Systematic Review Article

Posterior cranial base natural growth and development: *A systematic review*

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ABSTRACT

Objective: To provide a synthesis of the published studies evaluating the natural growth and development of the human posterior cranial base (S-Ba).

Materials and Methods: The search was performed on MEDLINE, Embase, PubMed, and all EBM Reviews electronic databases. In addition, reference lists of the included studies were hand-searched. Articles were included if they analyzed posterior cranial-base growth in humans specifically. Study selection, data extraction, and risk of bias assessment were completed in duplicate. A meta-analysis was not justified.

Results: Finally, 23 published studies were selected: 5 cross-sectional and 18 cohort studies. Articles were published between 1955 and 2015, and all were published in English. The sample sizes varied between 20 and 397 individuals and consisted of craniofacial measurements from either living or deceased human skulls. Validity of the measurements was not determined in any of the studies, while six papers reported some form of reliability assessment. All the articles included multiple time points within the same population or data from multiple age groups. Growth of S-Ba was generally agreed to be from spheno-occipital synchondrosis growth. Basion displaced downward and backward and sella turcica moved downward and backward during craniofacial growth. Timing of cessation of S-Ba growth was not conclusive due to limited identified evidence.

Conclusions: Current evidence suggests that S-Ba is not totally stable, as its dimensions change throughout craniofacial growth and a minor dimensional change is observed even in late adulthood. (*Angle Orthod.* 2017;87:897–910.)

KEY WORDS: Cranial base; Growth

INTRODUCTION

Understanding craniofacial growth and development is important for accurate diagnosis, treatment planning and posttreatment evaluation of orthodontic cases. Paramount to this is knowledge of the cranial base growth and development, since it is the foundation upon which the remaining facial structures develop.[1–4] Various methods to assess and analyze craniofacial growth and development have been described in the literature. These include craniometry, anthropometry, cephalometric x-rays, and, most recently, three-dimensional (3-D) cone-beam computed tomography (CBCT).[5,6]

The cranial base is said to reach 87% of its growth by 2 years and 98% by 15 years of age.[3] Around age 5, the cranial base has completed 90% of its growth and, from then on, can be considered relatively stable as the remaining 10% of change occurs in the next 10 years.[4] It is known that maturation of different components of the craniofacial skeleton reach their completion at different time points.[7] It is also considered that some components of the anterior cranial base are the earliest structures in the skull to reach maturity in shape and size at about 7–8 years.[8]

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A previous report on the posterior cranial base (S-Ba) changes showed that its length and angulation are differentially affected in different vertical facial types.[3] It was also shown that, within the S-Ba, the spheno-occipital synchondrosis is a cornerstone structure for growth of the cranial vault as well as craniofacial growth in general.[9] The spheno-occipital synchondrosis connects the occipital and sphenoid bones and is located anterior and superior to the foramen magnum and below the pituitary fossa.[10] To date, there are numerous reports that have studied growth of S-Ba and the spheno-occipital synchondrosis,[11–14] but there is no certainty as for when it completes its fusion and consequently stops growing.

As has been stated, the cranial base influences the growth and development of the remaining craniofacial structures. Knowledge of its stability is beneficial for proper diagnosis and treatment planning by orthodontists because what happens at the cranial base affects the position, size, angles, and structure of the overlying face.[3] A previous systematic review synthesized the changes in the anterior cranial base,[15] but did not consider changes in the S-Ba. As such, this systematic review aimed to provide a synthesis of the published studies evaluating the growth and development of S-Ba.

MATERIALS AND METHODS

Protocol and Registration

Neither systematic review registration nor a review protocol was completed.

Information Sources

With the assistance of a health sciences librarian, a computerized systematic search was performed up to July 17, 2016, in the following electronic databases: MEDLINE (Via OvidSP), Embase (via Ovid SP), PubMed, and all EBM Reviews databases (Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, and Cochrane Methodology Register). Using Google Scholar, a limited grey literature search was also performed, which consisted of key word searches with the first 15 Web pages of hits reviewed. The bibliographies of the finally selected articles were also hand searched for additional studies that may have been missed during the database searches. Related articles were also searched from the suggested article menu when an article was searched online. Additional articles were added as suggested by an expert in the field. No language limitations were applied, but the searches were limited to craniofacial studies in humans.

Table 1. Search Strategy for MEDLINE via OVIDSP (1950 to Present)

No.	Searches
1	Exp Maxillofacial development/ OR Growth/ OR human development/
2	Skull/ OR cranial fontanelles/ OR facial bones/ OR pterygopalatine fossa/ OR skull base/ OR spenoid bone/ OR basion.mp. OR articulare.mp. OR sella turcica/ OR exp cranial fossa, posterior/
3	Exp cephalometry/ab, cl, is, mt, st, sn, td, ut [abnormalities, classification, instrumentation, methods, standards, statistics & numerical data, trends, utilization OR exp Cone-beam computed tomographt/ ae, cl, is, my, st, sn, td, ut OR exp imaging, three-dimensional/ ae, cl, is, mt, st, sn, td, ut OR superimpose*.mp. OR exp methods/ is. Mt, st, ut [instrumentation, methods, standards, utilization]
4	1 AND 2 AND 3
5	4 limited to humans

Searches

When performing the above searches, specific subject headings and keywords were used first in MEDLINE (Table 1). The additional searches were modifications from this search, directed for the specific database.

Study Selection

Two reviewers independently reviewed the articles in both steps of the review process based on the decided inclusion and exclusion criteria. Disagreements in article selection were resolved via discussion; those that could not be resolved were brought to another reviewer for consultation.

The phase 1 selection process involved assessing titles and abstracts. Appropriate articles were considered if their abstracts assessed craniofacial growth or analyzed treatment outcome, but had a control group without treatment. Studies assessing fetal growth only or including syndromic patients were excluded.

Phase 2 involved obtaining full copies of the articles selected in phase 1. In this stage, articles were excluded if they did not specifically evaluate S-Ba growth (Appendix 1). Articles were also rejected if they were case reports or reviews. The articles selected to continue assessed the growth and development of S-Ba and surrounding structures.

Data Extraction

Data were extracted from the selected articles on the following items: study design, population characteristics (sample size, sex, age), method used to analyze cranial base growth, results (linear and angulation changes, shape change), and reliability and validity of reported methods (Table 2). The primary outcomes were dimensional changes (quantified as continuous

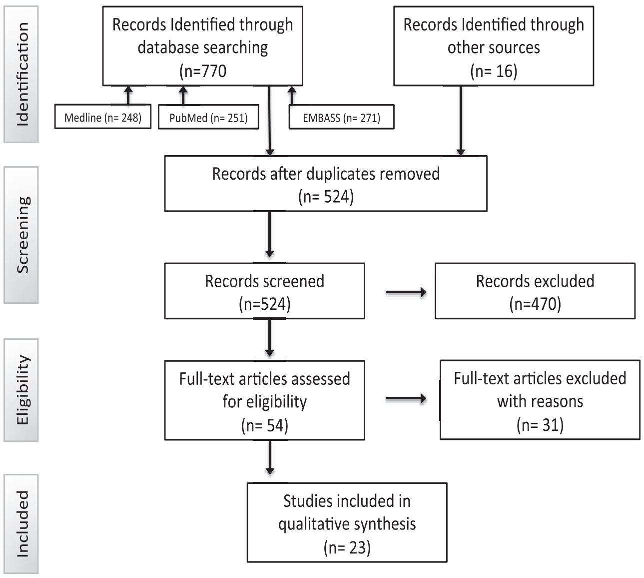

Figure 1. Flow diagram of the study selection.

variables) in S-Ba and surrounding structures during active craniofacial growth and development.

Risk of Bias Assessment

All selected studies were assessed for potential risk of bias using a nonvalidated quality assessment tool implemented in a previous systematic review[15] (Table 3). Two reviewers completed this process separately, and articles with a score of 50% or less were categorized as poor or low quality (high risk of bias). Good quality articles had scores over 50% and up to 75% (moderate risk of bias). Any article receiving a score greater than 75% was considered to have high or excellent quality (low risk of bias).

RESULTS

Study Selection

The selection process at each stage of this systematic review is represented in Figure 1. Twenty-three articles satisfied the selection criteria and were included in this systematic review.

Study Characteristics

A summary of the data and results of the selected articles are shown in Table 2. Of the 23 articles, 5 were cross-sectional in design,[13,16–19] while the remaining 18 were cohort studies.[2,20–36] Samples consisted of craniofacial measurements from living or deceased postnatal human skulls. Validity of the measurements was not determined in any of the studies, while only six reported some form of reliability assessment. All the articles measured multiple time points within the same population or data from multiple age groups.

Risk of Bias Within Studies

Table 4 summarizes results of the risk of bias assessment. The methodological quality of the studies ranged from poor to excellent. The most common weaknesses were failure to validate the accuracy of the findings (none of the studies reported this), insufficient statistical reporting, and failure to calculate or justify sample size.

Results of Individual Studies

Upon review of the pertinent information from the selected articles, we noted that there was a change in all S-Ba linear measurements (from Sella [S] to Basion [Ba]) among the various age groups studied.[16,20–22,25,29,34–36] In addition, there were variable changes in length and angulation among and between all stages of development.[13,27]

Knott observed that the largest absolute change in linear dimension over a 9-year period, from ages 6 to 15, occurred in the postsphenoid region with an annual average of 1 mm.[35] During a similar age interval, other studies also showed similar age-related changes in S-Ba.[31,32] Henneberke and Prahl-Anderson also reported constant growth velocity for S-Ba over 7 years from age 7 to 14 at 1 mm/y and 0.9 mm/y for boys and girls, respectively; the average length of S-Ba was 2.5 mm larger in boys than in girls.[24] On the other hand, other studies showed slightly different growth rates in different age groups and suggested that cranial base growth was closely related to skeletal age.[20,27] Malta et al. showed that the greatest amount of growth was 2.8 mm from time 1 to time 2, which correlated with CS1/2 change in growth to CS3/4.[27]

Five studies showed size and growth differences between males and females as the cranial base dimensions increased,[24,25,28,32,36] whereas the other three studies indicated no difference according to sex.[26,27,31]

Two studies reported changes in S-Ba length in adulthood.[22,26] Bishara observed a significant decrease in the cranial base angle (NSO) and increase in cranial base length from age 26 to 46 years.[22] In a group of adults ranging between the ages of 17 and 50 years, Lewis and Roche reported maximum values for S-Ba length at age 34.5 years in men and 35.0 years in women, with a growth rate of 0.3 mm/y in men and 0.2 mm/y in women.[26]

Growth directions of S-Ba were reported. Downward and backward displacement of basion was observed in one study,[21] which corresponded with the downward and slightly backward movement of the occipital

Table 2. Summary of Characteristics of Included Articles (CS = cervical stage, CVM = cervical vertebrae maturation, ICC = intraclass correlation coefficient, NR = not recorded)

Article	Study Design	Sample Size and Sex	Age	Measurement Method
Arat et al.[20] 2001	Mixed-longitudinal	78 M = 35 F = 43	Group 1: 10–12 y Group 2: 12–15 y Group 3: 15–17 y	3 groups divided based on skeletal maturation Cephalometric & hand-wrist films taken, followed for 4 to 7 y
Arat et al.[21] 2010	Longitudinal	30 Class II Division 1 M = 12 F = 18	T1: 11.98 ± 1.30 T2: 15.32 ± 1.12 T3: 32.12 ± 6.85	• Lateral cephs • Skeletal maturation assessed by CVM • Radiographs traced by one operator & superimposed with the new T-W method & common superimposition methods • Horizontal & vertical distances of cranial landmarks measured from reference lines
Bishara et al.[22] 1994	Longitudinal	30 M = 15 F = 15 Iowa Growth Study	M: 25–45 y F: 26–46 y	• Cephalometric analysis Linear & angular measurements • Dental cast analysis
Franchi et al.[23] 2007	Longitudinal	34 17 Class II Div 1–M (11), F (6) 17 Class I–M (13), F(4) University of Michigan & the Denver Child Growth Study	• T1, prepubertal (CS1) –10 y • T2, postpubertal (CS 6)	• Lateral cephs • Thin-plate spline analysis • Registered at nasion, sella, basion
Henneberke & Prahl-Andersen[24] 1994	Mixed-longitudinal	151 untreated–76 (M), 75 (F) 81 treated–40 (M), 41 (F)	7–14 y Age 7–9 Yearly radiographs Age 9–14 every 6 mo	• Lateral cephs: sella, nasion, basion • Linear measurement of S-N, N-Ba, S-Ba • Growth velocity curve for S-N, N-Ba, S-Ba
Jiang et al.[25] 2007	Longitudinal	28 M = 13 F = 15 • Chinese subjects • Normal occlusion	13–18 y	• Lateral cephs • Modified mesh diagram analysis by sex • Super imposed mesh diagrams at 13 & 18 y at nasion
Lewis & Roche[26] 1988	Longitudinal	20 M = 8 F = 12 Fels Longitudinal Growth Collection	17–50 y	• Lateral cephs linear measurement: S-N, N-Ba, S-Ba
Malta et al.[27] 2009	Longitudinal	36 M = 15 F = 21	10–16 y (M); 9–15 y (F) • T1 prepeak (CS 1 & 2): 10 y (M); 9.4 y (F) • T2 peak (CS 3 & 4): 13 y (M); 11.5;(F) • T3 postpeak (CS 5 & 6): 16 y (M); 15 y (F)	• Lateral cephs • Linear measurement at T1, T2, T3: S-N, Ba-N, Ba-S

Table 2. Extended

Measurement of Change Reported	Results	Validity/Reliability
• Correlated growth potential with growth stage • Linear measurement: tuberculum sella to Basion (S-Ba) • Intra- & inter group differences were examined	Posterior cranial base (S-Ba) showed substantial increase in all developmental phases & variance among developmental stages—growth differences most evident in group 2 & least in group 3—group 2 cranial base growth related to growth potential	NR
Graphed displacement (in mm) among superimposition methods	• Backward movement on Ba in all study periods • Downward displacement of Ba in all study periods	Same procedures repeated for 10 patients 1 mo later Reliability of measurements calculated by Cronbach alpha reliability test
Mean & difference reported: • Cranial base (NSO) angle • Anterior cranial base (S-N) • Posterior cranial base (S-O; "O" is occipital point)	• Posterior cranial base length (S-O) increased: 1.2 mm (F), 1 mm (M) • Cranial base length (N-O) increased: 1.8 mm (F), 1 mm (M) • Cranial base angle (NSO) decreased more in males: 0.4° (F); 1.2° (M)	• Landmarks identified by one investigator & inspected for accuracy by another • Each cephalometric measurement done twice or more until the readings fell within 0.5 mm or 0.5° error
• Thin-plate spline analysis—size & shape differences	No significant shape changes in cranial base from TI to T2 Centroid size changes were significant for Class I & Class II patients from T1 to T2	Traced by one investigator & checked by another
Velocity growth curve & growth percentile	• S-Ba distance increased 7–14 y: 7 mm (M), 6 mm (F) • Growth velocity for S-Ba was constant : 1 mm/y (M), 0.9 mm/y (F) • Sexual dimorphism in actual size, timing, & amount of growth—boys are larger than girls; differences approximately 2.5 mm for N-Ba, 2 mm for S-N, & 1.5 mm for S-Ba • Orthodontic treatment does not affect cranial base growth	Defined a tolerance limit of 0.2–1 mm between two tracings, & measurements were repeated when tolerance limits were exceeded
Proportional analysis Average elaborate mesh diagrams reported	• Uniform increase in craniofacial growth between 13 & 18 • Proportionate growth of posterior cranial base • From 13 to 18 y, both sexes with normal occlusion displayed different growth patterns	• Elaborate mesh diagrams of subjects generated twice 2–4 wk apart. • Measurement error no more than 0.04 from Dahlbergs formula
Reported total increments, age at maximum rate of growth, maximum rate of growth, age at maximum values	• Age at maximum values for S-Ba: 35 y (M), 29 y (F) • Total increment of S-Ba from 17–18 y: 1.5 mm (M), 1 mm (F) • Maximum rates of growth for S-Ba: 34.5 y (M), 35 y (F) • Maximum rates of growth of S-Ba (mm/y): 0.3 (M), 0.2 (F) • No difference between sexes	• One observer traced each radiograph & selected points Measurements between points done by another worker • Mean interobserver difference: 0.09–0.13 mm • Mean interobserver difference: 0.08–0.11 mm
Measurements to represent posterior cranial base (Se-Ba, CC-Ba, CF-Po, Ba-Na)	• During all studied periods posterior cranial base showed significant proportional growth increases • Se-Ba (T1–T3): 3.7mm increase for both sexes—no sex differences	• Inter-rater reliability determined for CVM & measurements (ICC $>$ 0.95)

Table 2. Continued

Article	Study Design	Sample Size and Sex	Age	Measurement Method
Melsen[13] 1969	Cross-sectional	132 skulls (sex unknown)	Grouped according to dental development • Deciduous dentition—48 • Mixed dentition—64 • Permanent (all 8s erupted)—20	• Direct inspection: Closure of speno-occipital synchondrosis (SOS) • Lateral cephs • Tomography of 5 skulls • 22 Linear & 2 angular measurements
Mitani[28] 1973	Longitudinal	30 M = 17 F = 13	7–15 y	• Lateral cephs • Linear measurement of cranial base growth: S-Ba, N-Ba, Ba-Ar
Palomo et al.[29] 2005	Longitudinal	32 (females) 16 Class II Div1 16 Class I – Bolton-Brush Growth Study	T1 = 6 y T2 = 11 y T3 = 15 y	Lateral & frontal cephs—use 3-D landmark frame
Phelan et al.[30] 2014	Longitudinal	24 M = 14 F = 10 University of Michigan & Denver Child Growth Study	T1 (CS 1–2): 8 y 9 m T2 (CS 2–3): 11 y 8 m T3 (CS 4–5): 14 y 2 m T4 (CS 6): 16 y 8 m	• Lateral cephs • Cervical vertebral maturation stage
Sejrsen et al.[17] 1997	Cross-sectional	45 skulls Children = 36 Adults = 9	Based on dental stage	• Direct skull measurement • Photo measurement
Singh et al.[18] 1997	Cross- sectional	142 73 Class III 69 Class I (equal males & females)	5–11	Pretreatment lateral cephs in patients with Class III molar & Class I molar 13 cranial landmarks digitized & traced
Thordarson et al.[31] 2006	Longitudinal	182 M = 95 F = 87	6–16 y	Lateral Cephs: 22 landmarks
Ursi et al.[32] 1993	Mixed-longitudinal	32 M = 16 F = 16 – Bolton-Brush Growth Study (Bolton standard)	6–18 y Records at ages 6, 9, 12, 14, 16, 18	Lateral cephs—measurements of cranial base, maxilla & mandible, vertical, dentoalveolar

Table 2. Extended Continued

Measurement of Change Reported	Results	Validity/Reliability
• Cranial base measurements: N-S, N-Ba, S-Ba, N-S-Ba, N-S-H (Hormion)	• Sella turcica moved 2 mm down & back • Distance between sella & distal surface of synchondral cartilage continued to increase until 2nd molars fully erupted interpreted as growth of synchondrosis • Incipient closure of spheno-occipital synchondrosis (SOS) occurred after complete eruption of all second molars	Duplicate measurements on 10 skulls Renewed markings & new radiographs taken Student's *t*-test did not reveal any systematic error
Mean curve of growth rate—-reported time difference in maximum annual increment of posterior cranial base to mandibular length	• Total increment for S-Ba was smaller in females: 10.3 ± 1.8 mm (M), 7.5 ± 1.7 mm (F) • Growth of S-Ba & mandibular condyle showed significant correlation • Total growth increment of S-Ba was smaller in females than in males compared with that of condyle • 60% of males & females showed coincidence in timing of maximum increment of posterior cranial base & mandibular length.	NR
Procrustes analysis—reported shape change in mm	Continuous shape change from 6 to 15 in both Class II & Class I samples	Intraoperator reliability—same operator identified all landmarks: 37.5% of total sample was digitized 3 times Reported average difference of 0.627 mm
Reported distances & angles • Cranial base measurements: N-S-Ba	No change in cranial base angle (N-S-Ba) T1 = 130.3° ± 5.3° T2 = 129.9° ± 5.1° T3 = 129.8° ± 5.5° T4 = 129.9° ± 6.1°	Cephs traced by one operator, then verified by another
• Reported lengths & widths in mm & plotted on graph • Measurements of the cranial base—3 widths & 3 lengths from external base • Measured between nerve canal openings	• External cranial base grows in width with increasing dental age • Cranial length increases with dental age	Reliability tested by creating local conversion factors which are ratios between distance to the measurement on the skull & same distance measured on photo
Thin-plate spline analysis	Changes in morphology if the posterior cranial base in Class III group— highest magnitudes affected Bolton, basion, & articulare. It indicated compression in the horizontal axis in the occipital region of the posterior cranial base in all age groups, as well as bending, vertical stretching, & narrowing	Upon duplicate digitation, landmarks with more than 1% discrepancy in *x*- & *y*- coordinates were considered unreliable & excluded
Posterior cranial base—angular & linear measurements: N-S-Ba, N-S-Ar S-N, S-Ba, S-Ar, N-Ba	• Posterior cranial base dimensions increased significantly from 6 to 16 y with greater changes in boys: S-Ba: 8.7 mm (M), 6.3 mm (F) N-Ba: 13.7 mm (M), 10.2 mm (F) • Cranial base flexures decreased significantly in both boys & girls: 1.6° (M), 1.0° (F), • No difference in cranial base flexures between boy & girls, either at 6y or at 16y. At 6 y: 130.3 ± 4.6° (M), 129.8 ± 4.8 ° (F) At 16 y: 128.7 ± 5.3° (M), 128.8 ± 5.2° (F)	Reliability—replicate measurement trial performed on 30 cephs of 16-year-olds Intraobserver error—cephs traced in 6-year- olds were double-checked by second observer.
Posterior cranial base—angular & linear measurements: S-N, S-Ba, N-S-Ba	• Sexual dimorphism not evident until age 16 at posterior cranial base length (S-Ba) when males had larger values After 12, females did not show large increments At 6 y: 42.1 mm (M), 38.6 mm (F) ns At 12 y: 44.7 mm (M), 43.9 mm (F) ns At 16 y: 47 mm (M), 44.9 mm (F) $P < .05$ 6 y-18 y: 6mm (M), 6.2 mm (F)	Cephs traced by one investigator & checked for accuracy by a second

Table 2. Continued

Article	Study Design	Sample Size and Sex	Age	Measurement Method
Wilhelm et al.[33] 2001	Longitudinal	43 (equal males & females) Class I group = 22 Class II group = 21– Fels Growth Study	1 mo–14 y T1: 1 mo T2: 2 y T3: 14 y	Lateral cephs
Bjork[2] 1955	Longitudinal	243 (males)	12–20 y T1: 12 y T2: 20 y	Lateral cephs Anterior cranial base superimposition technique
Lavalle[19] 1978	Cross-sectional	250 (males)	7–15 y— Class I, Class II— 4 age groups: 7–9, 9–11, 11–3, & 13–15	Lateral cephs taken & 177 data points placed. *X*- & *y*-coordinates recorded using strip chart digitizer. Data analyzed & placed into 6 categories (coordinates defining the cranial base are of interest here)
Ford[16] 1958	Cross-sectional	71 dry skulls—sex not specified	0–20 years of age	Dry skulls (measured by divider & ruler). 7 linear measurements Grouped based on eruption of dentition
Ohtsuki et al.[34] 1982	Mixed-longitudinal	397 M = 220 F = 177; Fels Growth Study	0–15 y Grouped into ages 0–3, 4–6, 7–18	Lateral cephs—9 landmarks identified
Knott[35] 1969	Longitudinal	37 females Iowa Growth Study	6–15 y T1 = 6 y T2 = 9 y T3 = 12 y T4 = 15 y	Lateral roentgenograms Values obtained by averaging measurements made 2 anthropometrists on 3 independent lateral roentgenogram films.

Table 2. Extended Continued

Measurement of Change Reported	Results	Validity/Reliability
	• No statistically significant changes in cranial base angle (N-S-Ba) and similar for both with a slight decrease with growth	
7 cranial base measurements: S-N, Se-N S-Se S-Ba, S-Occ, Ba-Occ N-S-Ba (°) Se = sphenoethmoidal point Occ = sphenoccipital point	• Growth occurred between all age groups with largest increases between 1 mo & 2 y • No differences in cranial base linear measurements between Class I & II • No differences in cranial base angle between Classes I & II	Reliability assessed by retracing & redigitizing 10 randomly selected radiographs ICC ranged from 0.61 to 0.97
Linear & angular measurements: S-N, S-Ba, S-Ar, N-Ba, N-Ar N-S-Ba (°), N-S-Ar (°)	• Dorsal elongation of cranial base due to endochondral growth at the clivus 12–20 y S-Ba: 3.8 mm, S-Ar: 3.2 mm, N-Ba: 8.1 mm • No marked change in shape of cranial base on average to remain stable with age (N-S-Ba, 0.7°); however, a marked individual variation with age as regards increased or decreased bending was noted • There is parallel lowering of the foramen magnum. • Age variations in growth magnitude, growth form, and size. Spheno-occipital synchondrosis acts as center of rotation in medial region of cranial base. Temporal bone and glenoid fossa can be displaced down,up, forward or back depending on cranial base rotation which affects mandibular position.	NR
Centroids (standard deviation units of the degree of separation between means)	Cranial base length contributed most to discrimination between the 3 categories Craniofacial & facial skeletons were similar to cranial base in sagittal growth	NR
Linear measurements (mm)	Pituitary point-Basion measurement showed continued growth between all grouped skulls	NR
Linear & angular measurements	• S-Ba length increasedconstantly but slowly after the age of 2 up to age 18 • Basion to sphenoocipital synchondrosis, & sella to sphenooccipital synchrondrosis dimensions increased steadily, but sella to sphenoccipital synchondrosis values were smaller. • N-S-Ba angle decreased until age 18	NR
• Linear measurements (mm) N-F: Frontal sinus F-W: ethmoid Presphenoid: W-P Postsphenoid: P-O • Angular measurements (°) —3 cranial base angles: NPO, FPO, WPO F = frontal sinus point W = sphenoidal wing point P = pituitary point, anterior wall of sella	• Postsphenoid segment showed greater dimensional change in mm between 6 & 12 years of age than anterior portions of cranial base. Annual increase of about 1 mm • Postsphenoid segment showed largest absolute change over the 9-y period Average 9-y dimensional change of 17% & averaged 6 mm • Downward & backward direction of change for occipital condylar point in relation to sphenoid plane.	2 anthropometrists measured 3 independent films; averages taken (nearest 0.1 mm & 0.1°)

Table 2. Continued

Article	Study Design	Sample Size and Sex	Age	Measurement Method
Knott[36] 1971	Longitudinal	66 F = 36 M = 30 Iowa Growth Study	6–25 y T1 = 6 y T2 = 11 y T3 = 15 y T4 = 25 y (22–29 y)	Lateral roentgenograms taken at all time points. Data was plotted in mm at all time points & descriptive statistics made

condylar point,[35] downward growth of the clivus,[28] as well as downward and backward growth of sella turcica that was reported in another study.[13]

Changes in the cranial base angulation were also noted. Bjork reported that the cranial base angle gradually bent throughout childhood up to about 10 years, at which point the cranial base reached its final shape and the cranial base angle remained relatively stable.[2,30,32] Conversely, Bishara,[22] Knott,[36] and Lewis and Roche[26] reported a slight decrease with age during adulthood.

A meta-analysis was not feasible because the methodologies of the selected articles were too heterogeneous.

DISCUSSION

This systematic review aimed to analyze published studies that evaluated growth of S-Ba and to evaluate their methodological quality. The results indicated that

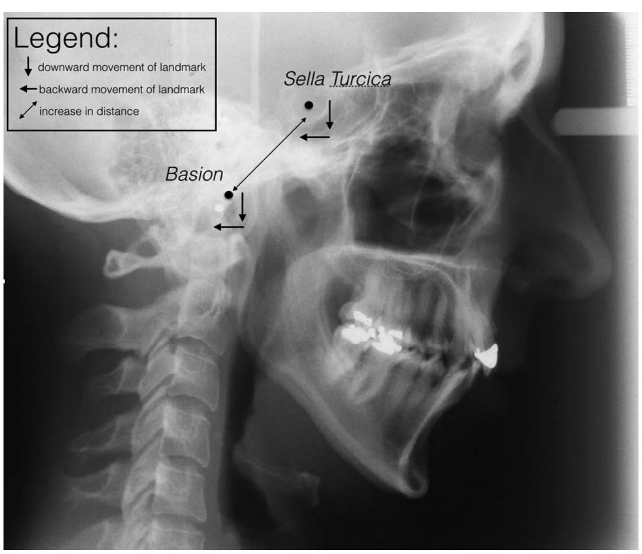

Figure 2. Diagram illustrating general movement of the posterior cranial base.

S-Ba is not a stable structure during craniofacial growth, and changes in S-Ba are primarily due to growth activity at the spheno-occipital synchondrosis, as well as sutural growth (eg, occipitomastoid changes) and cortical drift, in which bone is resorbed and deposited along the superior and inferior surfaces of the basicranium.[2,13,14] With no definitive agreement on timing of the cessation of growth and closure of the spheno-occipital synchondrosis,[13,14] S-Ba growth was reported to continue to grow even by small increments into adulthood and beyond.[22,26]

Proportional growth was reported[20,25]; differential growth rates were also seen. The more significant differential growth rates tended to correlate with pubertal growth spurts and growth potential.[16,20,27,28] A calculated length change over a 9-year period (ages 6–15) was shown.[35] All these studies supported this relationship between S-Ba length increase with activity of the spheno-occipital synchondrosis, since their study periods took place before the estimated closure of the synchondrosis at about age 11–18, based on laminagraphy, autopsy, and serial sections.[13,14,34] Bjork showed dorsal elongation of the cranial base due to endochondral growth at the clivus.[2]

In reference to direction of growth change, basion was shown to move backward and downward,[2,21] with an additional point measured in the general area of basion, occipital condyle point (Bolton), also showing downward and backward movement.[35] The anterior reference point for S-Ba, sella, was shown to move down and back as well[13,15] (Figure 2). Although both basion and sella were displaced in the same direction, these changes seemed to be due to different mechanisms. Movement of basion can be attributed to synchondrosis growth, whereas movement of sella can be attributed to eccentric growth of the sella turcica which remains stable at its anterior wall after around age 7. Intrinsic growth of sella turcica was also shown in a previous systematic review by Afrand et al.[15] As reported by Enlow, development of the endocranium

Table 2. Extended Continued

Measurement of Change Reported	Results	Validity/Reliability
• Linear measurements (mm) N-F: frontal sinus F-W: Ethmoid Presphenoid: W-P Postsphenoid: P-O • Angular measurements (°) —3 cranial base angles: NPO, FPO, WPO F = frontal sinus point W = sphenoidal wing point P = pituitary point, anterior wall of sella	• Postsphenoid segment (P-O) length increased by about 5.3 mm from 6 to 12 y At 6 y: 40.6 mm (M), 39 mm (F) At 12 y: 46.0 mm (M), 44.6 mm (F) At 15 y: 48.8 mm (M), 45.8 mm (F) At 25 y: 50.6 mm (M), 46.7 mm (F) • No differences between sexes at 9-12 After age 12, the difference in length of postsphenoid segment increased between males & females • No significant change in cranial base angle (NPO) for females, small decreases for males.	Two independent measurements made. If differences were greater than 0.2 mm, additional determinations were made & averages obtained.

also occurs by deposition on the outside and resorption from the inside, also referred to as *cortical drift*.[7] This can also explain small changes in location of landmarks from longitudinal cephalograms. Bjork also reported parallel lowering of the foramen magnum.[2]

Angulation changes of the cranial base showed mixed results. Numerous investigators have attempted to correlate cranial base angle with facial type but, in this systematic review, an attempt was made to address solely changes due to growth without analyzing the impact on facial characteristics. The longitudinal study by Ohtsuki et al. showed decreases in S-N-Ba angle up to age 18.[34] In contrast, Phelan et al. showed that there was no change in cranial base angle measured as SNBa.[30] This was also supported by Thordarson et al., who showed no difference in cranial base flexure from age 6 to 16 years.[31] In a longitudinal study by Wilhelm et al., there was no difference reported in cranial base angle between different facial classifications, specifically Class I and Class II.[3,34] In one of the studies by Knott, she concluded that the decrease in WPO angle (which was defined as the angle between the postsphenoid line from P to O and the presphenoid line from W to P) and increase in postsphenoid length corresponded to the movement of the occipital condyle point. She also concluded that angular changes within individuals were small and that statistically insignificant changes were present.[35]

Table 3. Methodological Scoring for the Included Studies (Y = Yes)

Study design (6 Y)
A. Objective clearly defined (Y)
B. Population adequately described (Y)
C. Sample size considered adequate (Y)
D. Selection criteria clearly described (Y) and adequate (Y)
E. Follow-up length clearly described (Y)
Study measurements (4 Y)
F. Measurement method mentioned (Y) and appropriate (Y)
G. Reliability described (Y)
H. Validity described (Y)
Statistical analysis (3 Y)
I. Statistical analysis appropriate (Y)
J. Presentation of data: Exact *P* value stated (Y), variability measures (SD or CI) stated (Y)
Maximum number of Y= 13

When comparing males with females, again we found conflicting data for the amount and rate of growth. Ursi et al. reported no differences in S-Ba length until age 16, when males had larger values and continued to show evidence of growth.[32] In the report by Thordarson et al., no differences were shown between males and females, even as S-Ba lengthened.[31] When comparing male and female longitudinal growth data, Knott showed an increase in postsphenoid length before the age of 6 years and no differences between sexes, but after the age of 12, males showed greater length change.[36] The longitudinal study by Lewis and Roche, which looked at adults up to the age of 50, showed a difference between males and females for maximal growth rate and maximal length of S-Ba. Although these values were small, they still show the potential for dimensional change in the S-Ba region into adulthood.[26] Overall, the present findings suggest that age-related changes in the craniofacial complex do not stop with the onset of adulthood, but continue, albeit at a significantly slower rate, throughout adult life. However, these changes tended to be of small magnitude, so that clinical relevance is somewhat limited and generally would not significantly influence orthodontic treatment planning.

Limitations

The use of a nonvalidated assessment tool[15] has its own drawbacks but, with the absence of one validated tool that clearly applied to the type of studies likely to be included, this was inevitable.

Changes in growth for all studies were reported in millimeters or degrees. Ideally, growth should be reported as a percentage to convey an idea of how

Table 4. Risk of Bias Among Selected Articles (Y = Yes, N = No, p = Partial)

	Study Design					Study Measurements			Statistics			
Article	A	B	C	D	E	F	G	H	I	J	Total	% of Total
Arat 2001	Y	Y	N	Yp	Y	Yp	N	N	Y	YN	7.5	57.7
Arat 2010	Y	Y	N	Yp	Y	Yp	Y	N	Y	NY	9	69.2
Bjork 1955	Y	P	N	NY	Y	YY	Y	N	p	NN	7	53.8
Bishara 1994	Y	Y	N	Yp	Y	YY	Y	N	Y	YY	10.5	80.7
Franchi 2007	Y	Y	N	YY	p	Yp	p	N	Y	YY	9.5	73.1
Henneberke 1994	Y	Y	Y	Yp	N	Yp	p	N	p	pp	8	61.5
Jiang 2007	Y	Y	N	Yp	Y	YY	p	N	p	YY	9.5	73.1
Lavalle 1978	p	Y	Y	Yp	N	Yp	N	N	p	NN	6	46.2
Lewis 1988	Y	p	p	Yp	Y	pp	N	N	p	pN	6.5	50.0
Malta 2009	p	p	N	YY	Y	pp	p	N	Y	YY	8.5	65.4
Melsen 1969	Y	Y	Y	pp	N	pp	N	N	p	NN	5.5	42.3
Mitani 1973	Y	Y	N	Yp	N	Yp	N	N	p	NN	5.5	42.3
Palomo 2005	Y	Y	N	YY	Y	YY	Y	N	p	NN	8.5	65.4
Phelan 2014	Y	Y	N	Yp	Y	YY	Y	N	Y	YY	10.5	80.7
Sejrsen 1997	Y	Y	N	Yp	N	Yp	Y	N	p	NN	6.5	50.0
Singh 1997	Y	Y	N	Yp	N	Yp	Y	N	p	YN	7.5	57.7
Thordarson 2006	Y	Y	Y	YY	Y	YY	Y	N	Y	YY	12	92.3
Ursi 1993	Y	p	N	Yp	N	Yp	Y	N	p	NY	7	53.8
Wilhelm 2001	Y	Y	N	Yp	Y	YY	Y	N	Y	NY	9.5	73.1
Ford 1958	Y	Y	N	YY	N	Yp	N	N	N	NN	5.5	42.2
Ohtsuki 1982	Y	Y	Y	YY	Y	YY	N	N	Y	NY	10	76.9
Knott 1969	p	Y	N	YY	Y	Np	N	N	p	NY	6.5	50.0
Knott 1971	p	Y	N	YY	Y	Np	p	N	p	NY	7	53.8

significant the changes were at any given age. This would also be important when different overall craniofacial sizes were considered.

For assessing growth, long-term longitudinal studies are the best option. Ideal growth studies would follow a large population and obtain records for many years with multiple time points at consistent time intervals. The selected articles varied greatly with regard to the age range studied, developmental stage, and data collection technique and analysis.

In addition, 10 of the 23 selected articles studied subjects from well-known growth studies conducted in North America during the 1930s–1970s. Although they were the best available sample, the same subjects may have been used in multiple studies.

Long-term aging studies that include late adulthood are inherently difficult to conduct, and, as a result, have a number of limitations such as wide variation in subjects' ages, different time spans between examination intervals, and particularly inclusion of 17–18-year-old subjects for whom later adolescent growth was still possible.[22,26]

In the past, two-dimensional lateral cephalometric radiographs were the most commonly used technique to evaluate growth of the cranial base. Measurements in 3-D would provide more accurate information on growth changes in the cranial base as a whole. No 3-D CBCT studies have yet been published on the growth of S-Ba.

CONCLUSIONS

Based on the identified published evidence and considering the stated limitations,

- A significant amount of growth in S-Ba was observed throughout the growth period. Even after pubertal growth had ceased at around 17–18 years, S-Ba was not yet 100% stable and dimensional changes continued into late adulthood, although at a slow rate.
- Growth of S-Ba was generally agreed to be from spheno-occipital synchondrosis growth. Change in length measured from sella to basion was most evident as S-Ba grew.
- Basion displaced downward and backward during craniofacial growth.
- Sella turcica moved downward and backward during craniofacial growth.
- The change in cranial base angle (N-S-Ba) with age was inconclusive.
- Angulation changes could not be consistently identified among different facial types or malocclusions.

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APPENDIX 1 Articles Excluded in Phase 2

Author	Reason
Bassed et al. 2010	Did not discuss posterior cranial base (S-Ba)
Battagel 1994	Only measured soft tissue and jaws
Bondevik 1995	Did not discuss S-Ba
Buschang et al. 1982	Did not measure S-Ba
Cevidanes and Heymann 2009	Did not discuss S-Ba
Cevidanes and Styner 2009	Evaluated a method for superimposition
Coben 1998	Did not measure S-Ba
Edwards et al. 2007	Did not mention S-Ba
Esenlik 2014	Did not discuss S-Ba
Gao et al. 2012	Did not discuss S-Ba
Haffner et al. 1999	Proposed a 3-D analysis technique
Hashemi 2015	Did not discuss S-Ba
Hilloowala et al. 1998	Did not measure S-Ba
Kean et al. 1982	No growth discussion
Klocke et al. 2002	Did not discuss changes of S-Ba
Kuroe et al. 2004	Discussed cranial bases of different populations
Latrou 2002	Not retrieved in English
Masaki 1980	Not retrieved in English
Moss 1983	Did not discuss S-Ba
Nie 2005	No growth measurement
Rosas et al. 2008	Growth not discussed
Sielaff 1991	Not retrieved in English
Steuer 1972	Discussed hypophyseal fossa for superimposition
Tallgren 1974	Did not discuss S-Ba
Tanabe et al. 2002	Did not discuss S-Ba
Thiesen et al. 2013	Discussed only one time point, not growth of cranial base
Viazis 1991	Could not obtain full article
Walker et al. 1972	Did not discuss S-Ba
West et al. 1999	Did not discuss S-Ba
Yang et al. 1990	Not retrieved in English, did not measure S-Ba
Yavuz et al. 2004	Measured only PA cephs