

The influence of asthma on face shape: a three-dimensional study

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SUMMARY Respiratory activity may have an influence on craniofacial development and interact with genetic and environmental factors. It has been suggested that certain medical conditions such as asthma have an influence on face shape. The aim of the study is to investigate whether facial shape is different in individuals diagnosed as having asthma compared with controls. Study design included observational longitudinal cohort study. Asthma was defined as reported wheezing diagnosed at age 7 years and 6 months. The cohort was followed to 15 years of age as part of the Avon Longitudinal Study of Parents and Children. A total of 418 asthmatics and 3010 controls were identified. Three-dimensional laser surface facial scans were obtained. Twenty-one reproducible facial landmarks (x, y, z co-ordinates) were identified. Average facial shells were created for asthmatic and non-asthmatic males and females to explore surface differences. The inter-ala distance was 0.4 mm wider (95% CI) and mid-face height was 0.4 mm (95% CI) shorter in asthmatic females when compared with non-asthmatic females. No facial differences were detected in male subjects. Small but statistically significant differences were detected in mid-face height and inter-ala width between asthmatic and non-asthmatic females. No differences were detected in males. The lack of detection of any facial differences in males may be explained by significant facial variation as a result of achieving different stages of facial growth due to pubertal changes, which may mask any underlying condition effect.

Introduction

The development of an individual's facial shape and form depends on the interactions of genetic factors with environmental factors, including the intensity and duration of the latter (Peng *et al.*, 2005; Paternoster *et al.*, 2012). Altered mechanics of breathing may influence the development of craniofacial structures (Cooper, 1989; Yamada *et al.*, 1997) and interfere with normal mastication and swallowing, which favour harmonious facial growth (Moss, 1962). Nasopharyngeal obstruction often results in the mouth-breathing (Straub, 1994), leading to a change in head posture to compensate for the decrease in nasal airflow (Josell, 1995), which can result in disharmony in the growth and development of orofacial structures (Rubin, 1980).

Numerous systemic medical conditions can influence facial shape, such as type 1 diabetes (El-Bialy *et al.*, 2000), growth hormone deficiency (Kjellberg *et al.*, 2000; Van Erum *et al.*, 1998) and asthma (Mattar *et al.*, 2004; Richmond *et al.*, 2009). Reduced somatic growth, which can accompany chronic asthma, is also associated with changes in facial structures in children (Kjellberg *et al.*, 2000; Pirinen *et al.*, 1994).

Asthma is a chronic disorder, characterized by the interaction of a number of asthma-related genes with environmental factors. The main characteristics include airway

inflammation, intermittent airway obstruction and bronchial hypersensitivity, of which not all are necessarily present in patients to the same degree (Kiley *et al.*, 2007). During the period of most rapid somatic growth after infancy, the prevalence of asthma changes. It has been reported that the prevalence of asthma is higher in boys under 15 years of age than girls of the same age and higher in females 15 years of age and above (To *et al.*, 1996; Krishnan *et al.*, 2001; Schatz *et al.*, 2003).

Patients with chronic asthma symptoms can present with an increased resistance of the lower airways with gas-trapping in the chest (Chaves *et al.*, 2010). The altered mechanics of breathing associated with these changes can lead to shortening of the cervical respiratory muscles, which could alter head and cervical spine posture (Hruska, 1997; Lopes *et al.*, 2007). This may cause dysregulation in the growth and development of the orofacial structures, including narrowing of the maxilla and lower development of the mandible (Bresolin *et al.*, 1984; Solow and Sandham, 2002).

The aim of this study is to investigate differences in facial features in 15-year-old children taking part in a longitudinal follow-up study that were reported as having asthma at 7.5 years of age and a control group drawn from the same population.

Subjects and Methods

Sample

The children involved in this study were recruited from the Avon Longitudinal Study of Parents and Children (ALSPAC). The study was designed to explore how an individual's genotype is influenced by environmental factors impacting on health, behaviour, and development of children (Golding *et al.*, 2001). The initial ALSPAC sample consisted of 14 541 pregnancies. This was the number of pregnant women enrolled in the ALSPAC study with an estimated date of delivery between April 1991 and December 1992. Out of the initial 14 541 pregnancies, all but 69 had known birth outcome. Of these 14 472 pregnancies, 195 were twins, 3 were triplets, and 1 was a quadruplet pregnancy, meaning that there were 14 676 fetuses in the initial ALSPAC sample. Of these 14 676 fetuses, 14 062 were live births, and 13 988 were alive at 1 year.

Mothers were asked to complete postal questionnaires that covered a range of health outcomes, including asthma symptoms and whether a doctor had ever diagnosed asthma in their children at 7.5 years of age (Henderson *et al.*, 2008).

The cohort was re-called when the children were 15 years of age. Invitations were sent to 9985 participants who reported that they were interested to take part in the clinics. Of these, 418 asthmatics (185 females, 233 males) and 3010 controls (1636 females, 1374 males) were included in the study. Body weight and height was measured. The BMI was calculated as follows: $BMI = \text{weight(kg)} / (\text{height(cm)} / 100)^2$. Ethical approval was obtained from the ALSPAC Law and Ethics Committee and the Local Research Ethics Committees prior to the commencement of the study.

Facial imaging

Three-dimensional facial images of the subjects were captured using a pair of high-resolution Vivid 900 laser scanners (Konica Minolta Sensing Europe, Milton Keynes, UK), with a reported manufacturing accuracy of 0.1 mm (Kau *et al.*, 2003). The scanners were controlled with Multi-scan

software (Cebas Computer GmBH, Eppelheim, Germany), and right and left facial scans were saved in a vivid file format. Rapidform 2006 (INUS Technology, Seoul, Korea) was used to process and analyse the facial scans in the manner described in the following paragraphs. The right and left facial scans of each participant were registered and merged using a locally developed subroutine using Rapidform software. Three-dimensional facial images were normalized within a reference framework using three planes: sagittal (Y-Z plane), coronal (X-Y plane), and transverse (X-Z plane), as shown in Figure 1. The origin of the co-ordinate system was the point between the inner corners of the eyes (mid-endocanthion) (men), which, as previous research has shown, is the most stable facial landmark (Toma *et al.*, 2009; Zhurov *et al.*, 2010).

Twenty-one facial soft tissue landmarks (Figure 2, Table 1) were manually identified on each facial image (Toma *et al.*, 2009, 2011), and the x, y and z co-ordinates were recorded. The reproducibility of these landmarks in the three dimensions has been reported previously, generally with an error of less than 1 mm for both intra- and inter-examiner assessments (Toma *et al.*, 2009).

Soft tissue parameters were evaluated as follows: exR-exL (inter-eye distance), al-al (nose width), n-pg (total face height), ls-pg (lower face height), ls-men (mid-face height), exR-pg-exL (mid-face angle), s-sn-pg (face convexity), n-pr-sn (nose prominence), and prn-sn-ls (philtrum depth). The 9 facial parameters included in the analysis were those that describe the main anterior-posterior, vertical and transverse relationships in facial shape analysis. For example, the inter-eye distance and nose width allow transverse analysis. The face height (total, lower and mid) allows for vertical relationships to be studied. Finally, the mid-face angle, facial convexity, nose prominence, and philtrum depth relate to anterior-posterior facial features.

Statistical analysis

The differences in weight, height, and BMI of both genders were estimated by *t*-test. The analysis of the data was carried

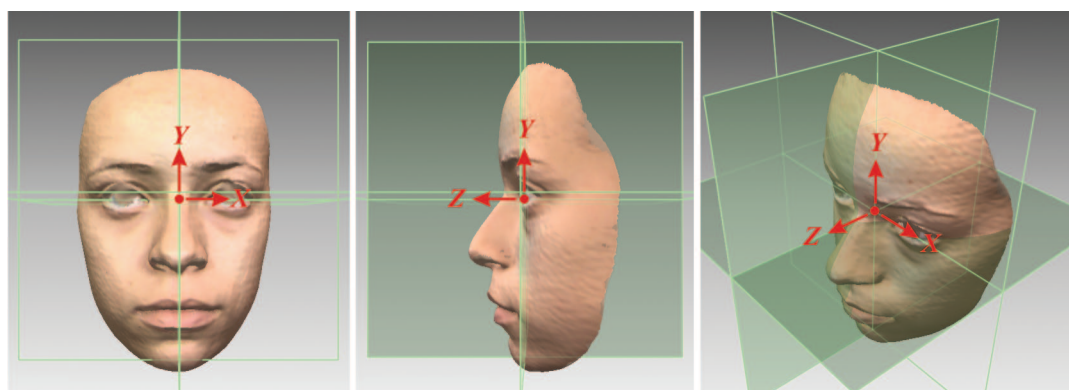


Figure 1 Normalization of facial shells to natural head posture.

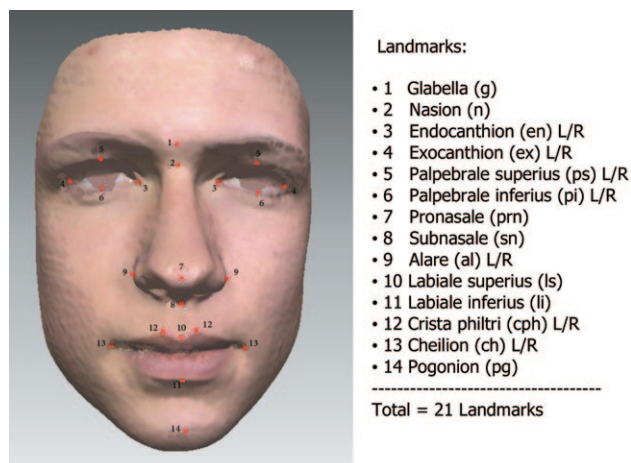


Figure 2 Facial soft tissue landmarks.

out using 95% CIs of the difference in facial parameters were used to examine the magnitude of the differences between the asthmatic and control groups. This was carried out for male and female groups separately as evidence suggests that both gender and asthma prevalence can influence facial growth (Kynnyk *et al.*, 2011; Wenzel *et al.*, 1985). Crouse and Laine-Alava (1999) have indicated gender differences on nasal airflow rate and nasal cross-sectional area. Average facial shells were created for the asthmatic and non-asthmatic females and males using a previously validated method (Kau and Richmond, 2010; Zhurov *et al.*, 2010).

Average faces were superimposed on the mid-endocanthion point (men). Differences in morphology were presented using colour maps, with a tolerance level of 0.25 mm to highlight significant topographical facial differences.

Results

A total of 5253 children attended the clinic at 15 years of age. Of this sample, 506 participants were excluded from analysis for the following reasons: not having their facial images recorded at the time of attending the clinic, poor quality facial scans, non Caucasian, and obvious facial dysmorphology. The sample therefore represented variation population-sample of 4747 Caucasian children (2514 females and 2233 males), of whom 418 children were reported to have asthma at 7.5 years of age (Henderson *et al.*, 2010).

The means of weight (kg), height (cm), and BMI for males and females of both asthmatic and non-asthmatic are shown (Table 2). In asthmatic females the mean BMI was greater than non-asthmatic males and females as well as asthmatic males. There was no significant difference in BMI between asthmatic and non-asthmatic males.

The summary data for the nine facial parameters used in this study are presented (Table 3). To compare the facial

features of asthmatics and non-asthmatics, 95% CIs of the differences in the measured facial parameters were used. When comparing asthmatics with non-asthmatics, there were no statistically significant differences in any of the 9 facial parameters in males. In contrast, three of the nine facial parameters differed in females; nose width, mid-face height, and mid-face angle. Females with an asthma history had on average a 0.4 mm wider nose compared with non-asthmatic females but could be as much as 0.7 mm. The mid-face height of asthmatic females measured from Is-men was on average 0.4 mm shorter than non-asthmatics but could be as much as 0.9 mm. And the mid-face angle of female non-asthmatics was more acute when compared with asthmatics (51.3 degree versus 51.7 degree).

Superimposition of average facial shells of asthmatic and non-asthmatic males showed no morphological differences. Whereas, superimposition of average asthmatic and non-asthmatic females facial shells confirmed the landmark measurements of a wider inter-ala distance. Differences of 0.4–0.5 mm were recorded in the nose width (Figure 3).

Discussion

This study is the first to investigate facial morphology of adolescents suffering from asthma in a large cohort of 15-year-old children using 3D facial imaging. Our findings suggest that there are small differences between the faces of asthmatic and non-asthmatic individuals; this was predominantly for females.

To understand the relevance of the results the underlying mechanisms of facial growth in the context of asthma should be considered. Moss (1997) theorizes that growth of the face occurs as a response to functional needs and is mediated by soft tissue in which the jaws are embedded. In simple terms, the soft tissues grow, and both bone and cartilage react. For example, the orbit grows as a result of growth of the eyes. The cranium increases in size as a result of growth of the brain, which separates the cranial bones at the sutures while new bone passively fills in at these sites (Moss, 1997). Nasal breathing encourages an increase in size of the nasal cavity in all directions with the floor of the nose developing in a downward and forward direction. Therefore the presence of any respiratory problems may affect normal craniofacial growth. Normal craniofacial growth seems to depend on normal physiological nasal breathing (Fricke *et al.*, 1993; Solow *et al.*, 1984; Vig *et al.*, 1981). It has been argued that mouth-breathing in children results from pharyngeal obstruction (Oulis *et al.*, 1994), affecting the position of the craniofacial muscles and the mandible, leading to occlusal and skeletal alterations (Subtelny, 1975).

Suppression of growth secondary to asthmatic conditions has been suggested (Nelson and Drash, 1959; Falliers

Table 1 Facial soft tissue landmarks (points).

Facial Region	Landmark name	Abbr.	Definition
Eyes	Endocanthion(R)	En	Inner commissure of the right eye fissure
	Endocanthion(L)	En	Inner commissure of the left eye fissure
	Exocanthion (R)	Ex	Outer commissure of the right eye fissure
	Exocanthion (L)	Ex	Outer commissure of the left eye fissure
	Palpebrale superius (R)	Ps	Superior mid-portion of the free margin of upper Rt eyelid
	Palpebrale superius (L)	Ps	Superior mid-portion of the free margin of upper Lt eyelid
	Palpebrale inferius (R)	Pi	Inferior mid-portion of the free margin of upper Rt eyelid
Forehead	Palpebrale inferius (L)	Pi	Inferior mid-portion of the free margin of upper Lt eyelid
	Glabella	G	Most prominent midline point between the eyebrows
Nose	Nasion	N	Deepest point of nasal bridge
	Pronasale	Prn	Most protruded point of the apex nasi, identified in lateral view of the rest position of the head.
	Subnasale	Sn	Mid-point of angle at columella base where lower border of nose and surface of upper lip meet.
	Alare (R)	Al	Most lateral point on right alar contour.
	Alare (L)	Al	Most lateral point on left alar contour.
Lips and Mouth	Labiale superius	Ls	Mid-point of the upper vermillion line
	Labiale inferius	Li	Mid-point of the lower vermillion line
	Crista philtri (R)	Cph	Point on right elevated margin of the philtrum just above the vermillion line
	Crista philtri (L)	Cph	Point on left elevated margin of the philtrum just above the vermillion line
	Cheilion (R)	Ch	Point located at right labial commissure.
	Cheilion (L)	Ch	Point located at left labial commissure.
Chin	Pogonion	Pg	Most anterior mid-point of the chin.

et al., 1961; Russell, 1993; Doull, 2004). Some studies have suggested that growth retardation in asthmatic children may occur for a number of reasons, including malnutrition (Snyder *et al.*, 1967; Murray *et al.*, 1976), chronic infection (Snyder *et al.*, 1967; Hauspie *et al.*, 1977), steroid therapy (Murray *et al.*, 1976; Falliers *et al.*, 1961; Morris, 1975; McCowan, 1998; Price, 2002), diminishing lung function (McNicol and Williams, 1973; Hauspie *et al.*, 1977), hypoxia (Murray *et al.*, 1976), and long-term stress (Hauspie *et al.*, 1977).

Several clinical studies have supported the theory of a relationship between head posture in breathing difficulties and craniofacial morphology (Solow and Tallgren, 1976; Thompson, 1978; Wenzel *et al.*, 1985). Wenzel (1985) studied the craniofacial morphology in children with asthma from lateral skull radiographs of a small sample of 50 asthmatic children with differing ages (6–16 years of age) compared with 50 control children and concluded that small differences were found in craniofacial morphology between asthmatic children and controls. The severely affected children tended to have a greater change in morphology and more likely to develop a retrognathic jaw associated with extension of the head.

Asthma or 'variable airflow obstruction' refers to episodic breathing difficulties that sometimes result in dysfunction, severe disability, and even death (Cecil *et al.*, 1940). Asthma is recognized from a pattern of one or more characteristic symptoms, including cough, wheeze, chest tightness and dyspnoea, and is better confirmed by evidence of variable or reversible airflow obstruction accompanying symptoms. Bresolin *et al.* (1983) found that the upper face height as well as maxillary and mandibular inclinations were increased in 30 mouth breathers and allergic children aged 6–12 years compared with 15 control children. In addition, they found that the mouth-breathing group was associated with retrognathism of the upper and lower jaws. The conflicting findings between the previous studies and the present study can be explained by diagnosis, age of children, sample size, and methods of recruitment and assessment.

The present study investigated children diagnosed as wheezing at 7.5 years of age, while Bresolin *et al.* evaluated dentofacial development in the mouth breather with allergy. Moreover, the use of the three-dimensional imaging

Table 2 Mean values for height, weight and BMI.

Facial Parameter	Asthmatic control difference in mean					
	Male (n = 233)	(n = 1374)	(95%CI)	Female (n = 186)	(n = 1636)	(95%CI)
Height (cm)	172.39 (7.711)	174.78 (7.493)	2.39 (1.36–3.42)	164.06 (5.840)	164.66 (6.011)	0.59 (–0.31–1.50)
Weight (kg)	61.87 (10.832)	64.31 (12.173)	2.44 (0.80–4.08)	61.29 (11.774)	58.64 (10.484)	–2.64 (–4.25–1.04)
BMI	20.76 (3.077)	20.97 (3.329)	0.21 (–0.23–0.66)	22.71 (3.841)	21.60 (3.513)	–1.11 (–1.65–0.57)

Table 3 Descriptive statistics of facial parameters and a test between asthmatic and non-asthmatic groups.

Facial parameter	Asthmatic control difference in mean (SD)					
	Male (<i>n</i> = 233)	(<i>n</i> = 1374)	(95%CI)	Female (<i>n</i> = 186)	(<i>n</i> = 1636)	(95%CI)
Eyes distance (mm) (exR-exL)	88.4 (4.27)	88.3 (4.04)	−0.09 (−0.65–0.46)	87.0 (3.60)	86.6 (3.96)	−0.4 (−0.96–1.94)
Nose width (mm) (al-al)	34.7 (2.86)	35.0 (2.51)	0.25 (−0.91–0.60)	32.7 (2.39)	32.2 (2.24)	0.4 (−0.72–0.03)
Total face height (mm) (pg-n)	104.3 (6.05)	104.8 (6.15)	−0.54 (−0.28–1.37)	98.9 (4.79)	99.0 (5.16)	0.12 (−0.65–0.89)
Lower face (mm) (ls-pg)	37.5 (3.53)	37.9 (3.80)	0.38 (−1.29–0.90)	35.6 (2.93)	35.6 (3.12)	0.07 (−0.39–0.54)
Mid-face (mm) (ls-men)	63.8 (3.55)	64.3 (3.39)	0.45 (−0.01–0.92)	58.9 (2.93)	59.4 (2.96)	0.49 (0.04–0.93)
Mid-face (angle) (exR-pg-exL)	49.8° (2.70)	49.5° (2.71)	−0.27 (−0.65–0.10)	51.7° (2.71)	51.3° (2.65)	−0.41 (−0.81–0.02)
Face convexity (n-sn-pg)	180.4° (1.51)	180.4° (1.83)	0.09 (−0.15–0.33)	180.5° (1.53)	180.4° (1.64)	−0.06 (−0.31–0.19)
Nose prominence (n-prn-sn)	179.8° (3.17)	180.0° (2.76)	0.20 (−0.25–0.65)	180.2° (2.73)	179° (4.63)	−0.06 (−0.53–0.40)
Philtrum depth (Prn-sn-ls)	127.5° (9.38)	127.3° (8.97)	−0.11 (−1.35–1.12)	127.7° (8.89)	126.9° (8.39)	−0.84 (−2.12–0.42)

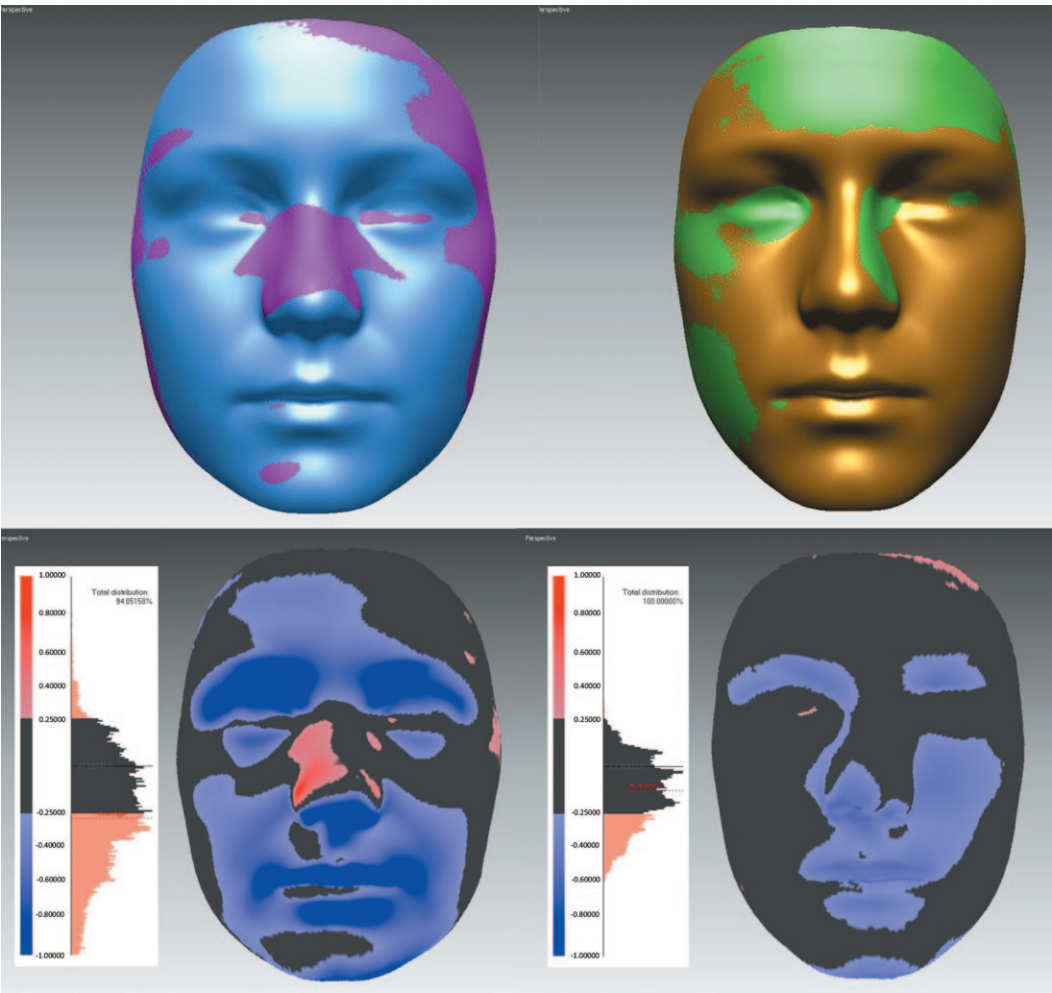


Figure 3 Superimposition of asthmatic and non-asthmatic females average facial shells (left) and males (right).

technique has provided more accurate and precise analysis of facial morphology, than using anthropometry, cephalometry, and photography (Kau *et al.*, 2004, 2005).

Epidemiologic studies of asthma show differences in asthma prevalence and severity related to age and gender.

The likelihood of developing asthma is about 10.5 per cent greater in women than men, with a significant increase in the severity of asthma in women after puberty (de Marco *et al.*, 2000; McCallister *et al.*, 2011). This could explain why females showed greater facial morphological

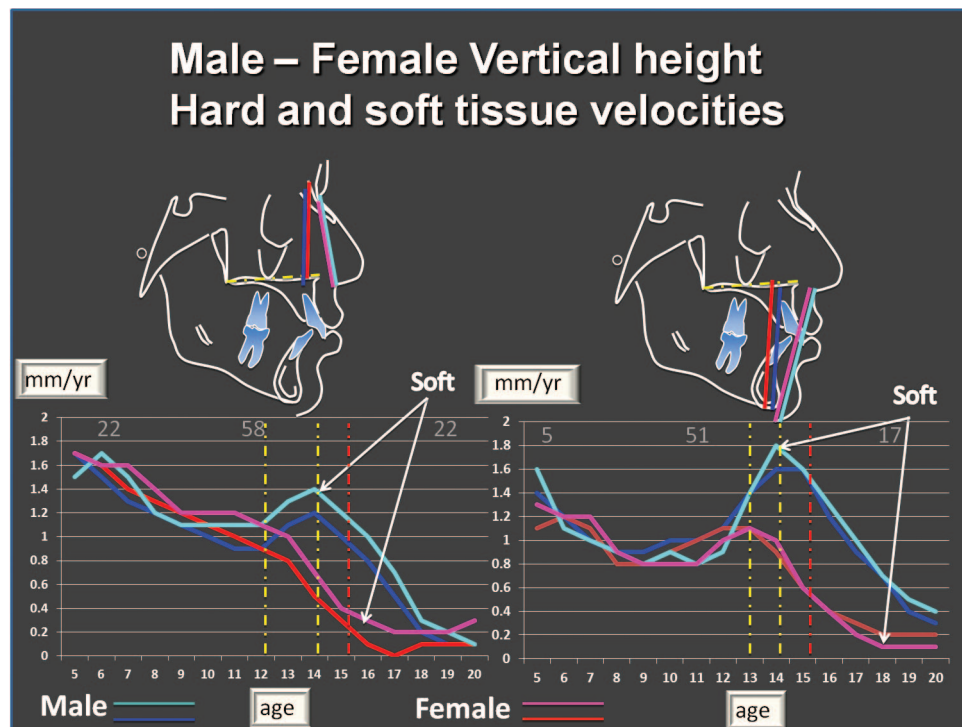


Figure 4 Soft and hard tissue velocities in relation to upper and lower face height. Both males and females show similar steady growth velocities (1–1.2 mm/year) from 7 to 11 years of age. Taken from Bhatia SN, Leighton BC A manual of facial growth. Oxford Medical Publications, 1993.

differences between the asthmatics and control groups when compared with males. It should be noted however that although statistical significance was inferred for some facial parameters in the female group, the linear differences were small. Therefore their clinical significance will require further investigation. Researchers continue to explore the potential influence of the female sex hormones, hormonal influences that are associated with both asthma and craniofacial growth, increased bronchial hyper-responsiveness, and altered perception of airflow obstruction (Kynyk *et al.*, 2011).

We found a slightly increased nasal width (al-al) in asthmatic females and might presume that size of nasal airway is related to body size in general, as BMI values of asthmatic females were slightly larger than males in this study. However, previous studies in children and young adults have indicated that BMI has an effect on airflow rate and nasal airway size (Laine-Alava and Minkinen, 1997; Crouse Uand Laine-Alava MT 1999). Laine-Alava and Minkinen, 1997 found that the values for airflow rate tended to increase with the increasing BMI, indicating that subjects with larger body size need higher air volumes. Therefore, asthmatic females showed an increased nasal cross-sectional area.

The other positive finding was the shorter mid-face height in asthmatic females. The design of the study was observational longitudinal, as such the analysis was facilitated to find association and not test for hypothesis. Therefore,

albeit a positive association was found but with asthmatic females with a reduced mid-face height, the clinical and potential statistical significance is likely to be minimal.

We were not able to detect any facial differences in asthmatic and non-asthmatic males. This may be explained by wide facial variation due to individuals reaching different stages in puberty which may mask any underlying condition effect.

Cephalometric investigations on longitudinal samples have identified a pubertal spurt in craniofacial growth that is characterized by wide individual variations in onset, duration, and rate (Ekström, 1982; Hunter, 1966; Nanda, 1955). Generally, puberty starts in females approximately 2 years before males and is shorter in duration. The mean peak height velocity occurs at around the age 12 years in females and 14 years in males. In a 15 year old population most of the facial growth will be completed in females but there would be still be significant growth potential in males. Therefore timing of assessment of the influence of medical conditions may be better conducted between 7 to 10 years of age when there are similar growth rates in males and females (Figure 4) or at 20 years of age or greater when facial growth has significantly reduced.

One of the limitations of the study is that the severity of asthma and the type of medication (i.e. inhaler or oral steroid) was not recorded. However, if these factors influence craniofacial growth and shape, they are likely to have small effects (Doull, 2004; Hauspie *et al.*, 1977; Price

et al., 2002; Russell, 1993). The loss to follow-up for the study group was 34 per cent, which is acceptable for a longitudinal study of this size (Fewtrell *et al.*, 2008). Another limitation is that co-morbidity (e.g. allergic rhinitis) was not considered. However this could be investigated retrospectively in the 15-year-old cohort to address this. Lastly as the study only recorded 3D facial shape at 15 years, there is no indication as to when the differences in facial morphology developed.

Despite these limitations, the results of the study are based on a population cohort of UK children that is broadly representative of the general population. In addition the imaging method is valid, and therefore, the methods are transferrable to other population groups (Kau *et al.*, 2005).

Conclusion

The research method provides a framework for the investigation of medical conditions and environmental factors that can influence child's health and development using a three-dimensional facial imaging.

The study found;

1. Statistically significant differences found between asthmatic and non-asthmatic females; inter-ala width was 0.4 mm wider and the face height was 0.4 mm smaller in asthmatic females.
2. There were no statistical differences in facial parameters for asthmatic and non-asthmatic males.
3. Three-dimensional facial imaging has sufficient resolution to detect small differences in facial morphologies and can be used to explore genetic and environmental effects on facial morphology.

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