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Perspective

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A roadmap of craniofacial growth modification for children with sleep-disordered breathing: a multidisciplinary proposal

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Abstract

Craniofacial modification by orthodontic techniques is increasingly incorporated into the multidisciplinary management of sleep-disordered breathing in children and adolescents. With increasing application of orthodontics to this clinical population it is important for healthcare providers, families, and patients to understand the wide range of available treatments. Orthodontists can guide craniofacial growth depending on age; therefore, it is important to work with other providers for a team-based approach to sleep-disordered breathing. From infancy to adulthood the dentition and craniofacial complex change with growth patterns that can be intercepted and targeted at critical time points. This article proposes a clinical guideline for application of multidisciplinary care with emphasis on dentofacial interventions that target variable growth patterns. We also highlight how these guidelines serve as a roadmap for the key questions that will influence future research directions. Ultimately the appropriate application of these orthodontic techniques will not only provide an important therapeutic option for children and adolescents with symptomatic sleep-disordered breathing but may help also mitigate or prevent its onset.

Key words: growth modification; rapid palatal expansion; craniofacial growth modification roadmap; sleep-disordered breathing in children; growth modification protocol; sleep; pediatric obstructive sleep apnea; sleep apnea

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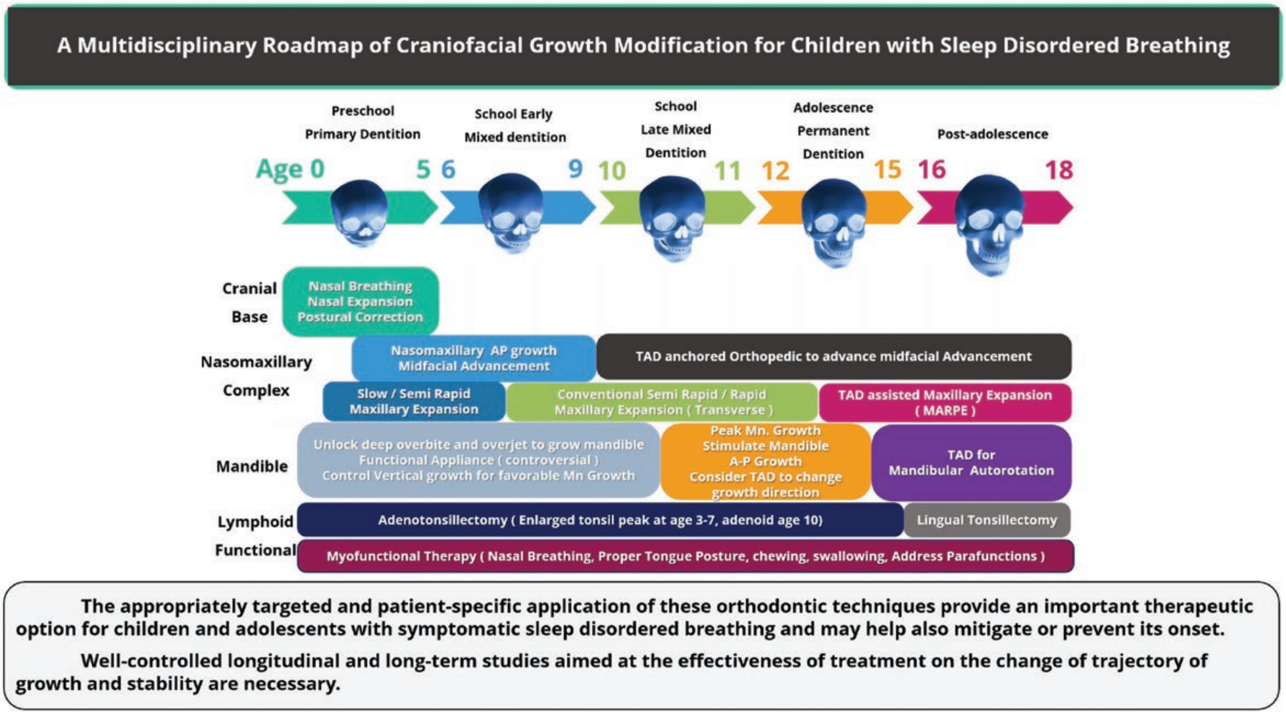
Graphical Abstract



Statement of Significance

This perspective provides a developmental approach to the application of orthodontic techniques for growth modification in the current treatment of children and adults with obstructive sleep apnea within a multidisciplinary team approach. This approach should allow for a more uniform application of orthodontic techniques and more reliable outcomes across all providers and their patients. In addition, the perspective offers potential research directions for the prevention of OSA through the application of these techniques considering the different physiological factors in the facial growth of children. This can potentially result in significant improvements in the clinical approach to the treatment of obstructive sleep apnea for all.

Introduction

The field of sleep medicine has grown significantly over the last several decades as clinicians uncover ailments and treatments for patients of all ages. Evidence supports the importance of early intervention for patients with sleep disorders to mitigate long-term adverse systemic effects. For pediatric patients, there are windows of opportunity to take advantage of their somatic growth and cranio-maxillofacial developmental plasticity to implement customized treatments. Therefore, it is critical that oral healthcare providers such as pediatric dentists and orthodontists to participate in the interdisciplinary care of pediatric patients with sleep disorders such as disordered breathing (SDB) and obstructive sleep apnea (OSA) [1]. There is a putative association between SDB and OSA with craniofacial disharmony resulting from abnormal growth patterns. A recent meta-analysis has questioned the strength of the evidence associating craniofacial morphology and OSA in children [2]. Craniofacial characteristics of pediatric SDB patients with mouth breathing include retrognathia, narrow high arch palate, increased vertical facial height, and increased mandibular plane angle [3–6]. Since orthodontic treatments can both alter and guide craniofacial growth patterns depending on a patient's age, clinical guidelines incorporating orthodontic, surgical, and medical interventions are needed for optimized and personalized care [4, 7].

The etiology of SDB and OSA is multifactorial. Although it can be questioned which comes first, there is a bidirectional influence of SDB and craniofacial development that seems to create a vicious cycle. A key contributor of its pathophysiology is craniofacial anatomy, and orthodontists can readily and effectively influence this factor with targeted therapy. Guilleminault *et al.* [8] concluded that orthodontic treatment is a powerful yet often overlooked intervention for pediatric OSA [8, 9]. Adenotonsillectomy surgery has been the primary, and often the only, intervention for SDB in children. However, residual and recurrence of SDB occur and often present after surgery. This occurs in less complex patients where adenotonsillar hypertrophy is the primary anatomic risk factor of OSA [10–13]. To this effect, Kaditis *et al.* proposed an interdisciplinary treatment approach algorithm for the diagnosis and treatment of pediatric OSA by using orthodontic treatment after adenotonsillectomy [9, 14]. A systematic review conducted in 2020 by Lin *et al.* revealed that although orthodontic rapid maxillary expansion (RME) may not directly reduce a patient's apnea–hypopnea index, RME therapy is one of the most effective interventions to improve oxygen saturation (SaO2) levels [15]. However, these RME results are based on limited samples with relatively short follow-up time, and should be taken carefully into consideration when evaluating these promising improvements. Despite these interventions, however, this review

Table 1. Craniofacial growth modification roadmap for sleep-disordered breathing in children

Developmental stages					
Chronological age in years	0–5	6–9	10–11	12–15	16–18
Dental stage	Primary dentition	Early mixed dentition	Late mixed dentition	Adolescent permanent dentition	Permanent dentition
Skeletal stage: cervical vertebral maturation stage	CS 1	CS 1	CS 2–3	CS 4–5	CS 5—6
Characteristics of skeletal growth					
Cranial base	• Up to 80% cranial and neural growth occurs by age 6 years • Cranial Base Flexion determines the frame of facial growth pattern • Elongation at synchondrosis	• Anterior cranial base growth is complete • Posterior cranial base growth continues: increase by 1 mm per year	• Anterior cranial base growth is complete • Posterior cranial base growth continues: increase by 1 mm per year	• Most growth completed	• Most growth completed
Nasomaxillary complex	• Development by anterior cranial base • Nasal cavity development	• Downward and forward growth • Nasal cavity development continues • Maxillary growth in horizontal direction	• Downward and forward growth • Nasal cavity development continues • Maxillary growth in vertical direction	• Downward and forward growth • Nasal cavity development continues • Maxillary growth in vertical direction	• Most growth completed
Mandible	• Body length and ramus development	• Increases in body length and ramus development	• Increases in body length and ramus development • Mn peak growth 11–13 years	• Increases in body length and ramus development • Mn peak growth 11–13 years	• Residual mandibular growth
Lymphoid/soft tissues and tongue	• Enlarged adenoid (peak at 10 years old) • Enlarged tonsil (Peak at 3–7 years old) • Hyoid bone descends, moves slightly anteriorly • Tongue displacement toward oropharynx affect mandibular development • Tongue strength increase rapidly from 3–6.5 years	• Enlarged adenoid (peak at 10 years old) • Enlarged tonsil (Peak at 3–7 years old) • Hyoid bone descends, moves slightly anteriorly • Increase tongue size • Tongue strength increases slowly	• Tonsil size reduced • Tongue size growth complete • Tongue moves inferiorly and forward • Tongue strength increases slowly	• Tongue strength increases slowly	• Hypertrophy of lingual tonsils (after puberty) • Tongue strength increases slowly until age 17
Functional	• Breathing-sucking-swallowing coordination • Breathing-chewing-swallowing coordination • Breathing-voice-speech coordination • Dissociation and grading of movement of tongue, lips and jaws • Speech development • Stability at rest and during movement of tongue, lips, and jaw	• Transition from immature swallowing to mature swallowing • Speech sounds development is completed	• Swallowing maturation through changes in dentition and palatal growth	• Swallowing maturation complete • Exclusive nasal breathing should be achieved	
Strategies for targeted therapy **Goal: Establish nasal breathing and guide favorable skeletal growth pattern**					
Cranial base	• Nasal breathing establishment • Postural correction	• Nasal breathing Establishment	• Nasal breathing establishment	• Nasal breathing establishment	• Nasal breathing establishment

Table 1. Continued

Nasomaxillary complex	• Expansion and advancement • Consider slow maxillary expansion therapy	• RME • Midface advancement with RPE and facemask therapy	• RME • Midface advancement with TAD anchored RPE/MARPE and facemask therapy	• TAD anchored maxillary expansion (MARPE) • Midface advancement with MARPE/facemask • Bollard mini-plates	• TAD anchored maxillary expansion (MARPE) • Limited success: Midface advancement with MARPE/facemask • Bollard mini-plates
Mandible	• Unlock deep overbite/overjet to allow mandibular growth • Consider myofunctional appliance for tongue posture and forward mandibular growth	• Unlock deep overbite/overjet to allow mandibular growth • Consider myofunctional appliance for tongue posture and forward mandibular growth	• Unlock deep overbite/overjet to allow mandibular growth • Functional orthodontic appliances (class II corrector) to influence mandibular growth direction	• Enhance mandibular growth • Functional orthodontic appliances to influence Mn growth direction • TAD to change growth direction (mandibular autorotation)	• Consider TAD for mandibular autorotation • Wait for orthognathic surgery
Lymphoid/soft tissues and tongue	• Adenotonsillectomy • Consider myofunctional appliance for tongue	• Adenotonsillectomy • Consider myofunctional appliance for tongue	• Adenotonsillectomy after expansion	• Adenotonsillectomy after expansion	• Lingual tonsillectomy
Functional	• Promote breastfeeding, weaning with chewable foods • Discontinue pacifiers (18 mos) • Promote prevention of orofacial functional disorders • Promote nasal breathing	• Active myofunctional therapy when needed • Promote nasal breathing, correct chewing, and swallowing, optimal resting position • Address parafunctions • Complete speech sounds correction	• Active myofunctional therapy when needed • Adjust chewing and swallowing to change of dentition • Promote proper resting position • Address parafunctions	• Implement active myofunctional therapy when needed • Promote life-style changes in nasal breathing, chewing, swallowing, resting position • Address parafunction	• Implement active myofunctional therapy when needed • Promote life-style changes in nasal breathing, chewing, swallowing, resting position • Address parafunction

The characteristics of skeletal growth of each craniofacial complex that is relevant to growth of the airway were outlined and growth modification strategies for each skeletal structures at different growth stages were suggested.
AP—anterior-posterior.
CS—cervical stage; cervical vertebral maturation stage (CVMS) is a method to identify the skeletal growth spurt and the peak in mandibular growth based on the analysis of the second through fourth cervical vertebrae in a single cephalogram (See Table 2).
Mx—maxilla.
Mn—mandible.
RME—rapid maxillary expansion; expansion in patients done within a short period of time typically 2–6 weeks of active expansion followed by a holding period to allow maxillary bone to fill into the split suture.
RPE—rapid palatal expander; orthodontic appliance used for RME; custom appliance banded to first molars, and sometimes first premolars with a jackscrew that is turned manually to help widen the maxilla in less skeletally mature patients.
MARPE—mini-screw-assisted rapid palatal expander; orthodontic expansion appliance anchored with mini-crews to the palate, to widen the maxilla. Developed and used for mature fused maxillary palatal suture.
TAD—temporary anchorage device; mini-screw with versatile applications to allow for skeletal and dental movement with bone anchored support.

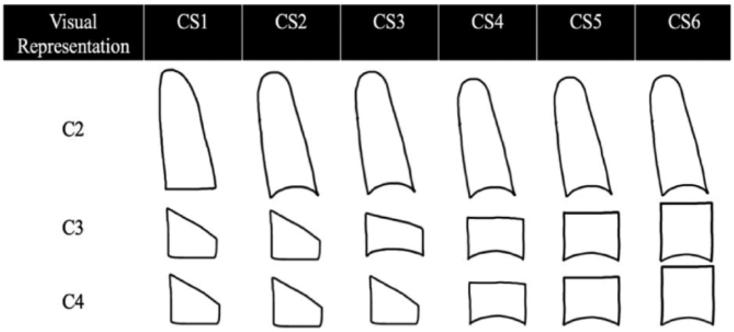
concluded that complete resolution of OSA was not achieved in most trials [15–19]. Notwithstanding more recent experience would lend support to the contention that RME can play a substantially beneficial role in the context of residual or relapsing OSA in children [16–19]. It is important that orthodontic interventions with the strong evidence for timely intervention of pediatric OSA is discussed within the context of interdisciplinary care.

Previous studies have established a robust and comprehensive understanding of the processes underlying craniofacial development and growth, and such expansive base of knowledge can be utilized to help improve how we address SDB in children. Because craniofacial differential growth is time-dependent, orthodontists can manipulate these craniofacial growth patterns by targeting specific structures [20] and change the trajectory of growth when interventions are timely implemented [9, 21, 22]. Here we review the differential growth of craniofacial structures, and suggest interventions aimed at achieving favorable growth modifications that alleviate SDB in children. Ideally, this may also prevent SDB recurrence later in life.

Growth Modification Roadmap (Table 1)

The growth modification roadmap (Table 1) serves as a guide to facilitate the understanding of a child's growth trajectory, in defined chronological age groups. The groups are based on stage of dental development and cervical vertebral maturation (Table 2) [23]. We outline the characteristics of skeletal growth in the craniofacial complex that affects the airway including cranial base, nasomaxillary complex, and mandible as well as lymphoid tissue, tongue, and functional development at each stage [22]. Although definitive evidence is lacking, it is hypothesized that chronic mouth breathing is detrimental to facial and airway growth [23–25]. Irrespective of whether a causal relationship exists between oral respiration and deceleration of specific

Table 2. CVMS staging table.



Stage	Inferior Border/Shape of Vertebrae	Growth Potential
CS 1	flat/trapezoid	peak in mandibular growth will occur on average 2 years after this stage
CS 2	C2 concavity	peak in mandibular growth will occur on average 1 year after this stage
CS 3	C2/C3 concavity; trapezoidal/rectangular	peak in mandibular growth will occur during the year after this stage
CS 4	C2/C3/C4 concavity; C3/C4 rectangular horizontal	peak in mandibular growth has occurred within 1 or 2 years before this stage
CS 5	C2/C3/C4 concavity; C3/C4 - square	peak in mandibular growth has ended at least 1 year before this stage
CS 6	C2/C3/C4 concavity; C3/C4 - rectangular vertical	peak in mandibular growth has ended at least 2 years before this stage

Cervical vertebral maturation (CVM) is a method for the detection of growth spurt and mandibular skeletal maturity in a single cephalogram. CS—cervical stage; CVMS—cervical vertebral maturation stage (CVMS). CVM cannot be solely relied upon. Other growth indicators also should be considered.

craniofacial growth, the main treatment objective is to enhance nasal breathing and favorable facial growth. Accordingly, we suggest strategies for targeted therapies at each developmental stage to enhance the growth trajectory and optimize upper airway size and function [19].

Toddlers and Preschool Stage (Chronologic Ages-Infancy up to 5 Years; Primary Dentition, CVMS 1)

At this age range, children have primary dentition and are in cervical vertebral maturation stage one (CVMS 1). After birth, breathing, chewing, and swallowing guide cranial bone remodeling. The cranial base provides the platform that drives craniofacial growth and upper airway development. The cranial base plays a key role in craniofacial growth by helping to integrate the anatomically and functionally different patterns of growth in various adjoining regions of the skull, such as the brain, the nasal cavity, the oral cavity, and the pharynx. The synchondroses formed via endochondral ossification in the cranial base are an important growth center for the neurocranium [24]. Within the nasomaxillary complex, there is development of the anterior cranial base and nasal cavity [22]. By the end of this stage up to 80% of cranial development is completed [25].

Cranial base lengthening and flexing is primarily controlled by genetics, but also can be influenced by respiratory patterning and by head posture. Cranial base flexion (basicranial flexion) occurs early in life which helps determine the facial phenotype. For example, an obtuse cranial base angle will displace the mandible more distally towards a class II (retrognathic mandible) sagittal jaw relationship tendency, while the opposite, craniofacial base angle closure will displace the mandible more anteriorly towards a class III (prognathic mandible) sagittal jaw relationship. Impaired cranial base flexion tends to keep the cranial base narrow and long (dolichofacial) and to displace the mandible distally [20].

During the first postnatal year, the mandible has the greatest growth velocity which secures the pharyngeal airway in infancy and make room for rapidly developing dentition. Thereafter, velocities of mandibular growth progressively decelerate. In this age group, the mandible develops both in the ramus length and anteroposterior (AP) growth (body length) more than in the vertical growth. By 5 years of age, ramus height grows to approximately 70% of adult size in males and 74% in females [25–27].

The tongue in newborns is large relative to the oral cavity. At birth, the tongue is positioned forward and fills up the oral cavity. As the larynx descends during first 5 years of life, the base of the tongue moves backward to the oropharynx and the base of the tongue becomes the anterior wall of the oropharynx. The volume of the tongue and the suprahyoid muscle guide the anterior growth of the mandibular symphysis. In addition, the hyoid bone descends and moves slightly anteriorly during this stage of growth [28].

Tongue strength increases rapidly from ages 3 to 6.5 years. This is a critical time from a functional development perspective. Initially, a primitive reflexive process such as deglution develops into a complex integrated voluntary and reflexive process. Breathing-sucking-swallowing, and subsequently breathing-chewing-swallowing coordination, dissociation, and grading of movement of tongue, lips, and jaw are developed. In this age group, it is common for the tongue to be displaced toward the oropharynx which affects the development of the mandible. As such, it is hypothesized that if a child is mouth breathing, the lower posterior tongue posture will result in a descent of the hyoid bone, which can impair mandibular growth [29–32]. Further studies are required to validate the tongue posture effects that will help formulate potential clinical guidelines.

As the key is to establish nasal breathing at this stage, clinicians need to understand the root causes of mouth breathing and treat accordingly [33]. Proper craniofacial development in children relies on nasal breathing, proper posture, and restoring normal function of the craniofacial complex. The impaired development of facial structures adversely affects daily functions such as chewing, suction, and nasal breathing [8]. This negative feedback impacts facial growth and airway development. Prevention of craniofacial disorders and establishment of unimpeded nasal breathing are the main functional strategies at this stage including but not limited to breaking bad oral habits, addressing, and eliminating parafunctional habits such as digit sucking, tongue thrusting, bruxism, mouth breathing, and nail biting, promoting breastfeeding and encouraging chewable food items [33].

Lymphoid tissues such as the adenoids and palatine tonsils can become enlarged at any age and are usually the result of viral or allergic stimuli [34]. In healthy children, the lower facial skeletal elements grow linearly along the sagittal and axial planes throughout the first 10–12 years of life. Lymphoid tissues in the upper airway grow proportionally to the craniofacial features. Adenotonsillar hypertrophy which peaks in children 3–7 years old coincides with peak incidence of childhood OSA. This may reflect an abnormal proliferation of these immune organs from inflammatory processes. If oral or nasal breathing are affected due to adenotonsillar hypertrophy, adenotonsillectomy is recommended as a treatment option [12, 35, 36]. In addition, the evaluation of limited tongue mobility and allergy testing and treatment should to be considered [37, 38].

In this age bracket, orthodontic strategies that can optimize the facial growth include maxillary expansion and advancement, as well as concurrent myofunctional therapy for appropriate speech and swallowing patterns [8]. Maxillary constriction with a high arch palate appears to be associated as a potential contributor to the development of SDB [39]. Hence, maxillary expansion has emerged as an effective treatment for OSA in patients with maxillary constriction [9]. Expansion across the midpalate suture can be done in two ways: (1) rapid expansion: 0.25–0.5 mm expansion per day (2–20 kg of force); (2) slow expansion: 0.5–1 mm expansion per week (900 g of force). At this age, the mid-palatal suture is very malleable, such that slow expansion treatment modalities are preferred over rapid expansion (Figure 1). Rapid expansion exerting heavy force is not recommended in preschool children because of the risk of producing undesirable facial changes especially in the nose. In addition to maxillary expansion, deep overbite or reverse overjet need to be corrected to allow proper mandibular growth. These approaches promote the restoration of nasal breathing at an early age [40]. Although controversial, myofunctional appliances that facilitate repositioning of tongue posture and encourage forward mandibular growth can be considered [41].

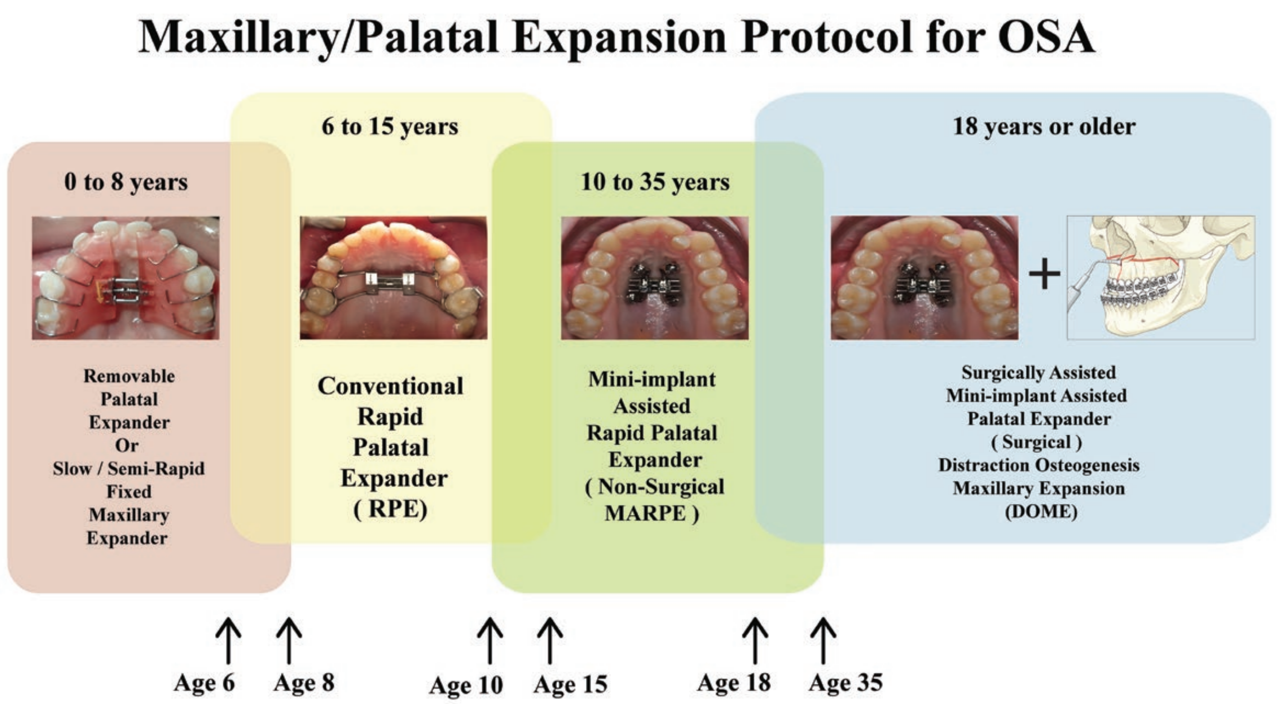


Figure 1. Maxillary (palatal) expansion protocol for OSA. Pink zone (up to 8 years: removable expander or slow/semi-rapid maxillary expander)—toddlers and preschoolers usually up to age 8 have malleable mid-palatal sutures, and can benefit from a removable maxillary expander or slow fixed maxillary expander; orthodontic appliances that have a jackscrew that is manually turned as part of a retainer appliance or a fixed appliance with slow release of force on the palate to widen the transverse. Yellow zone (6–15 years old: RPE)—children with a maturing mid-palatal suture can benefit from a conventional rapid maxillary expander, which is an orthodontic appliance that is cemented to the first molars, and sometimes first premolars with a jackscrew to manually expand the maxillary arch. Green zone (10–35 years old: MARPE)—late adolescents and young adults with a mature mid-palatal suture and airway issues can benefit from mini-implant/mini-screw assisted maxillary expander (MARPE) that is anchored into the palate with mini-implants and turned manually to split the mid-palatal suture. Blue zone (18 years old + to aging adult: surgical expansion or DOME)—adults with mature mid-palatal sutures and OSA can benefit from the mini-screw assisted maxillary expander in conjunction with surgery aka, distraction osteogenesis maxillary expansion (DOME) surgical procedure to expand maxilla.

Early Childhood (Chronologic Ages 6–9 Years; Early Mixed Dentition; CVMS 1)

In this age range, children have early mixed dentition and are in late cervical vertebral maturation stage one (CVMS 1). Anterior cranial base growth is now completed while the posterior cranial base continues to grow. The nasomaxillary complex continues to develop and nasal cavity enlarges. Overall, while the nasomaxillary complex grows downward and forward, the direction of maxillary growth is primarily in the horizontal plane [42].

The mandible continues to develop in both ramus and body length. Internal rotation of the mandible peaks along with the juvenile growth spurt. As the gonial angle, the angle of the posterior inferior region of the mandible, decreases, the overall shape of the mandible is determined [43]. However, the hyoid bone continues to descend and move slightly anteriorly [44].

The tongue slowly continues to increase in size and strength, which temporarily decreases the retroglossal airway. At this time, the child has transitioned from immature swallowing to a mature swallowing pattern and speech sound development is usually completed [28].

The main functional strategies that can be implemented at this stage consist of prevention of craniofacial disorders and establishing nasal breathing. Speech and swallowing therapy should be complete by this stage and proper tongue resting posture need to be addressed. More active myofunctional therapy, rather than passive approaches may be needed.

Orthodontic strategies at this age include targeted therapy for the nasomaxillary complex. These approaches include rapid palatal expansion (RPE) and midface advancement with reverse pull headgear (also called facemask) therapy. After this stage, skeletal advancement of the midface with traditional appliances is not likely to be effective. Additionally, deep overbite or reverse overjet need to be addressed to encourage mandibular growth [45, 46].

Myofunctional appliances can also assist in correcting tongue position and mandibular growth patterns. If upper airway lymphoid tissues are enlarged, then adenotonsillectomy should be considered [47]. Recent study reported RPE reduces the size of adenoid and tonsil around this stage [48]. RPE may be considered as a treatment option for children with narrow high arch palate and adenotonsillar hypertrophy.

Middle Childhood (Chronologic Ages 10–11 Years; Late Mixed Dentition; CVMS 2–3)

At this stage, children have late mixed dentition and are generally in cervical vertebral maturation stages two to three (CVMS 2–3). While growth of the nasomaxillary complex continues downward and forward with nasal cavity enlargement, the maxillary growth pattern is now primarily in the vertical direction as the width of the maxilla is determined [49]. Peak mandibular growth in both ramus and body length may start at this stage [44].

Recent MRI study reported that adenoid size peak around this age and palatine tonsils progressively become smaller [50]. Tongue growth is completed by this stage. The tongue moves inferiorly and forward, while tongue strength increases slowly. Swallowing maturation nears completion through changes in dentition and palatal growth [51].

Orthodontic interventions at this stage of development may still include RPE. However, if forward growth of the nasomaxillary complex is needed, a temporary anchorage device (TAD) with RPE or Mini-Implant Assisted RPE (MARPE) appliance with facemask therapy should also be considered [52, 53]. When TADs or mini-implants are used in the maxilla to secure a RPE appliance, it can directly apply forces to the nasomaxillary complex, effectively bringing the midface forward skeletally (Figure 1). Since nasomaxillary complex growth direction changed from horizontally to vertically around this stage, MARPE with facemask is more effective to develop nasomaxillary complex in horizontal direction than RPE. In addition, orthodontic functional appliances such as class II correctors can influence mandibular growth in a favorable direction at this stage. After expansion, the lymphoid tissues should be re-examined and if necessary, primary or revision adenotonsillectomy may be required [54, 55].

Adolescence Stage (Chronologic Ages 12–15 Years; Permanent Dentition; CVMS 4–5)

In this age group, children have adolescent permanent dentition and are mostly in late cervical vertebral maturation stages four to five (CVMS 4–5). Most growth is completed in the cranial structures. The nasomaxillary complex will continue to grow downward and forward, although at this stage the nasomaxillary complex will grow more vertically than horizontally [56].

The mandible will continue to increase in body length and ramus with peak growth occurring at age 11–13 years for girls and 13–15 years for boys. There is also vertical growth of the mandible and ramus, which results in counterclockwise external rotation and surface modeling of the mandible [57].

Lymphoid tissue changes include tonsil and adenoid size reduction. Swallowing maturation is complete and tongue strength continues to increase slowly.

Orthodontic targeted therapies for children in this age group with SDB are often more effective with bone anchored mini-implants to maximize orthopedic changes as the skeletal structures are mostly developed and past the peak growth potential. Strategies to help target the skeletal structures include a MARPE for transverse correction and/or midface advancement with MARPE/facemask therapy. Additionally, Bollard mini-plates can be utilized which allows directing force on skeletal components instead of dentition [55].

For the mandible, functional appliances can help guide a favorable growth pattern. For forward mandibular growth, the best time for therapy is when the child is about 1 year away from peak pubertal growth which is 11–13 years for females and 13–15 years for males [57]. The mandibular growth center, located in the condyle, is not well understood. There is a need for more extensive research about growth centers, their impairment and possible repair methods. It is also not well known whether the mandibular size can be increased with functional appliances. What we observe with these interventions may reflect the acceleration of mandibular growth, which can still be helpful in children with SDB for early alleviation of symptoms. More than the absolute extent of the growth, the direction and pattern of growth may be more important to the optimization of airway function. TADs may be used for posterior dental intrusion to encourage more favorable changes in growth pattern by mandibular counterclockwise autorotation [58].

Post Adolescence Stage (Chronological Age 16–18 Years; Permanent Dentition; CVMS 5–6)

Permanent dentition and late cervical vertebral maturation stages five to six (CVMS 5–6) are now apparent at this age. Most of the skeletal growth is completed except for residual mandibular growth. Cranial growth, nasomaxillary growth, and substantial mandibular growth, especially mandibular width are complete [20]. Only residual growth of the length and height of the mandible and surface remodeling continues at this stage. On the other hand, hyoid bone length continues to grow to age 18 years. The hyoid bone descends and moves slightly forward up to this age. The hyoid's forward translation is associated with mandibular forward displacement and the bone's descent is associated with vertical growth of cervical vertebrae and ramus height of mandible [57]. Tongue strength continues to increase slowly until approximately the same age [20].

Lingual tonsils which are in the dorsal surface at the base of the tongue develop later than other lymphoid tissues. Hypertrophy of the lingual tonsils frequently occurs after puberty and persists into adulthood. This can affect the retroglossal airway but is usually underrecognized because small to moderately sized lingual tonsils cannot be easily visualized during routine clinical oral examination. Enlarged lingual tonsils can be a significant cause of persistent OSA, especially in children with obesity or with craniofacial deformities [59]. Therefore, lingual tonsillectomy can be considered as a treatment option.

Once patients have reached complete maturation, targeted therapies become focused on direct skeletal interventions. There is limited success at this age group with midface advancement using MARPE/facemask appliances and Bollard mini-plates. MARPE remains an effective tool for palatal expansion in this stage to help treat a high arched narrow palate, bilateral posterior crossbite, and transverse problems. Alternatively, Distraction Osteogenesis Maxillary Expansion (DOME) for maxillary expansion can be considered for the patients with fully matured facial sutures or patients who failed with non-surgical skeletal expansion [60]. (Figure 1) Also orthognathic surgery including maxillomandibular advancement surgery can be planned after the patient's facial growth has fully matured. The use of TADs may be considered for mandibular autorotation. Throughout these stages of growth and development, lingual tonsillectomy may remain an option to help improve the airway along with myofunctional therapy [55, 61].

Conclusions

This roadmap of orthodontic growth modification aims to facilitate interdisciplinary communication among pediatric sleep medicine practitioners to develop comprehensive, patient-centered treatments of the upper airway. Universally accepted evidence of effectiveness of this roadmap is not available. Certainly, there is a role for clinical trials to establish the validity of this perspective. Such trials would also help increase the acceptance of orthodontic approaches to a wider population of practitioners and could help establish reimbursement and healthcare insurance coverage and diminish the disparate sleep healthcare outcomes that exist today. More targeted and patient-specific growth modifications are possible for younger children with OSA, and options will continue to emerge for the adolescent group as the plasticity of craniofacial-airway complex diminishes. However, unpredictability with orthodontic growth modifiers and potential burden of treatment costs should be carefully considered. OSA has a multi-faceted etiology and targeted therapy adapted to the patient's stage of development can maximize skeletal and functional growth potential in a favorable direction, significantly enhancing the sustainability of treatment success.

Future Research Directions

There are many clinical challenges and unanswered questions regarding craniofacial growth modification application for SDB in children. In order to justify incorporation of early orthodontic interventions, there is a need for better phenotyping of our potential patients to help select the best management options. In the future, personalized care will identify which specific children could benefit most from targeted craniofacial management as part of an interdisciplinary team. Well-controlled longitudinal and long-term studies aimed at the effectiveness of treatment on the change of trajectory of growth and stability of such changes will be necessary. For accuracy of phenotyping and proper treatment approaches at each of the different stages of development, current clinical challenges, and research questions are laid out for each chronological age group in Table 3.

For the proper direction of a collaborative approach there are several possibilities, such as randomized controlled trials (RCT) of RME with and without myofunctional therapy, or RCT of functional orthodontic appliances (class II corrector) after adenotonsillectomy compared to adenotonsillectomy alone in the appropriate age groups. Also, further work is needed to understand the proper sequence of any multidisciplinary treatments and what are the factors that inhibit access to multidisciplinary collaborative care from the patient side as well as the providers' aspects. Studies that involve all disciplines engaged in the evaluation and treatment of SDB patients will be necessary.

Also, a major challenge remains on how to provide appropriate orthodontic treatments to a greater sector of the population, irrespective of socio-economic background and to children and adolescents with various craniofacial syndromes. Since SDB is often a familial condition, these techniques may be incorporated in younger siblings of symptomatic patients to help prevent or ameliorate the impact of SDB in their lives. Further longitudinal work is needed to evaluate the disease prevention aspect of these therapies. If these preventive strategies are proven, then public health policy and insurance reimbursement considerations would need to take into account.

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Table 3. Partial list illustrating common clinical challenges and future research directions according to developmental stages

Developmental stage	Clinical challenges/questions	Examples of research directions
0–5 years	• What is patients' ability to participate in treatment in this age group? • What is the ability of parental involvement/ acceptance in this age group? • Can surgery avoid the need for future orthodontic treatment? • Any of SDB symptoms and craniofacial discrepancy are temporary/ transient and patient can naturally grow out of it without treatment?	• How early can we start expansion? Longitudinal study to investigate long-term effects of early treatment. • What is the best timing of expansion relative to tonsillectomy? • Patient and parent response survey; how willing are parents to treat early? • Twin studies to understand the genetic and environmental influences on treatment response and growth and development potential following intervention.
6–9 years	• Can myofunctional therapy avoid orthodontic treatment? • What is the consensus on the role of myofunctional therapy; type, timing, duration, sequences, compliance? • Rapid vs slow expansion trial? • Can orthodontic growth modification avoid the need for surgery?	• Randomized trial of myofunctional therapy with and without orthodontics? • Guidelines of myofunctional therapy in SDB • Randomized trials comparing rapid vs slow expansion protocols. • Longitudinal studies of growth modification with watchful observation vs with surgery
10–11 years	• Should orthodontic appliance such as RME and class II corrector be done before or after adenotonsillectomy? • Is RME indicated in all cases of post-operative residual SDB? • What is the best approach to controlling mandibular growth for OSA?	• Clinical trials of different orthodontic appliances and adenotonsillectomy sequence. • Cost effectiveness studies of RME for post-operative residual SDB
12–15 years	• Can MARPE avoid the need for PAP or future sleep surgery. • What dentofacial deformity is MARPE appropriate for?	• Randomized trials of MARPE vs PAP/sleep surgery • Outcome studies of MARPE in cranial facial syndromes such as cleft palate, Trisomy 21
16–18 years	• How does the care of older adolescents different from adult patients? • How will older adolescents accept these therapies in their lifestyles?	• Compare growth pattern modifications of MARPE vs DOME. • Study how these therapies impact mental health and academic performance

Disclosure Statement

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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