Sleep Medicine Reviews 24 (2015) 46–56

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

Pediatric sleep-disordered breathing: New evidence on its development

Christian Guilleminault*, Farah Akhtar

Stanford University Sleep Medicine Division, Stanford Outpatient Medical Center, Redwood City, CA, USA

ARTICLE INFO

Article history:
Received 14 April 2014
Received in revised form
7 November 2014
Accepted 26 November 2014
Available online 4 December 2014

Keywords:
Pediatrics
Sleep-disordered breathing
Craniofacial development
Functional impairment
Genetic involvement

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

* Corresponding author. Stanford University Sleep Medicine Division, Stanford Outpatient Medical Center, 450 Broadway, MC5704, Redwood City, 94063 CA, USA. Tel.: +1 650 723 6601; fax: +1 650 721 3465.
E-mail address: cguil@stanford.edu (C. Guilleminault).

http://dx.doi.org/10.1016/j.smrv.2014.11.008
1087-0792/

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

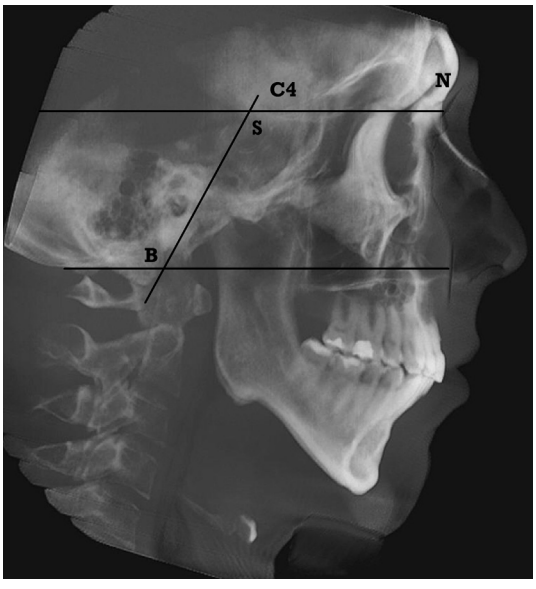

Fig. 1. Cephalometric X-ray with indication of basion-sella-nasion angle and "lines" investigated to evaluate position of odontoid and occipital hole. Basion-sella-nasion – Ba–S–Na-angle, also called sphenoidal angle is related to the vertical growth of the skull base and it is under the control of the 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.