ, <80, %***	10.6	13.2	14.6	18.1	15.1
IQ (mean, SD)***	105.76 (16.28)	103.33 (16.54)	102.67 (16.27)	100.99 (16.35)	101.80 (15.61)
Socioeconomic/family characteristics					
Maternal education, lower, %***	60.1	63.8	65.1	71.9	75
Paternal employment, manual, %***	39.9	45.0	45.5	52.0	48.0
Housing, inadequate, %***	10.5	14.3	15.3	18.2	20.6
Family adversity index, range 0–18, mean (SD)***	1.64 (1.81)	2.03 (2.08)	2.36 (2.15)	2.64 (2.39)	2.87 (2.27)
HOME score, mean 0–8, mean (SD)	5.76 (1.64)	5.77 (1.66)	5.75 (1.65)	5.69 (1.68)	5.71 (1.79)
Parity, ≥1, %***	57.5	53.5	49.9	46.8	48.9

HOME, Home Observation for the Measurement of the Environment.
* $P < .05$; ** $P < .01$; *** $P < .001$.

TABLE 4 BSP Odds of SEN Associated With Each Time Point of Reported BSP

Crude	OR (95%CI)
Crude	
Cumulative sleep problem score	1.12 (1.06–1.18)
Adjusted, without IQ[a]	
Cumulative sleep problem score*	1.07 (1.01–1.15)
Maternal age at delivery, higher vs lower	0.97 (0.95–0.98)
Child gender, male vs female	2.63 (2.26–3.06)
Child birth weight, low vs high	1.65 (1.16–2.34)
Paternal employment, manual vs professional	1.42 (1.22–1.65)
Family adversity index	1.10 (1.07–1.14)
Parity	1.29 (1.09–1.53)
1 vs 0	
≥2 vs 0	1.74 (1.42–2.14)
Adjusted, with IQ[a]	
Cumulative sleep problem score	1.08 (1.00–1.17)*
Child gender, male vs female	2.41 (2.00–2.90)
Family adversity index, increased	1.10 (1.06–1.15)
IQ <80	6.17 (5.10–7.48)

[a] Only significant covariate effects shown.
* $P < .062$.

problems, throughout early childhood, and SEN. Children with a history of BSPs and of SDB in the first 5 years of life were more likely to have an SEN at 8 years of age; even controlling for 16 putative confounders, BSPs were associated with a 7% increased odds of SEN, for each ∼1-year interval. Thus, for example, children with a BSP in at least 2 of the 4 intervals (∼1 of 5 children) had a 15% increased likelihood of SEN. SDB, overall, was associated with a near 40% increased odds of SEN. Children with the worst SDB symptoms were 60% more likely to have an SEN. Sleep problem effects remained significant, even after controlling for IQ, which itself was associated with five- to sixfold increased odds of SEN for both BSPs and SDB. Residual confounding is possible. Specifically, children with underlying neurodevelopmental issues, who are more likely to have SENs, may indeed have more sleep problems. However, given the persistence of sleep problem effects in analyses controlling for multiple putative confounders including IQ, such confounding is unlikely to negate our findings.

Our study differs from the few publications on sleep problems and SEN, in several ways. First, earlier work compared children from specialized versus mainstream schools.[18,19,46] In contrast, we use a population-based approach. Correspondingly, we applied the inclusive SEN designation, rather than the narrower "statement of SEN," most applicable to children in specialized schools. Second, in contrast to earlier work, our longitudinal cohort study's strengths include large sample size, control for multiple potential confounders, and ability to examine temporal relationships and estimate effects. Previous cross-sectional work analyzed data from ∼100 children or fewer from specialized schools, with limited control for confounders. Third, our work assesses SDB and BSP from infancy through 5 years of age, the peak period

TABLE 5 SDB Clusters Effects on SEN

	Crude OR (95% CI)	Adjusted,[a] Without IQ, OR (95% CI)	Adjusted,[b] With IQ, OR (95% CI)
Combined symptomatic vs normal	1.56 (1.37–1.77)***	1.38 (1.18–1.62)***	1.30 (1.05–1.61)*
Peak at 6 mo	1.52 (1.28–1.79)***	1.32 (1.08–1.62)**	1.40 (1.09–1.80)**
Peak at 18 mo	1.47 (1.24–1.75)***	1.31 (1.06–1.63)**	1.14 (0.87–1.50)
Worst	1.83 (1.48–2.25)***	1.60 (1.23–2.08)***	1.45 (1.05–2.00)*
Late	1.56 (1.32–1.85)***	1.43 (1.16–1.75)***	1.26 (0.98–1.63)

* $P < .05$; ** $P < .01$; *** $P < .001$.

[a] In adjusted models without IQ (based on symptomatic versus normal SDB clusters), the following variables were significant: maternal age at delivery, child gender (male), low birth weight, paternal employment (manual), family adversity (increased), and parity (≥2).

[b] In adjusted models with IQ (based on symptomatic versus normal SDB clusters), the following variables were significant: child gender (male), family adversity (increased), and IQ (<80).

for both disorders,[27,47] enabling us to predict cumulative effects during this vulnerable period on later SEN.

Several population-based studies have examined cognitive and academic outcomes (ie, not special education) with mixed results. In 1 study, school-aged children with objectively measured mild SDB did no poorer on most intelligence measures assessed,[48] in contrast to most research linking SDB to poorer academic performance,[12,14] while in another, objectively measured SDB was significantly associated with cognitive outcomes.[49] Regarding BSPs, our findings differ from an Australian study finding no concurrent or longitudinal association between "sleep problems" and cognitive outcomes measured at 4 to 5 and 6 to 7 years of age.[50] In that study, "sleep problems" was defined by just 1 item (ie, whether the parent considered the child to have a sleep problem [none, mild, moderate, severe]), in contrast to our scale-based measure of 7 specific sleep behaviors.

Regarding school outcomes of interventions, adenotonsillectomy to treat SDB is associated with improved neurocognition among 4-year-olds[51,52] and school performance among the lowest performing first graders.[53] Limited data are available on school-related outcomes of BSP interventions, despite their known efficacy among young children.[54–57] The 1 published randomized controlled trial did not find improved learning outcomes among 5- to 6-year-olds identified via school screening. Authors posit that the brief instrument that was used may have been insufficiently sensitive to detect changes in skills (eg, working memory) that affect school outcomes or that learning effects might lag beyond the study's 6-month follow-up.[58]

This study has several limitations. First, neither sleep problem was assessed with validated pediatric sleep questionnaires,[18,19,46] in part, because none were available at the time.[59] Still, the SDB items are similar to those validated against objective measures,[60–64] while the clusters themselves may better capture the dynamic, multisymptom expression of SDB.[24] Our BSP measure corresponds to one used in earlier ALSPAC analyses.[25,26] Second, ALSPAC data did not specify the disabilities that qualified a child for SENs. At the time, the bulk of classifications were for learning versus socioemotional or physical disorders.[21] In contrast, "behavioral, emotional, and social difficulty," "speech, language, and communication difficulty," and "autism spectrum disorder" are now more prevalent among those with SENs, compared with when our study's SEN outcomes data were collected.[65] Given overlap between the functional effects of these disabilities and sleep disorders,[66] our effect sizes may actually be underestimates based on present SEN classifications.

Findings presented here strongly support an association between early childhood sleep problems and later SEN, on a population basis. This highlights the need for early screening, because early treatment is often effective for SDB[67] and BSPs.[56] The magnitude of potential benefit from early screening and treatment is greatest for young children with behavioral, cognitive, and language delays/disabilities, because sleep disorders affect functioning in these areas. Currently, US-based early intervention programs do not systematically screen for sleep disorders,[68] which are underdiagnosed in routine pediatric care.[69,70] Future research should focus on timely and systematic screening and on testing potential interventions, particularly for BSPs, among young children at risk for developmental delay/disability.

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Pediatric Sleep Disorders and Special Educational Need at 8 Years: A Population-Based Cohort Study

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Sleep-Disordered Breathing in a Population-Based Cohort: Behavioral Outcomes at 4 and 7 Years

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KEY WORDS

sleep-disordered breathing, behavior, longitudinal

ABBREVIATIONS

ALSPAC—Avon Longitudinal Study of Parents and Children
CI—confidence interval
HOME—Home Observation for Measurement of the Environment
OR—odds ratio
SDB—sleep-disordered breathing
SDQ—Strengths and Difficulties Questionnaire
SES—socioeconomic status

All authors meet the criteria for authorship; Dr Bonuck conceptualized and designed the study, drafted the initial manuscript, reviewed and modified the analyses in collaboration with Drs Freeman and Xu, and incorporated coauthor feedback into the final manuscript; Dr Freeman worked to develop the methods, carried out initial analyses, supervised final analyses of Dr Xu, and reviewed and revised the final manuscript; Dr Chervin advised on study design and analyses, and carefully reviewed and revised multiple versions of the manuscript; Dr Xu collaborated on statistical design issues, completed final analyses, and reviewed and revised the final version of the article.

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WHAT'S KNOWN ON THIS SUBJECT: Sleep-disordered breathing is associated with neurobehavioral morbidity in children. Prior related research has generally been cross-sectional or short (ie, 1–2 years) follow-up studies of a single symptom (ie, snoring, obstructive sleep apnea, mouth breathing), with limited control for confounders.

WHAT THIS STUDY ADDS: Sleep-disordered breathing was assessed as a trajectory of combined symptoms from 6 months to 69 months, in more than 11 000 children. Sleep-disordered breathing was associated with 40% and 60% more behavioral difficulties at 4 and 7 years, respectively.

abstract

OBJECTIVES: Examine statistical effects of sleep-disordered breathing (SDB) symptom trajectories from 6 months to 7 years on subsequent behavior.

METHODS: Parents in the Avon Longitudinal Study of Parents and Children reported on children's snoring, mouth breathing, and witnessed apnea at ≥2 surveys at 6, 18, 30, 42, 57, and 69 months, and completed the Strengths and Difficulties Questionnaire at 4 (n = 9140) and 7 (n = 8098) years. Cluster analysis produced 5 "Early" (6–42 months) and "Later" (6–69 months) symptom trajectories ("clusters"). Adverse behavioral outcomes were defined by top 10th percentiles on Strengths and Difficulties Questionnaire total and subscales, at 4 and 7 years, in multivariable logistic regression models.

RESULTS: The SDB clusters predicted ≈20% to 100% increased odds of problematic behavior, controlling for 15 potential confounders. Early trajectories predicted problematic behavior at 7 years equally well as at 4 years. In Later trajectories, the "Worst Case" cluster, with peak symptoms at 30 months that abated thereafter, nonetheless at 7 years predicted hyperactivity (1.85 [1.30–2.63]), and conduct (1.60 [1.18–2.16]) and peer difficulties (1.37 [1.04–1.80]), whereas a "Later Symptom" cluster predicted emotional difficulties (1.65 [1.21–2.07]) and hyperactivity (1.88 [1.42–2.49]) . The 2 clusters with peak symptoms before 18 months that resolve thereafter still predicted 40% to 50% increased odds of behavior problems at 7 years.

CONCLUSIONS: In this large, population-based, longitudinal study, early-life SDB symptoms had strong, persistent statistical effects on subsequent behavior in childhood. Findings suggest that SDB symptoms may require attention as early as the first year of life. *Pediatrics* 2012;129:e857–e865

Neurobehavioral morbidity is common in childhood sleep-disordered breathing (SDB) that can range from snoring to obstructive sleep apnea. Mouth breathing is another frequent clinical finding.[1,2] SDB causes abnormal gas exchange, interferes with sleep's restorative processes, and disrupts cellular and chemical homeostasis.[3] The supposed resultant dysfunction of the prefrontal cortex impairs attention, executive functioning, behavioral inhibition, self-regulation of affect and arousal, and other socio-emotional behaviors.[4] Behavioral manifestations include both externalizing (eg, hyperactivity, aggression, impulsivity) and internalizing (eg, somatic complaints, social withdrawal) behaviors.[5] SDB reportedly peaks from 2 to 6 years of age,[6] but also occurs in younger children.[7] SDB's neurologic effects may be irreversible,[8] highlighting the saliency of underdetection.

SDB presents as a heterogeneous disorder in children. Understanding how and when SDB symptom patterns in early life affect neurobehavioral outcomes has clinical implications for deciding whether, how, and in whom to intervene.[9] Yet, existing studies of SDB's neurobehavioral effects in children are primarily cross-sectional, and limited by poor sampling, insufficient consideration of confounders, and imprecise use of statistical tools.[10,11] The few longitudinal studies are either before or after tonsillectomy or follow children for ≤2 years.

This study describes the combined trajectory of 3 hallmark SDB symptoms (snoring, mouth breathing, and witnessed apnea) and their longitudinal statistical effects on behavior. Our research questions were (1) What effect do early SDB trajectories, from 6 through 42 months of life, have on social-emotional behavior at 4 and 7 years? and (2) What effect do SDB trajectories from 6 months through 69 months have on behavior at 7 years of age? We analyzed previously collected observational data from a critical period in SDB development, from 6 months through nearly 7 years of age in a prospective, population-based cohort.

METHODS

Population

The Avon Longitudinal Study of Parents and Children (ALSPAC), a geographically based cohort study of children, enrolled pregnant women residing in a defined part of the former county of Avon in southwest England with an expected date of delivery between April 1991 and December 1992. A total of 14 541 pregnant women were enrolled. The cohort, described in detail elsewhere,[12] is broadly representative of the UK population in terms of socioeconomic status (SES), although with a slight underrepresentation of ethnic minority families, and overrepresentation of wealthier families. Our analyses excluded twin, triplet, and quadruplet births; children who did not survive to 1 year; and children with conditions, such as major congenital disorders, that are likely to affect SDB or behavioral assessment. The resulting base sample, used to derive SDB clusters and behavioral outcomes, was 13 467infants.

ALSPAC's internal law and ethics committee reviews all proposals for secondary analyses and approves policies for data handling and analysis. Ethical approval for this analysis was obtained from the ALSPAC Law and Ethics Committee and UK Local Research Ethics Committee. All participants provided informed consent.

SDB Assessment

Questionnaires, designed and mailed as part of the original ALSPAC study when children were 6, 18, 30, 42, 57, and 69 months of age, asked parents to report on their child's snoring, apnea, and mouth breathing. These items were as follows: (1) Mouth breathing: "Does he or she breathe through the mouth rather than the nose?" At 57 months and older, parents were asked to report separately for mouth breathing when awake versus asleep, although only the latter was used in analyses. (2) Snoring: "Does he or she snore for more than a few minutes at a time?" (3) Apnea: "When asleep, does he or she seem to stop breathing or hold breath for several seconds at a time?" The ALSPAC parent-reported SDB measures are similar or identical to items validated against polysomnographic data from sleep laboratories. Some validated questionnaires have included parent report of all 3 SDB symptoms,[13–17] whereas others have included only snoring and apnea.[18,19]

Responses were categorized along ordinal scales of 3, 4, or 5 levels. Given this inconsistency in (preexisting) response categories, we extrapolated the values to a common scale (0–100) with the "Always" responses anchored at one end and the "Never" or "Rarely/Never" responses anchored at the other, and proportionate spacing in-between (ie, a 4-category scale was recoded as 0, 33, 66, 100). Variables were then transformed to *z* scores, with higher scores indicating greater symptom burden.

Behavior Assessment

The Strengths and Difficulties Questionnaire (SDQ),[20] a widely used behavioral screen, was completed by mothers when children were ∼4 and 7 years old. The 25-item SDQ has 5 scales: inattention/hyperactivity, emotional symptoms (anxiety and depression), peer problems, conduct problems (aggressiveness and rule breaking), and a pro-social scale (sharing, helpfulness, and so forth). A total difficulties (range = 0–40) score is generated by summing all but the latter scale because the absence of pro-social behavior is conceptually different from the

presence of psychological difficulties. Higher scores denote more problems. Missing data were prorated according to SDQ instructions.[21] The SDQ scores were dichotomized at the upper 10% based on psychometric testing,[22] ALSPAC,[23,24] and other UK cohort studies.[25]

Covariate Assessment

Initial covariate selection was guided by previous ALSPAC studies of SDQ outcomes,[24,26–32] and non-ALSPAC studies of sleep problem effects on SDQ outcomes.[33,34] Based on this literature review, and exploratory analyses, 15 potential confounders were incorporated into analyses.

SES was measured by paternal employment (manual versus professional), maternal education (higher versus lower), and housing inadequacy (if either >1 person/room or homeless). Family adversity was measured by an 18-item index of stressors (eg, maternal psychopathology, crime, financial insecurity) used in other ALSPAC analyses[35]; higher values signify more adversity. Intrauterine exposures of maternal smoking or alcohol use in the first trimester (yes/no) and fish intake at 32 weeks' gestation (servings/week) were assessed, as was whether the child was ever breastfed and the mother's age at delivery. Household variables included family size (0, 1, or ≥2 children in household at 6-month interview) and the Home Observation for Measurement of the Environment (HOME) Inventory[36] to assess the quality of parenting and home environment. Child demographics included race (white versus other) and gender, low birth weight (<2500 g) and prematurity (<37 weeks). Analyses of the subsample with BMI z score data are in Supplemental Tables.

To predict behavior at 4 years, "Early" clusters were derived from the 11 049 participants in the base sample with SDB data for ≥2 of the first 4 time points (ie, 6, 18, 30, and/or 42 months). To predict behavior at 7 years, "Later" clusters were derived for the 11 235 participants in the base sample with SDB data for ≥2 of the first 6 time points (ie, 6, 18, 30, 42, 57, and/or 69 months). Through a process described in detail elsewhere,[37] we produced 5 conceptually and statistically distinct Early clusters (6–42 months), and 5 comparable Later clusters (6–69 months) that were extensions of Early clusters.

STATISTICAL ANALYSIS

For SDQ scores at 4 and 7 years, we calculated the mean (SD) and proportions above and below the 10% cutoff for the base sample, and their associations with putative covariates either from χ^2 test or analysis of variance. We describe the association between SDQ mean (SD) total scores at 4 and 7 years and the Early and Later clusters, by analysis of variance. Only participants not missing SDQ data are included in analyses of behavioral outcomes.

Multivariate logistic regression analyses examined adjusted and unadjusted relationships between clusters and SDQ total and subscales at 4 and 7 years. To streamline presentation, unadjusted analyses are in the Supplemental Tables. Initial models included all putative covariates. Only those variables that were significant ($P \leq .05$) were retained in multivariate models. Odds ratios (ORs) and 95% confidence intervals (95% CIs) represent the odds of being in the top 10% versus the remaining 90% of SDQ scores. To address multicollinearity, variance inflation factors were derived to assess the effects of individual independent variables on variance. A conservative variance inflation factor threshold of 10 was used in model testing.[38] Analyses were conducted by using SAS version 9.1 (SAS Institute, Inc, Cary, NC).

RESULTS

Data Completion and Attrition

SDB longitudinal data were relatively complete. Early cluster analyses of the 7996 participants with SDQ 7-year outcomes included 7716 (96%) with SDB data for ≥3/4 time points. Likewise, Later cluster analyses (SDQ 7-year data) for 8064 participants, included 7383 (92%) with SDB data for ≥5/6 time points. Missing SDQ or SDB data were significantly associated with nonwhite race, prematurity, low birth weight, manual (versus professional) paternal employment, lower (versus higher) maternal educational status, housing inadequacy, not being breastfed, and higher levels of wheezing (not shown).

Sample Characteristics and Association With Top 10% of SDQ Total Scores

Characteristics of the base sample and associations with behavioral outcomes are shown in Table 1. Children in the upper 10% of SDQ scores had significantly more adverse characteristics (eg, higher maternal smoking, older delivery age, lower maternal education, higher Family Adversity Index scores, lower HOME scores, housing inadequate, prematurity, low birth weight, and being male) than the remaining 90% at 4 and 7 years, but there were no differences by race, maternal alcohol intake during pregnancy, or tonsils removal.

Cluster Description and Association With Sample Characteristics

Cluster analyses yielded 1 asymptomatic ("Normals," 45% of sample) and 4 symptomatic (55% of sample) trajectories. Early clusters, shown in Fig 1, can be summarized as (1) symptoms "Peak @ 6" and then abate, (2) symptoms "Peak @ 18" months and then abate, (3)

TABLE 1 Demographics for Total Sample and by SDQ Scores at 4 and 7 Years

	Total Sample[a] n = 13 467	SDQ Total Score, 4 y		SDQ Total Score, 7 y	
		Top 10% n = 1218	Lower 90% n = 7922	Top 10% n = 889	Lower 90% n = 7055
Maternal					
Smoked during pregnancy, any	25.0%	30.5%[b]	20.0%	30.9%[b]	18.7%
Alcohol during pregnancy, any	54.6%	55.6%	55.5%	58.3%	55.6%
Fish intake during pregnancy, mean (SD)	1.87 (1.75)	1.94 (1.76)	1.88 (1.75)	1.96 (1.86)	1.88 (1.73)
Age at delivery, mean years (SD)	27.96 (4.98)	27.47 (4.80)[b]	28.86 (4.65)	28.08 (4.76)[b]	29.02 (4.57)
Breastfed this child, ever	75.5%	73.0%[b]	78.6%	76.5%	79.3%
Child					
Gender, male	51.5%	55.1%[c]	51.1%	59.5%[b]	50.6%
Race, white	97.4%	98.1%	98.4%	98.1%	98.3%
Premature, <37 wk	4.9%	5.6%[c]	4.3%	6.1%[c]	4.1%
Low birth weight, <2500 g	4.3%	4.7%[c]	3.5%	5.0%[b]	3.3%
Adenoids removed, ever	7.4%	—	—	9.4%[b]	6.2%
Tonsils removed, ever	4.5%	—	—	5.0%	3.8%
BMI z score at 42 mo	0.27 (1.06)	0.24 (1.10)	0.27 (1.04)	0.29 (1.12)	0.26 (1.03)
Socioeconomic and family					
Maternal education,[d] lower (%)	64.6%	71.5%[c]	58.9%	69.0%[b]	57.8%
Paternal employment, manual (%)	44.0%	52.4%[b]	39.2%	48.5%[b]	39.0%
Housing, inadequate, (%)	12.3%	18.9%[b]	11.6%	18.3%[b]	10.9%
Family Adversity Index, mean (range: 0–18)	1.77 (1.98)	2.65 (2.28)[b]	1.73 (1.87)	2.87 (2.39)[b]	1.70 (1.85)
HOME score, mean (range: 0–8)	5.74 (1.66)	5.60 (1.77)[b]	5.80 (1.62)	5.48 (1.74)[b]	5.84 (1.61)
Parity, ≥1	55.1%	52.3%	54.3%	50.8%[c]	54.5%

P values are calculated from χ^2 test for categorical variables and analysis of variance for continuous variables. HOME, Home Observation for Measurement of the Environment.

[a] These 13 467 constitute the base sample used to derive the clusters and SDQ outcomes.

[b] $P < .01$ for difference between top 10% versus lower 90%.

[c] $P < .05$ for difference between top 10% versus lower 90%.

[d] "Lower defined as "0" level education or less (equivalent to school-leaving certificate at 16 in the UK), from 5 original groupings.

symptoms peak at 30 months and then persist ("Worst Case"), (4) symptoms emerge at 42 months and then persist ("Late Symptom") and (5) "Normals" who are asymptomatic throughout. Snoring levels were nearly double those of apnea or mouth breathing in Worst Case and Late Symptom versus comparable symptom levels in other clusters. Whether assessed as a continuous or dichotomous (10% vs 90%) variable, SDQ total scores differed significantly across the 4 symptomatic clusters, and in combined symptomatic clusters versus Normals (Table 2). Early clusters' descriptive characteristics are shown in Supplemental Table 6.

Five comparable Later clusters are illustrated in Fig 2. Patterns are similar to the Early clusters, except that in this Late Symptom cluster, snoring and mouth breathing peak together at lower levels at 57 months with no marked apnea, and the Peak @ 6 apnea levels are nearly double those of the Early clusters.

SDQ Total Score

The SDB clusters significantly predict SDQ total scores at 4 and 7 years (Table 3). Early cluster effects are 20% to 70% in multivariate analyses. The strongest and most persistent is for Worst Case, with comparable outcomes at 4 (OR = 1.49, 95% CI = 1.11–1.99) and 7 years (OR = 1.72, 95% CI = 1.31–2.25). Later clusters' effects are 40% to 100% in multivariate analyses, including a ≈40% effect for Peak @ 6 and ≈50% effect for Peak @ 18. Membership in any symptomatic cluster is associated with being in the upper 10% of total SDQ scores (versus Normals), an effect that increases slightly from 4 (OR = 1.33, 95% CI = 1.14–1.56) to 7 years (OR = 1.52, 95% CI = 1.24–1.85: Later clusters). Multivariate effects are strongly attenuated from unadjusted effects (Supplemental Table 7).

SDB effects exceeded those of maternal smoking, maternal education, and paternal employment in multivariate analyses (Table 3). Race, prematurity, low birth weight, maternal fish intake, or maternal age were not significant in any multivariate analyses, total or subscale (not shown). Only male gender and not being the second or later-born child had greater adverse effects. Greater family adversity was associated with poorer behavioral outcomes, whereas higher home environment scores were associated with improved outcomes. Gender-cluster interactions were not significant for any total or subscore analyses.

SDQ Subscores

In adjusted analyses, nearly every cluster-subscale association was significant (Table 4), with effects of 20% to 100% (see Supplemental Table 7 for unadjusted effects.) Details are in the following paragraphs.

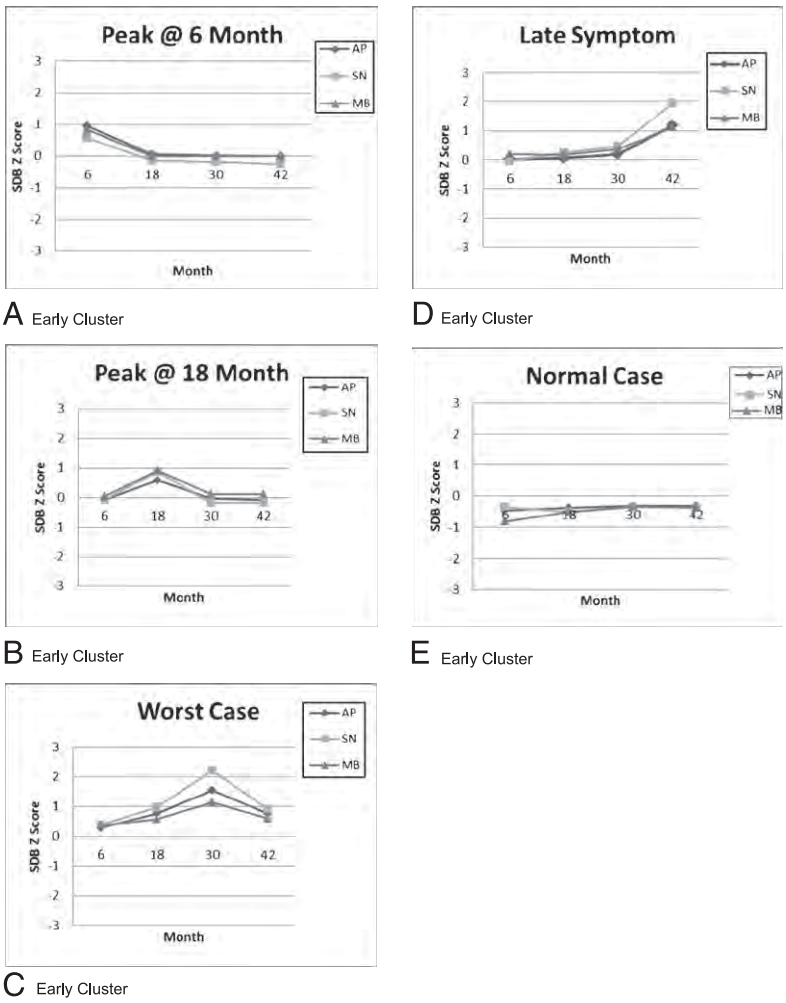


FIGURE 1
Early clusters.

Pro-social

Peak @ 6 was associated with ≈30% greater odds of being in the lowest decile across outcomes at 4 and 7 years. All of the remaining associations were not significant.

Hyperactivity

With 1 exception, all effects (≈20%–100%) were significant, and increased from 4 to 7 years. Furthermore, Early cluster effects at 4 years for Worst Case and Late Symptom equaled or increased at 7 years.

Emotional

With 1 exception at 4 years, all effects were significant (range ≈20%–65%), and most increased from 4 to 7 years. Late Symptom had the strongest effect at 4 and 7 years based on Early cluster models, with effects persisting to 7 years in Later cluster models.

Conduct

With 1 exception, all effects were significant (range ≈30%–70%). Both Worst Case and Peak@18 effects increased from 4 to 7 years, whereas Late Symptom and Peak @ 6 effects attenuated over that time.

Peer

Half of the cluster-subscale associations were significant, and SDB effects were more modest (range ≈30%–50%) and stable over time, compared with the other subscales. Effects were strongest for Worst Case.

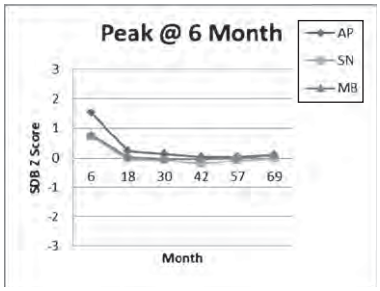
DISCUSSION

We examined the effects of snoring, apnea, and mouth-breathing patterns (clusters) on behavior, from infancy through 7 years in more than 11 000 children. By 4 years, children in the symptomatic clusters were ≈20% to 60% more likely to exhibit behavioral difficulties consistent with a clinical diagnosis; by 7 years, they were ≈40% to 100% more likely. These effects, in a population-based cohort that controlled

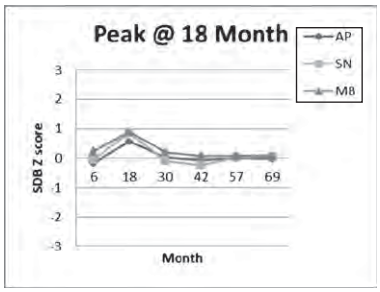
TABLE 2 Association Between Early Clusters (n = 11c049) and SDQ outcome

	Peak at 6 *n* = 2277 (20.6%) (1)	Peak at 18 *n* = 1881 (17.0%) (2)	Worst Case *n* = 878 (8.0%) (3)	Late Symptom *n* = 1023 (9.3%) (4)	Normals *n* = 4990 (45.2%) (5)
Outcome SDQ					
SDQ top 10% at 4 y[a]	13.7%	15.0%	18.8%	19.5%	10.1%
SDQ top 10% at 7 y[a]	12.1%	12.9%	17.7%	14.2%	8.4%
SDQ continuous at 4 y, mean (SD)[a]	14.59 (3.59)	14.66 (3.70)	15.32 (3.96)	15.35 (3.91)	13.88 (3.44)
SDQ continuous at 7 y, mean (SD)[a]	8.13 (4.98)	7.94 (4.93)	8.83 (5.31)	8.36 (4.91)	6.76 (4.49)
SDQ top 10% at 4 y[a]			15.74%		10.07%
SDQ top 10% at 7 y[a]			13.46%		8.41%
SDQ continuous at 4 y, mean (SD)[a]			14.84 (3.74)		13.88 (3.44)
SDQ continuous at 7 y, mean (SD)[a]			8.20 (5.01)		6.76 (4.49)

P values are calculated from χ^2 test for categorical variables and analysis of variance for continuous variables.
[a] $P < .01$ for difference between top 10% versus lower 90%.

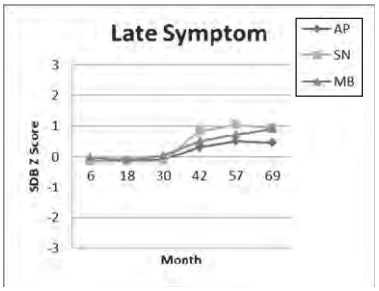


A Later Cluster

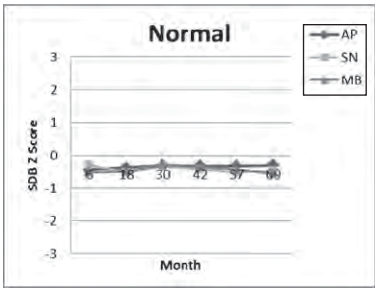


B Later Cluster

C Later Cluster



D Later Cluster



E Later Cluster

FIGURE 2
Later clusters.

for 15 putative confounders, exceeded those of any measured prenatal (ie, maternal age, smoking or alcohol use), gestational age, birth weight, breastfeeding, SES, family adversity, or home environment exposure. Furthermore, SDB effects at 4 years were as predictive of behavioral difficulties at 7 years. The worst symptoms were associated with the worst behavioral outcomes. Among the neuroehavioral domains assessed, hyperactivity was most affected.

Compared with previous parent-reported effects of SDB on Later behavior, our findings are conservative. In a study of ≈1000 third graders, snoring at baseline was associated with 2- to 10-fold increases in SDQ-assessed hyperactivity, and emotional, conduct, and peer difficulties at 1-year follow-up in age- and gender-adjusted analyses.[39] A pediatric clinic sample of 229 2- to 13-year-olds found that baseline SDB symptoms predicted fourfold increases in hyperactive behaviors at 4-year follow-up, after adjustment for age, gender, and baseline hyperactivity.[40] These studies differed from ours, with smaller, less representative samples, lack of data from the earliest years, use of other (non-SDQ) behavioral measures, and limited control for confounders. Alternatively, several cross-sectional studies that used different operational definitions of SDB and SDQ outcomes found no effects. One, a large nationally representative cross-sectional sample of ≈5000 Australian 4- to 5-year-olds, found that neither SDQ total, nor the Hyperactivity, Peer, or Emotional scale (actual) scores were greater among children with "snoring and/or breathing difficulties" during sleep ≥4 times per week.[33] Likewise, among 635 6- to 8-year-olds, snoring ≥1 time per week in the past 6 months was not associated with high (upper 10th percentile) SDQ scores.[34]

This is the first study to assess SDB as a trajectory of combined symptoms, across a key period of SDB development from 6 months to 81 months, in a large sample. Previous studies had smaller samples that were often cross-sectional, or had shorter follow-up. Many were not population-based, involved school-age children only, or did not adjust for as wide a range of confounders.[8,41] The potential impact of confounders is illustrated by the fact that several covariates independently associated with the clusters were not significant in multivariate analyses, and most unadjusted effects of SDB attenuated in controlled analyses. Although residual confounding is possible, covariates were selected based on previous ALSPAC analyses of SDQ outcomes, and non-ALSPAC studies of sleep problem effects on SDQ outcomes.

The current study has several limitations. First, SDB data were derived from parent report, rather than objective testing; however, the symptom-items used reflect widely accepted and well-validated SDB risk factors. Second, because parents may hear snoring from another room, they may be more likely to report it than either apnea or mouth breathing. Third, observed apnea during infancy is difficult to distinguish from the more common central apnea; however, our finding that observed apnea in infancy tracked with more clearly obstructive symptoms through 7 years suggests that observed apneas of infancy may not always have

TABLE 3 Cluster Effects on SDQ Total Scores at 4 and 7 Years

	Early Cluster Models		Later Cluster Models
Top 10% vs Lower 90% OR (95% CI)	4 y[a] n = 9007	7 y[a,b] n = 7996	7 y[a,b] n = 8064
Adjusted without BMI[c]			
Peak at 6 (1)	1.23 (1.00–1.51)[e]	1.25 (1.02–1.53)[e]	1.39 (1.11–1.74)[d]
Peak at 18 mo (2)	1.26 (1.01–1.57)[e]	1.39 (1.12–1.72)[d]	1.50 (1.21–1.86)[d]
Worst Case (3)	1.49 (1.11–1.99)[d]	1.72 (1.31–2.25)[d]	2.00 (1.53–2.62)[d]
Late symptom (4)	1.56 (1.19–2.03)[d]	1.46 (1.12–1.91)[d]	1.68 (1.35–2.10)[d]
Smoking during pregnancy	N.S.	1.21 (1.01–1.45)[e]	NS
Gender, male	1.18 (1.01–1.37)[e]	1.50 (1.29–1.76)[d]	NS
Maternal education, lower	1.40 (1.18–1.66)[d]	1.31 (1.11–1.55)[d]	1.33 (1.13–1.57)[d]
Paternal employment, manual	1.28 (1.08–1.51)[d]	NS	NS
Family Adversity Index	1.20 (1.15–1.24)[d]	1.25 (1.20–1.30)[d]	1.25 (1.21–1.30)[d]
HOME score	NS	0.91 (0.87–0.95)[d]	0.91 (0.87–0.96)[d]
Parity 1 vs 0 ≥2 vs 0	1.00 (0.85–1.19) 0.66 (0.53–0.83)[d]	0.72 (0.61–0.86)[d] 0.58 (0.46–0.72)[d]	0.72 (0.61–0.86)[d] 0.59 (0.47–0.74)[d]
Clusters 1, 2, 3 and 4 vs Normals (5)	1.33 (1.14–1.56)[d]	1.24 (1.02–1.51)[e]	1.52 (1.24–1.85)[d]

HOME, Home Observation for Measurement of the Environment; NS, not significant.

[a] Adjusted for fish intake, Family Adversity Index, mother and home score, smoke during pregnancy, alcohol during pregnancy, race, breastfeeding ever, housing inadequacy, parity, gestation age, paternal social, maternal education, birth weight, maternal age, gender.

[b] Additional adjusted for tonsils or adenoids removed.

[c] Covariates shown are only those that were significant ($P < .05$) in reduced models with each of the 4 symptomatic models incorporated as a separate variable (versus combined clusters 1, 2, 3, and 4).

[d] $P < .01$.

[e] $P < .05$.

TABLE 4 Adjusted Clusters Effects on SDQ Subscales at 4 and 7 Years

Top 10% vs Lower 90% OR (95% CI)	Early Cluster Models		Later Cluster Models
	4 y[a]	7 y[b]	7 y[b]
Pro-social			
Peak at 6	1.28 (1.05–1.55)[c]	1.26 (1.02–1.54)[c]	1.29 (1.04–1.60)[d]
Peak at 18 mo	1.18 (0.95–1.46)	1.25 (0.99–1.56)	1.21 (0.99–1.49)
Worst Case	1.14 (0.85–1.52)	1.24 (0.91–1.68)	1.05 (0.78–1.41)
Late Symptom	1.01 (0.76–1.34)	1.01 (0.74–1.37)	0.91 (0.71–1.16)
Hyperactivity			
Peak at 6	1.19 (1.00–1.42) [d]	1.50 (1.23–1.83) [c]	148 (1.12–1.97) [d]
Peak at 18 mo	1.12 (0.92–1.35)	1.40 (1.13–1.74) [c]	1.51 (1.15–1.98) [c]
Worst Case	1.56 (1.23–1.98) [c]	1.98 (1.52–2.58) [c]	1.85 (1.30–2.63) [c]
Late Symptom	1.51 (1.21–1.89) [c]	1.57 (1.20–2.05) [c]	1.88 (1.42–2.49) [c]
Emotional			
Peak at 6	1.20 (0.99–1.44)	1.38 (1.15–1.66) [c]	1.45 (1.18–1.78) [c]
Peak at 18 mo	1.24 (1.02–1.52) [d]	1.32 (1.09–1.61) [c]	1.47 (1.21–1.78) [c]
Worst Case	1.47 (1.14–1.89) [c]	1.41 (1.08–1.85) ‡	1.58 (1.21–2.07) [c]
Late Symptom	1.50 (1.19–1.91) [c]	1.62 (1.27–2.06) [c]	1.65 (1.35–2.02) [c]
Conduct			
Peak at 6	1.47 (1.24–1.73) [c]	1.31 (1.06–1.63)[d]	1.29 (1.01–1.65) [d]
Peak at 18 mo	1.26 (1.04–1.52) [d]	1.32 (1.05–1.67) [d]	1.42 (1.13–1.78) [c]
Worst Case	1.52 (1.20–1.92) [c]	1.53 (1.13–2.08) [c]	1.60 (1.18–2.16) [c]
Late Symptom	1.68 (1.34–2.09) [c]	1.13 (0.83–1.54)	1.40 (1.09–1.79) [c]
Peer			
Peak at 6	1.27 (1.04–1.56)[d]	1.14 (0.94–1.38)	1.03 (0.82–1.29)
Peak at 18 mo	1.29 (1.04–1.60) [d]	1.18 (0.96–1.46)	1.22 (0.99–1.49) [d]
Worst Case	1.33 (1.01–1.77) [d]	1.48 (1.13–1.93) [c]	1.37 (1.04–1.80) [d]
Late Symptom	1.21 (0.92–1.59)	1.19 (0.91–1.55)	1.17 (0.93–1.46)

[a] Adjusted for fish intake, Family Adversity Index, mother and home score, smoke during pregnancy, alcohol during pregnancy, race, breastfeeding ever, housing inadequacy, parity, gestation age, paternal social, maternal education, birth weight, maternal age, gender.

[b] Additional adjusted for tonsils or adenoids removed.

[c] $P < .01$.

[d] $P < .05$.

a central etiology. Fourth, missing SDB and SDQ data were associated with identified SDB risk factors (eg, maternal smoking, lower SES). Although biases that involve selective dropout may alter prevalence estimates, other ALSPAC analyses found only marginal effects on regression models predicting behavioral outcomes.[42] This is likely the case in our study, in which such biases would render our findings more conservative.

These findings, from the largest-ever cohort study of SDB exposure and neurobehavioral morbidity, provide epidemiologic evidence that early childhood SDB effects may only become apparent years later. The most significant long-term effects occurred in children with the greatest overall levels of snoring, apnea, and mouth breathing throughout, peaking at 30 months. Even very early symptom peaks at 6 and 18 months are associated with ≈40% and 50%, respectively, increased behavioral morbidity at 7 years of age. This may be because of the increased vulnerability to SDB effects during this early critical period of brain development,[43] when there is the greatest need for sleep.[44]

SDB is relatively common in childhood. In previous analyses of this cohort, the prevalence of habitual snoring ranged from 10% to 21%, from 6 months to 81 months.[45] The potential clinical and educational implications of untreated SDB, therefore, are notable. As an example, we found significant (nearly twofold), and sustained effects on hyperactivity. In national survey data, children with attention-deficit/hyperactivity disorder had increased adjusted risks of comorbid learning disability (eightfold), anxiety (eightfold), and low social competence (threefold).[46] Further, 40% to 80% of the nation's 3 million 6- to 21-year-olds who receive special education for a developmental disability or delay also have attention-deficit/hyperactivity.[47]

CONCLUSIONS

These population-based data found a strong and persistent association between SDB symptoms and behavior. This has clinical implications for screening and treatment. A 2009 consensus statement by UK pediatricians and pediatric specialists noted that "the natural history of SDB, where a child changes from normality to abnormality, and where the risks of developing complications of the condition outweigh the risks of the surgical intervention, has not been established."[48] Although data from multicenter, randomized controlled trials, such as the current National Institutes of Health–funded Childhood Adenotonsillectomy study, will provide some evidence of cause-and-effect relationships, our findings provide further epidemiologic evidence to support attention to SDB symptoms beginning as early as the first year of life.

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Sleep-Disordered Breathing in a Population-Based Cohort: Behavioral Outcomes at 4 and 7 Years

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Three-dimensional assessment of pharyngeal airway in nasal- and mouth-breathing children

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ABSTRACT

Objectives: The aim of this study was to assess the pharyngeal airway space (PAS) in nasal and mouth-breathing children using cone beam computed tomography (CBCT).
Methods: Volume, area, minimum axial area and linear measurements (PAS-NL, PAS-UP, PAS-OccL, PAS-UT, PAS-Bgo, PAS-ML, PAS-TP) of the pharyngeal airway of 50 children (mean age 9.16 years) were obtained from the CBCT images. The means and standard deviations were compared according to sexes (28 male and 22 female) and breathers patterns (25 nasal breathers and 25 mouth breathers).
Results: There were no statistically significant differences ($p > 0.05$) between all variables when compared by sexes. Comparisons between nasal and mouth breathers showed significant differences only in two linear measurements: PAS-OccL ($p < 0.001$) and PAS-UP ($P < 0.05$). Airway volume ($p < 0.001$), area ($p < 0.001$) and minimum axial area ($p < 0.01$) had significant differences between the groups.
Conclusions: The CBCT evaluation showed that pharyngeal airway dimensions were significantly greater in nasal-breathers than in mouth-breathers.

1. Introduction

Heredity has an important function in determining size and shape of the face, however, environmental factors such as breathing habit is essential to the harmonic and balanced development of the craniofacial complex. In this context, mouth breathing habit has been associated with some dentofacial deformities. According to Moss' functional matrix theory [1], nasal breathing allows proper growth and development of the craniofacial complex interacting with other functions such as masticatory and swallow. On the other hand, when nasal obstruction leads to mouth breathing habit, this could result not only in changes of the tongue and lip positions, but also causes mouth opening posture, downward and backward rotation of mandible, long face, constricted maxillary arch, incompetent lip seal, flat noses, narrow nasal base [1–5]. Predisposing factors of nasal obstruction can include adenoid and tonsil hypertrophy, polyps, allergies, infections, and nasal deformities.

Naso-breathing function and its relation to craniofacial growth are of great interest today, not only because the basic biological relationship of form and function but also because of the great practical concern to pediatricians, otorhinolaryngologists, allergists, speech therapists, orthodontists, and other members of health-care community as well [3].

Traditionally, the airway space has been evaluated by the use of cephalometric radiographs, however, this method results in superimposition of all bilateral structures of the craniofacial complex. Nowadays with the advent of Cone Beam Computed Tomography (CBCT), the airway evaluation became more accurate and reliable, generating information more comprehensive than the 2D radiographs [6,7].

Accordingly, the purpose of this study was to carry out a CBCT evaluation of the pharyngeal airway space (PAS) in nasal-breathing and mouth-breathing children.

2. Materials and methods

This study was revised and approved by the Institute of Collective Health Studies Research Ethics Committee of Rio de Janeiro Federal University. Free informed consent was signed by all the responsible of the patients before they took part in the clinical procedures.

A total of 50 healthy children ranging 8–10 years old (mean age of 9.16 years and standard deviation of 0.64), were selected from a group of 68 children who attended the Orthodontics clinic of the Federal University of Rio de Janeiro. The orthodontic diagnosis of

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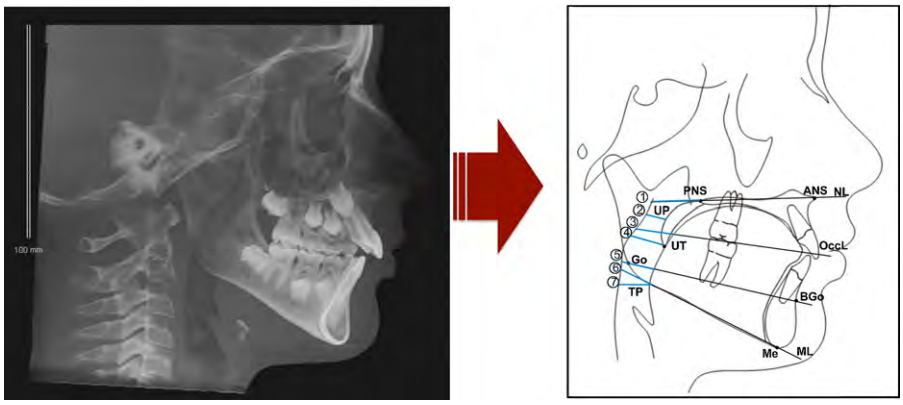

Fig. 1. 2D-lateral cephalometric image with the use of a ray-sum technique (*Dolphin Imaging® software, version 11.0*/Orientation function) and linear distances: 1, PAS-NL; 2, PAS-UP; 3, PAS-OccL; 4, PAS-UT; 5, PAS-BGo; 6, PAS-ML; 7, PAS-TP.

the respiratory function was realized through clinical evaluation of the habitual posture of the lips, size and shape of the nostrils, control reflex muscle alares and Glatzel mirror test [8]. In addition, all the patients were evaluated in the Otorhinolaryngology sector of the University Hospital Clementino Fraga Filho. All the rhinoscopy examination were conducted by the same otorhinolaringologist and the respiratory pattern of the subjects was confirmed according to the degree of adenoid hypertrophy. Patients with more than 60% airway obstruction due to adenoid hypertrophy were considered mouth breathers.

Twenty-five subjects were diagnostic as nasal breathers (mean age of 8.94 years) and 25 as mouth breathers (mean age of 9.27 years). Eighteen patients that had symptoms of upper respiratory infection at the time, pharyngeal pathology or a history of adenoidectomy or tonsillectomy were excluded.

All CBCT scans were taken with the same cone beam machine (i-CAT, Imaging Sciences International, Hatfield, PA, USA), according to a standard protocol (120 kV, 5 mA, 13 × 17 cm FOV, 0.4 mm voxel and scan time of 20 s) used for orthodontic records in this University.

Because the volume of the airway is influenced by head posture [9], all patients seated in the upright position with Frankfort Horizontal (FH) plane paralleled to the floor, maximum intercuspation and lips and tongue in position of filling the oral cavity. The patients were instructed not to swallow and not to move the head and tongue during the scanning.

Data were imported in DICOM (Digital Imaging and Communications in Medicine) format and handled by Dolphin Imaging® software, version 11.0 (Dolphin Imaging, Chatsworth, California, USA). Once the image head 3D-reconstructions of each patient were oriented [10,11], the airway analysis tool in Dolphin 3D Imaging software was used to define the superior [12,13] and inferior [14,15] border of the airway. The update volume was generated and the airway volume, airway area and minimum axial area were obtained (Fig. 1).

Furthermore, the software was used to create a 2D lateral cephalometric image (ray-sum technique). These lateral cephalometric images were printed by HP colorjet (HP Color LaserJet 2600n, Hewlett-Packard Company, Palo Alto, Califórnia, USA) and seven linear measurements (PAS-NL, PAS-UP, PAS-OccL, PAS-UT, PAS-BGo, PAS-ML, PAS-TP) were realized in different levels of the PAS (Fig. 2, Table 1) as previously described by Pracharktam et al. [16] and Hochban and Brandenburg [17]. The linear measurements were hand-traced and calculated by the same author.

The intra-class correlation test (ICC) was applied in order to assess the intraexaminer concordance (95% confidence interval) for all variables (airway volume, airway area, minimum axial area and linears measurements). Sixteen CBCT were randomly selected and all measurements were repeated within a 1-week interval. Descriptive statistical analysis (mean and standard deviation) was carried out for all variables. Differences between sexes were tested with the independent *t*-test. Kolmogorov–Smirnov's test confirmed normal sample distribution and independent *t* test was used to compare the airway volume, airway area, minimum axial area and the linear distance between the nasal and mouth breathers group. $p < 0.05$ was considered statistically significant.

All statistical analyses were performed by using SPSS software (18.0 version).

3. Results

The orthodontic diagnostic of the respiratory function and rhinoscopy examination became possible to classify the patients according to the respiratory pattern (25 nasal breathers and 25 mouth breathers). Some authors emphasize that rhinoscopy examination should always be performed because it allows the visualization of the entire nasopharynx, providing reliable data the relationship between content and the continent [18].

Concordance index was greater than 0.98 for all variables analyzed, except for minimum axial area (0.91) and PAS-UP (0.92).

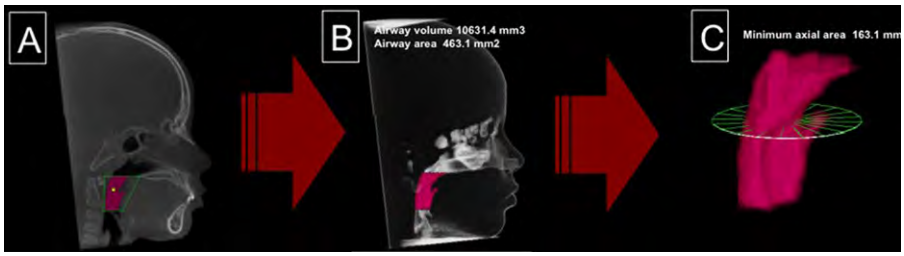

Fig. 2. (A) Pink area denotes defined airway portion of interest; (B) obtainment of airway volume and airway area; (C) obtainment of minimum axial area (*Dolphin Imaging® software, version 11.0*/Orientation function). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Table 1
Linear measurements (mm) of the pharyngeal airway space.

PAS-NL	Pharyngeal airway space on nasal line
PAS-UP	Minimal pharyngeal airway space between the uvula and the posterior pharyngeal wall
PAS-OccL	Pharyngeal airway space on occlusal line
PAS-UT	Minimal pharyngeal airway space between the uvula tip and the posterior pharyngeal wall
PAS-BGo	Pharyngeal airway space on B-Go line
PAS-ML	Pharyngeal airway space on mandibular line
PAS-TP	Minimal pharyngeal airway space between the back of the tongue and the posterior pharyngeal wall

Table 2
Comparison between sexes of the descriptive analysis (mean and standard deviation) of linear measurements, airway volume, airway area and minimum axial area.

Variables	Male ($n=28$)		Female ($n=22$)		p
	Mean	*SD*	Mean	*SD*	
PAS-NL (mm)	11.48	5.70	14.20	5.81	0.172
PAS-UP (mm)	6.39	2.67	6.46	2.18	0.928
PAS-OccL (mm)	8.34	3.59	8.93	2.21	0.547
PAS-UT (mm)	8.43	2.84	10.12	2.33	0.074
PAS-Bgo (mm)	9.53	2.85	11.13	2.84	0.106
PAS-ML (mm)	9.62	2.52	11.46	4.09	0.105
PAS-TP (mm)	8.81	2.95	9.62	3.17	0.447
Airway volume (mm^3)	6898.07	2646.24	6775.02	1399.93	0.855
Airway area (mm^2)	383.48	108.26	405.49	38.04	0.388
Minimum axial area (mm^2)	106.01	51.45	119.44	45.89	0.422

In our study, there was no difference in the airway measurements between sexes. Initially means and standard deviations for all variables were compared by sex, which showed (Table 2) no statistical significant differences ($p > 0.05$) and, therefore, the groups were divided according to the respiratory pattern (nasal and mouth) for subsequent analysis.

Table 3 showed that among the linear measurements, only the PAS-OccL and PAS-UP variables were statistically significant ($p < 0.05$) between nasal and mouth breathers. The others variables, PAS-NL, PAS-UT, PAS-BGo, PAS-ML and PAS-TP, showed no statistically significant differences ($p > 0.05$). The airway volume, airway area and minimum axial area showed statistically significant differences ($p < 0.05$) between the groups. Volumetric size variability was seen in our children sample. This result shows

Table 3
Comparison between nasal and mouth breathers of the descriptive analysis (mean and standard deviation) of linear measurements, airway volume, airway area and minimum axial area.

Variable	Nasal breathers ($n=25$)		Mouth breathers ($n=25$)		p
	Mean	*SD*	Mean	*SD*	
PAS-NL (mm)	14.49	6.20	10.93	5.05	0.067
PAS-UP (mm)	7.90	2.39	5.09	1.62	0.000***
PAS-OccL (mm)	9.84	3.48	7.46	2.18	0.018*
PAS-UT (mm)	10.01	2.58	8.35	2.71	0.075
PAS-Bgo (mm)	10.61	2.76	9.83	3.07	0.431
PAS-ML (mm)	11.25	3.19	9.62	3.37	0.145
PAS-TP (mm)	10.07	3.09	8.35	2.81	0.095
Airway volume (mm^3)	8171.31	1710.28	5594,70	1878.76	0.000***
Airway area (mm^2)	446.35	57.31	341.30	79.1	0.000***
Minimum axial area (mm^2)	137.42	44.91	86.85	39.97	0.001**

* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

that the assessment by 3D reconstruction were more sensitive than linear distances to detect differences between the two groups.

Fig. 3 shows the comparison of the airway volume between two subjects, a nasal breather and a mouth breather. In this specific case, the volume shown in the nasal breather was almost twice greater than in the mouth breather.

4. Discussion

It is known that breathing pattern is of great importance in orthodontic diagnosis and treatment planning, as well as in the stability of the treatment results. When breathing function undergoes throw significant changes, it may have negative impact on the stages of facial growth, and also in the occlusion development [1,17,19–21]. Despite there are a lot of studies on the different patterns of breathing and its influence on pharyngeal airway space and development, the majority used only two-dimensional analysis, evaluating the lengths and areas. Kluemper et al. [22] suggested that cephalometric analyses are poor indicators of nasal impairment and should not be used as clinical decision-making.

CBCT is widely accepted diagnostic tool for this purpose. Differently from the radiographic methods which structures are projected onto one-dimensional plane through X-ray, CBCT scan provides cross-sectional images while structural relationships can be investigated through 2D scrolling or 3D volume rendering [23,24]. In our study, the CBCT allowed not only the actual view of

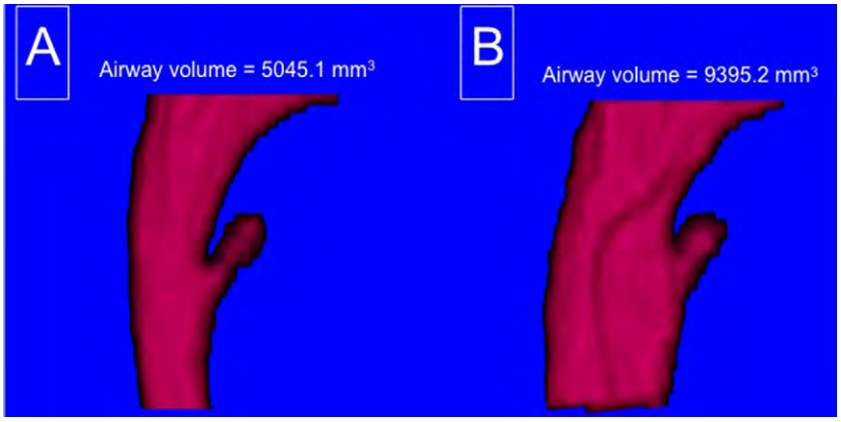

Fig. 3. Digital image reconstructed and measured by means of *Dolphin Imaging software*, demonstrating the differences in volume between a mouth (A) and nasal (B) breather.

the airways, as well as measuring of the airway volume, airway area and minimum axial area.

In Table 2, no statistically significant differences between sexes ($p > 0.05$) were found. Juliano et al. [25] evaluating 27 children and also did not find difference between mouth and nasal breathers regarding sex ratios. Sheng et al. [26] also showed no statistically significant differences ($p > 0.05$) between sexes in four linear measures localized in PAS between the hard palate and the epiglottis tip. They evaluated 239 Taiwanese subjects during mixed dentition stage. In other study, Martin et al. [27] assessed nasopharyngeal soft-tissue patterns in patients with ideal occlusion and showed no statistically significant differences ($p > 0.05$) for measurements similar to PAS-UP and PAS-UT.

Table 3 shows no statistically significant ($p > 0.05$) differences between the two breathing patterns in the linear measurements variables, except for PAS-OccL ($p = 0.018$) and PAS-UP ($p = 0.000$). However, as only two of the seven linear variables were statistically significant, we suspect that these could have been influenced by the adenoids size, which is located in this region. Despite the patients who had adenoid and tonsillitis hypertrophy had been previously excluded, it is known that the absence of lip seal and lower tongue position, often found in the mouth breathers, interfere the airway permeability [28] and could cause lymphatic-tissue increase of the pharynx and consequently change in such measures.

Juliano et al. [23] reported statistically significant differences ($p < 0.05$) between mouth and nasal breathers in the variable SPAS (similar PAS-UP in our study). This study showed that mouth-breathing children had more oxygen desaturation during sleep. Furthermore, the mouth breathers showed reduced linear measurement of the upper airway space with narrowed area at the level of the nasopharynx, hypopharynx, or both. In the other hand, Gouveia et al. [29] evaluating the relationship between patients with different breathing patterns found no statistically significant differences ($p > 0.05$) in two linear measurements made at PAS. In this study were assessed 88 subjects by lateral cephalograms, which 45 were mouth breathers and 43 nasal breathers.

Recently, some authors have used the 3D reconstruction for different purposes, such as to determine accurate relationship between airway patency and mandibular advancement [14], to compare the 3D pharyngeal airway volume in healthy children with different anteroposterior skeletal patterns [15], Class III malocclusion and to assess the differences in the airway shape [12] and in the volume among subjects with various facial patterns [30]. But, there are no studies that evaluate the pharyngeal airway space in differences breathing patterns using CBCT.

Table 3 showed statistically significant differences between airway volume ($p = 0.000$), airway area ($p = 0.000$) and minimum axial area ($p = 0.001$) between the two groups. Only two of the seven linear distances showed significant statistically differences ($p < 0.05$) while all the 3D variables showed significant statistically differences ($p < 0.05$).

Minimum axial area was greater in nasal breathers than mouth breathers ($p = 0.001$). This effective airway resistance can be great enough to affect nasal airway function. Resistance to airflow is not only related to airway size, but also to airway shape [31–33].

All CBCT scans were realized with the patient seated in upright position and Frankfort Horizontal (FH) plane paralleled to the floor, because the airway volume is influenced by the head posture. Muto et al. [9] reported changes in airway dimensions related to the cranio-cervical inclination. The changes in cranio-cervical inclination produced by head extension were correlated with changes in the variables describing the PAS.

Despite the patients had been instructed not to swallow and not to move the head and tongue during CBCT acquisition, some patients did not follow the instructions and, therefore, new tomography were made. The acquisition times for our iCAT scanner was 20 s; sometimes, this was too long to ask the patient not to move the head and tongue during the scan. Newer scanners have reduced the acquisition time to about 5 s, and allows control of this limitation. Futhermore, reduces the loss of quality for patient movement during scanning and minimizes the radiation dose.

The evaluation of pharyngeal airway space in the present study, indicated that the use of CBCT was an important method of diagnosis, especially when it takes into account the detection and correction of the abnormalities in the airway during development can influence the normal dentofacial growth [34].

5. Conclusion

According to our results, there are differences between nasal and mouth breathers in the measurements PAS-OccL, PAS-UP, airway volume, area and minimum axial area, suggesting that pharyngeal airway dimensions are higher in nasal-breathers than mouth-breathers. The authors believe, that once detected airway constriction, multidisciplinary approach involving pediatricians, physicians, dentists, and ear–nose–throat specialists is required. The treatment aim should be the improvement of the children breathing condition and consequently all its associated medical, social, and behavioral problems.

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Sleep Breath
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PEDIATRICS • ORIGINAL ARTICLE

Can myofunctional therapy increase tongue tone and reduce symptoms in children with sleep-disordered breathing?

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Abstract
Purpose Data in the literature suggest that myofunctional therapy (MT) may be able to play a role in the treatment of children with sleep-disordered breathing (SDB). Our study investigated the effectiveness of MT in reducing respiratory symptoms in children with SDB by modifying tongue tone.
Methods Polysomnographic recordings were performed at baseline to assess obstructive sleep apnea (OSA) severity in 54 children (mean age 7.1 ± 2.5 years, 29 male) with SDB. Patients were randomly assigned to either the MT or no-MT group. Myofunctional evaluation tests, an assessment of tongue strength, tongue peak pressure, and endurance using the Iowa Oral Performance Instrument (IOPI), and nocturnal pulse oximetry were performed before (T0) and after (T1) 2 months of treatment.
Results MT reduced oral breathing (83.3 vs 16.6%, $p < 0.0002$) and lip hypotonia (78 vs 33.3%, $p < 0.003$), restored normal tongue resting position (5.6 vs 33.4%, $p < 0.04$), and significantly increased mean tongue strength (31.9 ± 10.8 vs 38.8 ± 8.3, $p = 0.000$), tongue peak pressure (34.2 ± 10.2 vs 38.1 ± 7.0, $p = 0.000$), and endurance (28.1 ± 8.9 vs 33.1 ± 8.7, $p = 0.01$) in children with SDB. Moreover, mean oxygen saturation increased (96.4 ± 0.6 vs 97.4 ± 0.7, $p = 0.000$) and the oxygen desaturation index decreased (5.9 ± 2.3 vs 3.6 ± 1.8, $p = 0.001$) after MT.
Conclusions Oropharyngeal exercises appear to effectively modify tongue tone, reduce SDB symptoms and oral breathing, and increase oxygen saturation, and may thus play a role in the treatment of SDB.

Keywords Children · Obstructive sleep apnea · Myofunctional therapy · Oropharyngeal exercises

Introduction

Sleep-disordered breathing (SDB) is an upper airway dysfunction that occurs during sleep and is characterized by snoring and/or a greater respiratory effort caused by increased upper airway resistance and pharyngeal collapsibility [1].

Obstructive sleep apnea (OSA) is the most severe clinical type of SDB, and the most common cause of OSA is adenotonsillar hypertrophy, though other anatomical and neuromuscular factors such as craniofacial dysmorphism, obesity, and hypotonic neuromuscular disease are also involved [2, 3].

The multidisciplinary therapeutic approach to OSA is based on adenotonsillectomy, orthodontic and medical treatments, weight loss, and non-invasive ventilation [1, 4, 5]. Treatment interventions are applied in a stepwise fashion until the complete resolution of SDB is achieved. Different treatment modalities are often combined depending on the severity and underlying conditions predisposing to upper airway obstruction during sleep [1, 4, 5]. Oral breathing and lip hypotonia, which are peculiar characteristics of children with OSA, increase nasal resistance and are associated with malposition of the tongue, thereby exacerbating the impaired development and further hampering the growth of the maxilla and mandible [6–8]. Persistence of oral breathing during sleep directly affects the position and strength of the tongue as well as that of the orofacial muscles, thereby causing abnormal airway

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development and SDB [8]. Myofunctional re-education is performed to avoid this evolution and may prove useful as a means of restoring a correct stomatognathic function and of treating OSA associated with other treatments so as to avoid residual OSA [9, 10].

The aims of our study were to evaluate the efficacy of myofunctional therapy (MT) as a first step designed to reduce oral breathing in children with SDB and to evaluate the increase in tongue tone using the Iowa Oral Performance Instrument (IOPI).

Methods

This prospective, case–control study was based on children who were referred to our Pediatric Sleep Center (S. Andrea Hospital, Rome, Italy) for SDB. The diagnosis of OSA was confirmed by the presence of SDB symptoms combined with a polysomnography (PSG) yielding an obstructive apnea/hypopnea index (AHI) >1 event/h [1].

Exclusion criteria were a positive history of acute or chronic cardiorespiratory or neuromuscular diseases, chronic inflammatory diseases, major craniofacial abnormalities, chromosomal syndromes, and epilepsy.

Age- and sex-matched control healthy Caucasian children were randomly recruited from a school in the same urban area of the study group. The inclusion criterion was as follows: none of the controls was obese. No history of sleep problems (snoring, apnoeas, and restless sleep) were reported. The control group underwent only IOPI measurements.

A clinical examination was performed and a sleep clinical record (SCR) obtained for all the SDB patients.

Polysomnographic recordings were performed before MT to define OSA severity. Thereafter, patients with SDB were randomized to two groups—an SDB case group (MT group) treated with MT plus nasal washing, consisting of the application of a saline solution in each nostril three times a day, and an SDB control group (no-MT group) treated with nasal washing alone. We measured tongue strength, tongue peak pressure, and endurance using the IOPI, and performed nocturnal pulse oximetry before (T0) and after (T1) 2 months of treatment in all the patients. We compared the baseline IOPI measurements of the SDB groups with normal values obtained from 38 sex- and age-matched, healthy school children.

The "Sapienza" University institutional review board approved the study, and written informed consent was obtained from the parents of the children upon admission to the study.

Sleep clinical record

All the children underwent the SCR, which has been validated previously [11]. Briefly, the SCR consists of three main sections. The first section takes into consideration the data yielded by a physical examination of the nose, oropharynx, and dental and skeletal occlusion. The following signs are considered: signs of oral breathing; nasal obstruction, inferior turbinate hypertrophy, or rhinolalia; visual evaluation of soft-palate position according to Friedman classes (grades 3 and 4 considered as positive); nasal septum deviation; tonsillar hypertrophy, with grades 3 and 4 being considered as tonsillar hypertrophy [12]; obese or adenoid phenotype; dental/skeletal malocclusion, and narrow hard palate. The dental/skeletal malocclusion, i.e., the intermaxillary divergence, includes jaw deviation from normal occlusion such as retrognathia; prognathia; open, deep bite; crossbite; and overjet. These signs were scored as either two points (positive sign) or zero point (negative sign).

The second section describes the patients' subjective symptoms as summarized by the Brouillette OSAS score. Questions investigated sleep symptoms (habitual snoring, witnessed apnoeic episodes, frequent awakenings, or agitated sleep). Questions were kept simple and concise, and a yes/no response format was chosen. We calculated the Brouillette score, considering a score equal to or higher than −1 as positive [13] and scoring it as 0.5. The third section consists in assessing the presence of inattention and hyperactivity symptoms using the attention deficit hyperactive disorder (ADHD) rating scale for school-aged children [14]. A score higher than 6 was considered as positive and scored as 1. A total sleep clinical record score of 6.5 or more was considered to be positive, as has previously been approved [11].

Sleep analysis

All the children underwent a laboratory overnight PSG assessment, using a Grass Heritage polygraph, in our Pediatric Sleep Center, to define the severity of OSA. The variables recorded included an electroencephalogram with at least eight channels (frontal, central, temporal, and occipital, referred to the contralateral mastoid), an electro-oculogram, a submental electromyogram, and an electrocardiogram (one derivation); chest and abdomen movements were measured by strain gauges. Airflow was recorded from an oronasal thermocouple and a nasal pressure transducer. Arterial oxygen saturation was monitored using pulse oximetry. Sleep stages were scored according to the standard criteria of the American Academy of Sleep Medicine (AASM). Arousals were detected visually according to the criteria reported in the recent manual for the scoring of sleep and associated events by the AASM [15].

Central, obstructive, and mixed apnoea events were counted according to the criteria established by the AASM [15]. The AHI was defined as the average number of apnoea and hypopnea events per hour of sleep. The diagnosis of OSA was confirmed if the laboratory PSG yielded an AHI ≥1 event/h combined with SDB symptoms [1].

Nocturnal pulse oximetry

The Nonin 2500A pulse oximeter (Nonin Medical; Plymouth, MN) was used to perform nocturnal oximetry recordings. A physician analyzed the recordings using the PROXYnet 10.1 software package (MedicAir, Italia). In brief, oximetry recordings with at least three clusters of desaturation events and at least three dips in SaO_2 below 90% were regarded as being diagnostic for OSA (abnormal or positive oximetry). Recordings not meeting these diagnostic criteria were considered as negative/inconclusive for OSA [16].

Myofunctional evaluation and treatment

The myofunctional therapist filled in a myofunctional evaluation form that assessed the respiratory pattern (nasal or oral), labial seal (competent or not), lip tone (normal or not), and tongue position at rest and during swallowing (normal or not normal) [17, 18].

The MT consisted of isometric and isotonic exercises involving the tongue, soft palate, and lateral pharyngeal wall designed to improve suction, swallowing, chewing, breathing, and speech functions.

Oropharyngeal exercises were divided into three categories: (1) nasal breathing rehabilitation, (2) labial seal and lip tone exercises, and (3) tongue posture exercises. The types of exercises used were described in a previous article [10].

Children were required to perform the exercises every day at home, at least three times a day, doing 10–20 repetitions each time. The MT group underwent two monthly meetings with a myofunctional therapist. In the first meeting (T0), the therapist carried out a myofunctional evaluation and taught the patients and their parents how to perform the rehabilitation exercises, which children were required to perform daily at home for 2 months.

In order to reduce a possible observer bias, one therapist performed all the myofunctional evaluations in both groups at T0 and T1, while another taught the children and their parents how to perform the exercises.

Nasal washing was performed using Rinowash with 2.5% saline hypertonic solution. All the patients performed nasal washing twice daily, in the morning and evening, for 2 months.

IOPI measurements

The IOPI objectively measures tongue and lip strength and endurance. Tongue strength is assessed by measuring the maximum pressure exerted when an individual presses a disposable, standard-sized tongue bulb against the roof of the mouth. The peak pressure achieved is displayed on a large, easy-to-read LCD. The units displayed are kilopascals (kPa), according to the internationally recognized unit of pressure, the pascal (Pa). The standard procedure and standard values

Table 1 PSG parameters and myofunctional evaluation of the two groups of children with SDB

	MT group 36)	No-MT group (18)	*p* value
Total sleep time (min)	440.5 ± 71.1	452.6 ± 67.7	0.8[a]
N1 NREM sleep (%)	13.6 (7.7–18.9)	13.5 (10.3–23.3)	0.9[a]
N2 NREM sleep (%)	40.5 (32.9–49.4)	34.2 (29.4–44.0)	0.2[a]
N3 NREM sleep (%)	26.1 (16.9–30.0)	28.7 (21.9–35.1)	0.2[a]
REM (%)	15.4 (9.8–18.6)	19.0 (12.3–22.5)	0.2[a]
Arousal index (*n*/h)	0.0 (0.0–4.5)	0.0 (0.0–3.2)	0.6[a]
AHI (ev/h)	1.5 (1.0–2.8)	1.8 (1.0–2.5)	0.9[a]
SpO_2 (%)	97.9 (96.6–98.0)	96.95 (95.7–98.0)	0.1[a]
Children with OSA (%)	26 (72.2%)	14 (77.7%)	0.7[b]
Oral breathing (%)	25 (69.4)	15 (83.0)	0.3[b]
Lip competence (%)	15 (41.6)	10 (55.0)	0.9[b]
Lip hypotonia (%)	27 (75.0)	13 (72.0)	0.8[b]
Normal tongue resting position (%)	5 (13.8)	2 (16.6)	0.7[b]
Normal tongue position during swallowing (%)	6 (16.6)	3 (16.6)	0.6[b]
Nasal cartilage hypotonia (%)	19 (52.7)	10 (55.5)	0.7[b]
Positive Glatzel test (%)	11 (30.5)	4 (22.2)	0.5[b]
Positive Rosenthal test (%)	14 (38.8)	6 (33.3)	0.7[b]

MT myofunctional therapy, *AHI* apnea–hypopnea index, *SpO_2* mean oxygen saturation, *OSA* obstructive sleep apnea

[a] Mann–Whitney *U* test

[b] Chi-square test

Table 2 Differences in IOPI measurements between the three groups of children

	MT group (36)	No-MT group (18)	Healthy group (38)	*p* values[a]
Tongue strength (kPa)	31.9 ± 10.7	32.4 ± 9.4	51.3 ± 13.6	Healthy vs no-MT group, <0.001
				Healthy vs MT group, <0.001
				MT group vs no-MT group, 0.5
Peak pressure (kPa)	34.2 ± 10.2	34.4 ± 9.9	54.2 ± 12.7	Healthy vs no-MT group, <0.001
				Healthy vs MT group, <0.001
				MT group vs no-MT group, 0.9
Endurance (s)	28.1 ± 8.9	23.3 ± 5.9	15.8 ± 7.2	Healthy vs no-MT group, <0.001
				Healthy vs MT group, <0.001
				MT group vs no-MT group, 0.06

MT myofunctional therapy

[a] Mann–Whitney *U* test

by age were previously validated by Potter et al. [19]. Maximal pressure for the tongue was determined by recording three maximal force efforts, each lasting approximately 1 s, with a 1-min rest period between trials.

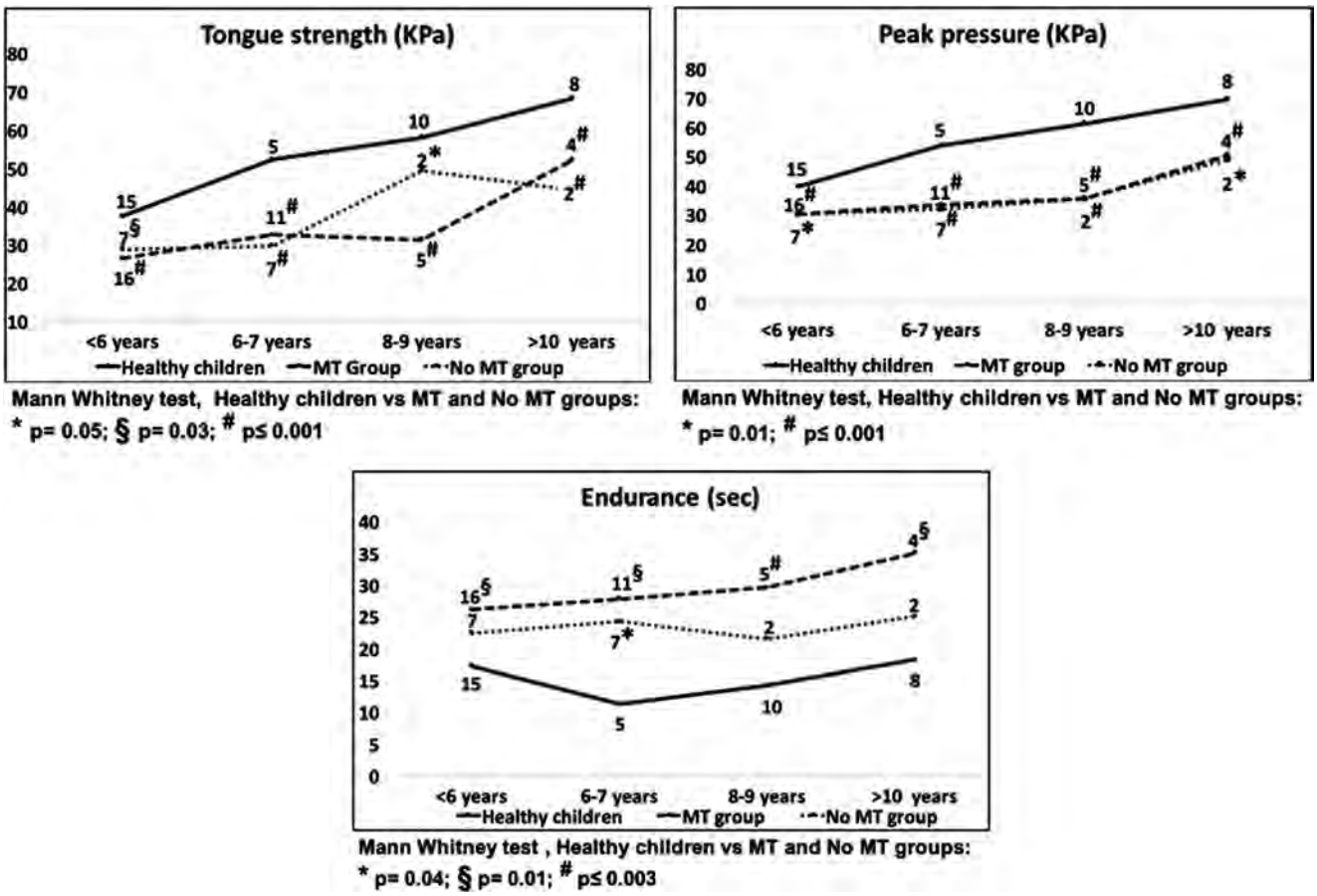

Fig. 1 Iowa Oral Performance Instrument (IOPI) measurements in the overall population divided according to age groups

Endurance was measured by asking the subjects to maintain 50% of their maximal pressure for as long as possible. The length of the endurance trial was measured in seconds.

Statistical analysis

All variables were tested for normality. Accordingly, the values are expressed as a number and percentage (%) for categorical variables, mean ± standard deviation (SD), or median and interquartile range (25–75 percentile) for continuous variables according to the normal distribution of the data. The chi-square test or Fisher's exact test was used for categorical variables, and the independent *t* test or Mann–Whitney test for continuous variables according to the normal distribution of the data. The Wilcoxon signed-rank test was used to compare paired data before and after MT. All the tests were two-tailed and a p value <0.05 was considered significant. The SPSS package (PASW Statistics for Windows, Version 23.0, Chicago: SPSS Inc. 2009) was used for all the analyses.

Results

We enrolled 54 children with sleep-disordered breathing (mean age 7.1 ± 2.5 years, 29 male) and 38 healthy children (7.8 ± 2.2, 25 male). According to the PSG records, 14 children suffered from primary snoring (PS, AHI 0.35 ± 0.3 ev/h) and 40 from mild–moderate OSA (AHI 2.2 ± 2.0 ev/h).

We divided the children into two groups: 36 were assigned to the MT group (mean age 6.7 ± 2.3 years, 14 male) and 18 (mean age 6.7 ± 2.8 years, 8 male) to the no-MT group. Table 1 shows the PSG parameters and myofunctional evaluation for each group.

SCR

No differences emerged between the SCR of the children in the MT group and those in the no-MT group (8.3 ± 2.1 vs 8.35 ± 2.1, $p = 0.9$), nor were any differences observed between the phenotype characteristics in the two groups: tonsillar hypertrophy (53 vs 77%), arched palate (75 vs 61%), skeletal malocclusions (44 vs 60%), and presence of obesity (2 vs 2%).

IOPI measurements

The IOPI, which was performed in all the SDB children and 38 healthy children, revealed significant differences between the MT and no-MT groups and the healthy children (Table 2). There were differences in IOPI measurements depending on age and between groups (Fig. 1). When we compared the IOPI measurements in the MT group before and after 2 months of treatment, we observed a significant improvement in all the parameters, whereas no differences were observed in the no-MT group (Fig. 2). Moreover, the myofunctional evaluation improved after 2 months of treatment in 18 children, as shown by a reduction in the oral breathing habit and lip hypotonia (Table 3).

When all the children with SDB repeated the pulse oximetry after 2 months, higher minimum and mean minimum oxygen saturation values and a lower oxygen desaturation index (ODI) were observed in the MT group, whereas no differences in the pulse oximetry values were observed in the no-MT group (Table 4).

Discussion

Our data demonstrate that MT reduced the respiratory symptoms during the night and oral breathing, and increased tongue tone as measured by means of the IOPI, an instrument easy to administer, in all the children with SDB. Moreover, subjects with SDB were found to have lower tongue strength as measured by the IOPI than healthy children.

The lower tongue strength and endurance observed in children with SDB are likely to be due to the persistence of oral breathing during sleep, which affects tongue position and strength as well as the orofacial muscles, and ultimately leads to abnormal craniofacial and airway development [8].

Oral breathing in children with SDB [20] results in an abnormal tongue position at rest and during sleep, which in turn reduces tongue movement and probably induces tongue hypotonia. These aspects are associated with skeletal malocclusions, as has been demonstrated by other authors [21], and

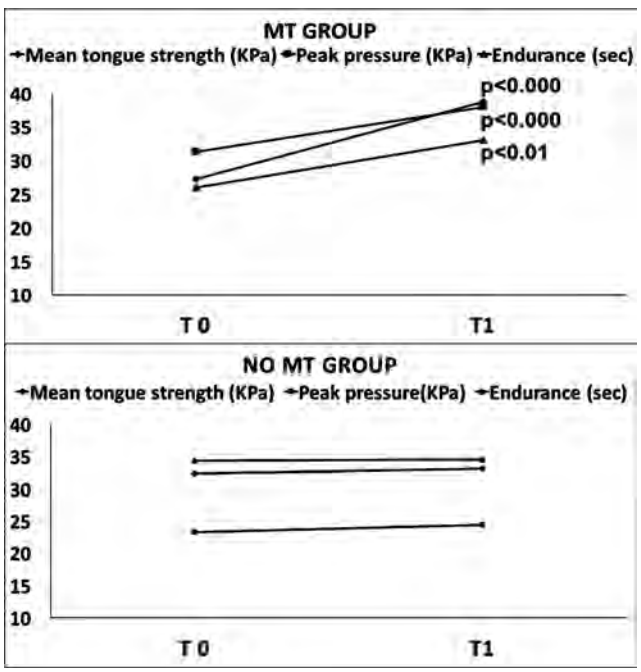

Fig. 2 Iowa Oral Performance Instrument (IOPI) measurements before and after 2 months of treatment in the MT and no-MT groups

Table 3 Myofunctional evaluation at T0 and at T1 in children with sleep-disordered breathing

	MT group (18)			No-MT group (18)		
	T0 18	T1 18	p^a	T0 18	T1 18	p^a
Oral breathing	15 (83.3)	3 (16.6)	0.0002	15 (83.0)	14 (78.0)	1.0
Lip incompetence	11 (61.1)	7 (39.0)	0.3	8 (44.4)	9 (50.0)	1.0
Lip hypotonia	14 (78)	6 (33.3)	0.003	13 (72.0)	12 (66.7)	1.0
Abnormal tongue resting position	17 (94.4)	12 (66.6)	0.03	16 (88.8)	16 (88.8)	1.0
Abnormal tongue position during swallowing	15 (83.3)	11 (61.1)	0.3	15 (83.3)	15 (83.3)	1.0
Nasal cartilage hypotonia	9 (50.0)	7 (38.8)	0.7	10 (55.5)	9 (50.0)	1.0
Positive Glatzel test	8 (44.0)	7 (38.8)	1.0	4 (22.2)	7 (38.8)	0.5
Positive Rosenthal test	8 (44.0)	4 (22.2)	0.3	6 (33.3)	8 (44.0)	0.7

MT myofunctional therapy

[a] Chi-square test

when the tongue is not in its normal position (i.e., lying against the maxillary incisors and hard palate) but sits on the mouth floor, the modelling role played by the tongue on the oral cavity, upon every deglutition, is strongly reduced [22].

Reduced tongue tone and endurance in children with SDB (i) may be a consequence of oral breathing and/or (ii) could be associated with sucking habits (bottle- or breastfeeding) and delayed chewing [23].

When the tongue is placed high in the palate, it correctly stimulates the intermaxillary synchondrosis, leading to normal orofacial growth and normal nasal breathing [24, 25]. Previous data have demonstrated that MT restores nasal breathing and re-establishes tongue position [10].

In our study, MT had a positive effect on tongue behaviour, restoring the normal tongue resting position after 2 months of treatment and enhancing tongue strength, maximum peak pressure, and endurance, as evaluated by means of the IOPI.

These aspects are associated with the restoration of nasal breathing and a reduction in mouth breathing, which in turn improve nocturnal breathing and reduce OSAS in both adult and pediatric populations [9, 10, 26].

These changes are related to nocturnal symptom reduction and result in a higher oxygen saturation, as has previously been demonstrated [10]. Moreover, the fact that oral breathing and lip hypotonia disappeared indicates that MT not only restores normal orofacial function but also may, if performed as a routine exercise, prevent tongue hypotonia [21]. The improvement in tongue function after 2 months of MT was accompanied by improved pulse oximetry values in mean oxygen saturation and a lower ODI. These results may be ascribed to the restoration of normal nasal breathing and the resulting increased supply of oxygen, nitric oxide, and alveolar ventilation during the night [27].

It is not clear how dental malocclusions are associated with stomathognatic myofunctional anomalies. There is, however, a consensus among orthodontists across Europe that myofunctional re-education of the oral–facial region plays an important role in correcting abnormal maxillary and mandibular growth, as well as in normalizing bite and teeth positioning. These effects are believed to be due to the restoration of normal local muscle activity [17].

The creation of oral–facial muscle re-education programs led to the creation of specific university training for the staff involved in such programs. Combined orthodontic and myofunctional re-education has since been applied to children with narrow jaws [8]. With regard to long-term outcomes, combined therapy has proved to be more effective than either treatment used on its own. Ever since maxillary–mandibular growth was shown to be

Table 4 Oxygen saturation values before and after myofunctional treatment

	MT group (18)			No-MT group (18)		
	T0	T1	p^a	T0	T1	p^a
Oxygen desaturation index (ODI)	5.9 ± 2.3	3.6 ± 1.8	0.000	6.3 ± 2.7	7.1 ± 3.2	0.7
Mean oxygen saturation (%)	96.4 ± 0.6	97.4 ± 0.7	0.000	96.1 ± 2.2	96.2 ± 1.5	0.9
Minimum oxygen saturation (%)	91.1 ± 1.4	91.2 ± 1.3	0.9	85.2 ± 4.1	87.7 ± 4.9	0.2
Mean minimum oxygen saturation (%)	94.3 ± 1.3	95.4 ± 1.3	0.000	93.7 ± 2.1	94.2 ± 1.4	0.5

[a] Wilcoxon signed-rank test

involved in SDB, children have been treated with both myofunctional re-education and orthodontia [8, 17].

We know that tongue function may play a role in stomatognathic remodelling and that the restoration of correct normal tongue function needs to be integrated in orthodontic and surgical treatments.

Limitations of the study

One limitation of this study is that the polysomnography was not repeated in children with SDB after 2 months of MT. However, the pulse oximetry, which was repeated, yielded good results. The decision not to repeat the polysomnography was taken to avoid the high costs involved in readmitting the children to hospital, to spare the children and their families any further discomfort as well as because of the parents' opposition, who were already satisfied with the improvement in their children's respiratory symptoms and deemed a repeat examination unnecessary.

Moreover, this study included children with mild–moderate OSA; further research is needed to determine if MT could be effective in patients with different OSA severities and complementary to other treatments.

Conclusions

Children with SDB may exhibit tongue thrusting and abnormal swallowing patterns caused by nasal obstruction and a persistent mouth breathing posture. MT may be used to integrate medical and surgical treatments for OSA and help to restore a normal resting posture of the tongue; appropriate oral, lingual, and facial muscle patterns; nasal breathing; normal lip posture; and a correct swallowing pattern.

Compliance with ethical standards

Funding source There were no sources of funding or support for this research.

Conflict of interest The authors declare that they have no conflict of interest. All authors certify that they have no affiliations with or involvement in any organization or entity with any financial or non-financial interest in the subject matter or materials discussed in this manuscript.

None of the authors has any relevant financial activities outside the submitted manuscript (over the 3 years prior to submission).

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

This article does not contain any studies with animals performed by any of the authors.

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Declaration of authorship

Prof. Maria Pia Villa had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.