

A three-dimensional analysis of the effect of atopy on face shape

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SUMMARY Three-dimensional (3D) imaging technology has been widely used to analyse facial morphology and has revealed an influence of some medical conditions on craniofacial growth and morphology.

The aim of the study is to investigate whether craniofacial morphology is different in atopic Caucasian children compared with controls.

Study design included observational longitudinal cohort study. Atopy was diagnosed via skin-prick tests performed at 7.5 years of age. The cohort was followed to 15 years of age as part of the Avon Longitudinal Study of Parents and Children (ALSPAC). A total of 734 atopic and 2829 controls were identified. 3D laser surface facial scans were obtained at 15 years of age. Twenty-one reproducible facial landmarks (x, y, z co-ordinates) were identified on each facial scan. Inter-landmark distances and average facial shells for atopic and non-atopic children were compared with explore differences in face shape between the groups.

Both total anterior face height (pg–g, pg–men) and mid-face height (ls–men, sn–men, n–sn) were longer (0.6 and 0.4 mm respectively) in atopic children when compared with non-atopic children. No facial differences were detected in the transverse and antero-posterior relationships.

Small but statistically significant differences were detected in the total and mid-face height between atopic and non-atopic children. No differences were detected in the transverse and antero-posterior relationships.

Introduction

Atopy is the tendency to develop immunoglobulin E (IgE) antibodies to commonly encountered environmental allergens (Jarvis and Burney, 1998). The most common clinical manifestations of atopy are asthma, allergic rhinitis, and atopic dermatitis (Burney *et al.*, 1989). Development of atopic responses has been linked to several genes and gene products (Steinke *et al.*, 2008). Thus, atopic diseases represent a complex gene and environmental interaction in which environmental antigens interact with the immune system, producing atopic (IgE) responses (Peden, 2000). In epidemiological studies, skin prick testing provides an expedient test for atopy (Oryszczyn, 1991; Cookson *et al.*, 1989; Zimmerman, 1988), and/or elevated total serum IgE level (Cookson *et al.*, 1989; Stempel, 1980).

Coca and Cooke (1923) introduced the term ‘atopy’, which mainly indicates people with asthma, fever, eczema, urticaria, and the food allergies. The author gave another definition of the atopy: ‘it is the abnormal condition of immunology and it would cause inflammation of organs in the body’. The combination of mast cells and basophils are used to differentiate atopy from non-atopy. The author stated that atopy is the genetic predisposition that would produce mast cells and may

cause eosinophilia. The term atopy represents the group of diseases that mainly develops in allergic conditions.

The relevance of atopy in facial growth is that environmental stimuli and irritations may cause chronic swelling of the nasopharyngeal mucous membranes in atopic individuals. Obstruction of the nasal airway due to atopic allergy can therefore be associated with mouth breathing and facial anomalies, including malocclusions such as increased overjet, a higher palatal plane, narrowing of both upper and lower arches, and proclination of incisors (Jefferson, 2010; Faria, 2002; Koski and Lähdemäki, 1975; Linder-Aronson, 1974, 1970; Ricketts, 1968). The switch from nasal to oronasal breathing results in functional adaptation including an increase in total face height and vertical development of the lower anterior face (Tourne, 1990).

A retrospective cephalometric comparative study of 55 paediatric patients who suffered from nasal obstruction and 61 controls indicated that naso-respiratory obstruction was associated with mouth breathing. In the children with nasal obstruction there was a higher tendency for a backward rotation of the mandible associated with an increase in anterior face height by 3 degree (SD 5) of the mandibular plane angle (Harari *et al.*, 2010).

The influence of asthma on face shape has been reported previously in a large sample indicating that the mid-face height was 0.4 mm (95% CI) shorter in asthmatic when compared with non-asthmatic females (Al Ali *et al.*, 2012).

The effect of atopy on craniofacial structures (determined cephalometrically) was studied in 100 11-year-old school children and indicated a backward rotation of the mandibular body and an anterior lowering of the nasal floor in the moderate and severe nasal allergy groups. Differences were more pronounced in children presenting with atopy and enlarged adenoids (Hannuksela, 1981).

Cephalometric analysis was undertaken for 30 chronically allergic mouth-breathing subjects and 15 nonallergic nose breathers (Bresolin and co-workers in 1983) and revealed that the upper anterior face height and the total anterior face height were significantly larger in the mouth breathers. The maxilla and mandible were more retrognathic in mouth breathers. Maxillary intermolar width was narrower in the mouth breathers and was associated with a higher prevalence of posterior crossbite.

Three-dimensional (3D) analyses of facial surface anatomy are fundamental in determining deviations from normal facial morphology. 3D imaging technologies have provided both reliable and accurate data capture for facial analysis (Kau and Richmond, 2010; Kau *et al.*, 2005; Kevin and Oleh, 1996, Toma *et al.*, 2009, 2011; Kau *et al.*, 2005). Quantitative analysis of facial morphology is of vital importance in determining facial discrepancies in individuals with craniofacial deformities (Kevin and Oleh, 1996). Two-dimensional techniques such as cephalometry and photographs are of limited value in describing the complex 3D topography of the facial surface.

The aim of the present study is to investigate the influence of atopy on craniofacial morphology using 3D laser scan imaging technology and to assess the null hypothesis that there is no difference in face shape in atopic and non-atopic Caucasian children.

Subjects and Methods

Sample

The children involved in this study were recruited from the Avon Longitudinal Study of Parents and Children (ALSPAC), which was designed to explore genetic and environmental factors impacting on health, behaviour, and development of children (Golding *et al.*, 2001). Ethical approval was obtained from the ALSPAC Law and Ethics Committee and the Local Research Ethics Committees prior to the commencement of the study.

All children were invited to attend a clinic at 7.5 years of age, where skin-prick tests were performed to a panel of six allergens (house dust mite, cat, mixed grass, mixed nuts, peanut, and milk) and a positive (1 % histamine solution) and negative (diluent) controls (Henderson *et al.*, 2008).

Skin tests were carried out on the anterior surface of the left arm using new disposable sterile lancets for each allergen tested. The skin was pricked through a drop of allergen solutions, which were blotted off after five minutes, and the test were read after a further 10 minutes (Henderson *et al.*, 2008). The maximum weal diameter was measured and a second measurement performed at 90 degree to the first, and the mean weal diameter was calculated. Atopy was defined as a positive skin-prick test to the above allergens (weal diameter ≥ 1 mm with as negative diluents response, Henderson *et al.*, 2008).

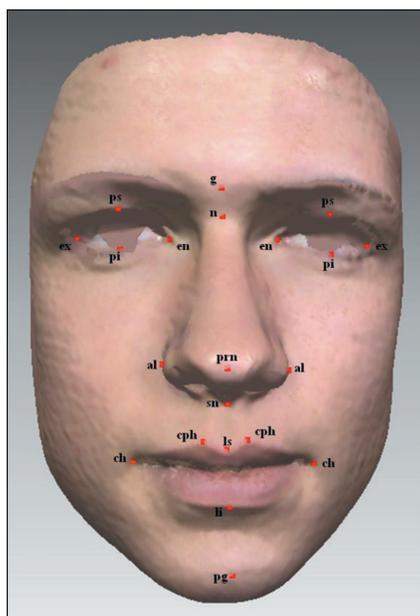
The cohort was re-called when the children were 15 years of age where 3D laser facial scans were acquired. Body weight and height were also measured for all children. The final sample in this study consisted of 734 atopic and 2829 non-atopic control group children.

Facial imaging

3D facial images of the children 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). Rapidform 2006 (INUS Technology, Seoul, Korea) was used to process and analyse the facial scans. The right and left facial scans of each child were registered and merged using a locally developed subroutine for above mentioned software. Quality of registration of right and left facial scans for all subjects was determined using average distance between shells and percentage of overlap between the right and left shells. The facial scan was evaluated as having good quality when the average distance between right and left facial scan is 0.3 mm and below and is the most suitable for merging (Kau and Richmond, 2008). Generally, 70–100 per cent overlap of the right and left facial shells with a tolerance level set at 0.5 mm indicates facial shells suitable for merging, and any non-suitable scans were excluded from the sample of the study (Toma *et al.*, 2008; Kau and Richmond, 2010).

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

Antero-posterior, vertical and transverse relationships in face shape analysis were determined using the following soft tissue parameters: exR–exL (inter-eye distance) and al–al (nose width) allows transverse analysis, pg–g, pg–men (total face height), sn–men, Is–men, n–sn (mid-face height) allows vertical relationship analysis, s–sn–pg (face convexity) relate to antero-posterior features. The statistical analysis used 95% confidence intervals (CIs) of the difference in facial parameters between the atopic and non-atopic group.



Glabella (g): Most prominent midline point between the eyebrows
 Nasion (n): Deepest point of nasal bridge
 Endocanthion (en) L/R: Inner commissure of the left and right eye fissure
 Exocanthion(ex) L/R: Outer commissure of the left and right eye fissure
 Palpebrale superius (ps) L/R: Superior mid-portion of the free margin of upper left and right eyelid
 Palpebrale inferius (pi) L/R: Inferior mid-portion of the free margin of upper left and right eyelid
 Pronasale (pm): Most protruded point of the apex nasi
 Subnasale (sn): Midpoint of angle at columella base
 Alare (al) L/R: Most lateral point on left and right alar contour
 Labiale superius (ls): Mid-point of the upper vermillion line
 Labiale inferius (li) L/R: Mid-point of the lower vermillion line
 Crista philtri (cph) L/R: Point on right elevated margin of the philtrum just above the vermillion line
 Cheilion (ch) L/R: Point located at left and right labial commissure
 Pogonion (pg) L/R: Most anterior mid-point of the chin

Figure 1 Facial soft tissue landmarks.

The facial parameters included in the analysis were the most common parameters reported that might be influenced by different modes of breathing (Harari *et al.*, 2010; Kerr *et al.*, 1989; Wenzel *et al.*, 1985; Bresolin *et al.*, 1983).

Average facial shells were created for atopic and non-atopic children using a previously validated method (Kau and Richmond, 2010; Zhurov *et al.*, 2010). Average faces were superimposed on the mid-endocanthion point. Differences in morphology were presented using colour maps, with a tolerance level of 0.1 mm to highlight significant topographical facial differences.

Body weight was measured using Tanita scales to the nearest 0.1 kg. Height was measured to the nearest 0.1 cm using Harpenden stadiometer (Lawlor *et al.*, 2010). Body mass index (BMI) was then calculated as weight (kg) divided by the square of height (m^2).

Statistical analysis

To compare the facial features of atopic and non-atopic children, independent *t*-test, 95% CI of the differences in the measured facial parameters were used.

Results

The sample represented 3563 Caucasian children (1692 male/ 1871 female) with no obvious facial dysmorphology. Of the 3563 ALSPAC children, 734 children (411 male/ 323 female) were recorded as atopic at age 7.5 years (Henderson *et al.*, 2008). Mean BMI of the study sample was within the range (21.2 kg/m^2 ; reported normal range $17\text{--}24.2 \text{ kg/m}^2$, Cole *et al.*, 1998; Cole *et al.*, 1995) with

no significant differences between the atopic and the non-atopic group.

Generally, the parameters describing transverse distances and the antero-posterior features in atopic children did not differ significantly from the non-atopic group (Table 1). However, all the parameters that describe vertical relationships showed significant differences between the atopic and non-atopic children. Both total anterior face height (pg–g, pg–men) and mid-face height (ls–men, sn–men, n–sn) were longer (0.6 and 0.4 mm, respectively) in atopic children when compared with non-atopic children. Superimposition of average facial shells of atopic and non-atopic children showed a significant morphological difference between the groups in the z direction. The direction of the differences for the average facial shells for the atopy and non-atopic groups are shown in three presentations of colour deviation maps (Figure 2). The cheeks and chin are less prominent in the atopic group, and the atopic children showed an increased nose width (0.49 mm) compared with non-atopic children.

Discussion

This study is the first to investigate the influence of atopy on facial morphology in a large cohort of 15-year-old children using 3D facial imaging. Currently available 3D soft tissue imaging technologies allow clinicians to evaluate facial differences as a result of medical and surgical interventions. The 3D laser scanning system has the advantage of being quick, non-invasive, and easy to use unlike other 3D hard tissue imaging systems, such as Cone Beam Computed Tomography (CBCT) and Magnetic Resonance

Table 1 Summary of the statistics of 3D co-ordinates.

	Atopic (n = 734)		Non-atopic (n = 2829)		Mean difference	95% confidence interval
	Mean	Standard deviation(SD)	Mean	SD		
Eyes Distance (mm, exR–exL)	87.4	3.97	87.5	4.05	0.06	–0.26–0.39
Nose width (mm, al–al)	33.8	2.86	33.6	2.68	–0.18	–0.40–0.03
Mid-face (mm, ls–men)	62.0	4.22	61.6	3.95	–0.45	–0.79–0.11
Mid-face (mm, sn–men)	48.5	3.69	48.0	3.43	–0.42	–0.71–0.13
Mid-face (mm, n–sn)	52.6	3.94	52.3	3.83	–0.34	–0.65–0.03
Total face height (mm, pg–g)	114.2	6.38	113.6	6.23	–0.60	–1.09–0.07
Total face height (mm, pg–men)	94.1	5.85	93.6	5.66	–0.60	–1.03–0.11
Face convexity (angle, n–sn–pg)	162.0	5.51	162.5	5.64	0.41	–0.04–0.86

Imaging (MRI), which are both expensive, time-consuming, and with CBCT presenting a radiation risk (Kau *et al.*, 2007).

The present study revealed that laser scanner can be used in large-scale population studies and is able to detect small facial differences (0.6 mm) in atopic children who had longer faces when compared with non-atopic children.

While craniofacial morphology is primarily determined by heredity (David and Carlson, 2005), environmental stimuli also markedly influence the growth of the bones, as for instance in patients with partially or totally obstructed nasal airways (Kiliç & Oktay, 2008; Dunn *et al.*, 1973). Atopic conditions are associated with chronic swelling of the nasopharyngeal membrane that can affect normal

breathing (Hannuksela, 1981). The mode of breathing and its effect on craniofacial growth has been a controversial issue within orthodontics for decades. It has been described that obstructed nasal breathing leads to mouth breathing and the so called ‘adenoidal face’ (long face syndrome) with an increased anterior face height (Chaves *et al.*, 2010; Bresolin *et al.*, 1983; Linder-Aronson, 1970; Subtelny, 1954). This craniofacial development has been explained by changes in the muscular balance. Mouth breathing leads to a lower tongue position in the oral cavity that will alter the force balance from the cheeks and tongue, which may be associated with an increased anterior face height, a steep mandibular plane angle resulting in a retrognathic mandible. In addition, incompetent lips, a narrow upper dental arch, retroclined mandibular incisors are also seen, in children

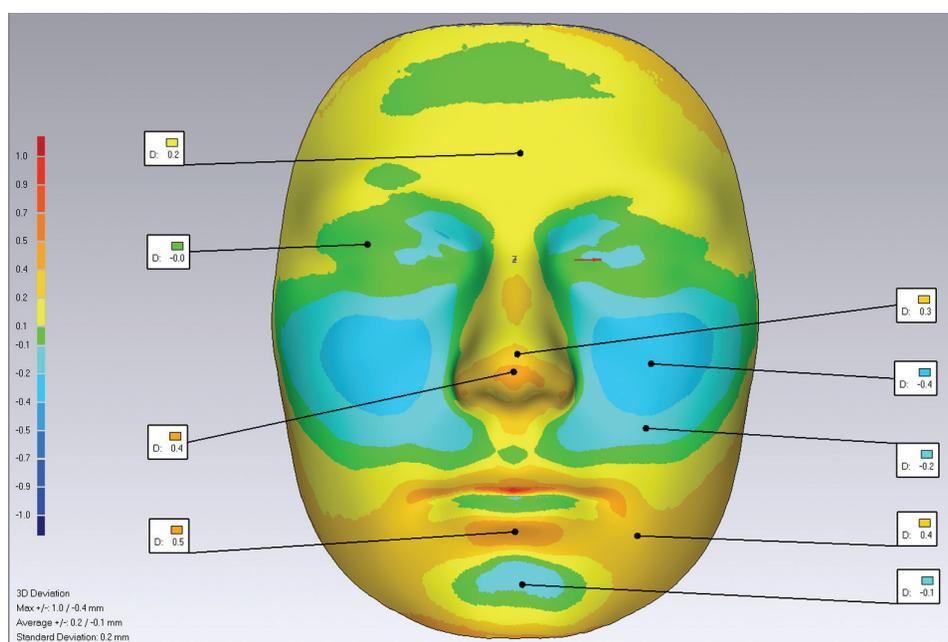


Figure 2 The green areas represent no difference in the atopy and control groups (0 mm). The blue area indicates less prominent cheeks and chin point in the atopic group (0.1–0.4 mm) the deeper blue representing greater facial retrusion in the atopic group. The yellow areas are those prominent features in the atopic face—prominent forehead, nose, lower lip and wider forehead, nose and lower jaw (0.1–0.5 mm).

with reported nasal breathing compared with healthy controls (Solow *et al.*, 1984; McNamara, 1981; Linder-Aronson, 1979; Solow and Kreiborg, 1977).

Previous data and results from the 3D study of the influence of asthma on face shape of 4747 children from Avon Longitudinal Study of Parents and children (Al Ali *et al.*, 2012) showed shorter mid-face height in asthmatic females (0.4 mm) compared with non-asthmatic children. The confliction with results in this study could be explained by the fact that the relationship between atopy and asthma is not straightforward (Carroll *et al.*, 2006). The available epidemiological evidence suggests that the proportion of asthma cases that are attributed to atopy is less than one-half, indicating that the importance of atopy as a cause of asthma in individuals may have been overemphasized (Pearce *et al.*, 1999).

Findings in the present study are consistent with the proposed possible contribution of environmental stimuli, such as atopic allergic conditions and breathing difficulty on craniofacial growth and morphology. Atopic diseases, therefore, should be taken into consideration when examining orthodontic patients and when planning treatment for the correction of malocclusion.

Although results have revealed an association between mouth breathing in atopic allergy and modification in craniofacial growth and morphology, there is a need to know how much nasal obstruction has to occur before an effect on facial growth is observable? Is this a reversible condition and is there a time dependent relationship? These questions required a fundamental premise of being able to define nasal obstruction its position and severity (Vig, 1998).

Conclusion

The results of this study indicate that face shape differences were present in atopic children compared with matched control. The major features included increased mid-face height and total anterior face height. The research methodology provides a framework for the investigation of environmental factors that can influence craniofacial development using 3D facial imaging.

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