Three-dimensional analysis of cranial growth from 6 to 12 months of age

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SUMMARY The aim of this study was to generate three-dimensional data of the physiological growth of the infant’s cranium in the significant growth phase from 6 to 12 months of age. In a longitudinal observational study non-invasive 3D data using an optical surface scanner were generated of the entire head of 52 Caucasian infants (27 females and 25 males) between the ages of 6 (T1) and 12 (T2) months.

The circumference of the head increased by 6.51 per cent (from 43.50 to 46.33 cm). Analysis of width and length showed that the head grows 2.84 per cent more in length, resulting in a decrease in the cranial index of 2.52 per cent (from 83.87 to 81.76 per cent). The highest increment observed was in the total volume of the cranium, with an increase of 18.76 per cent (from 1229.01 to 1459.57 cm³). Comparison of the left and right sides of the head by measuring the diagonal symmetry difference showed a difference of only 0.37 cm. Overall, the symmetry-related parameters showed an almost symmetric development of the cranium in infants.

The findings should provide valuable information on physiological growth and development of the infant’s cranium. Therefore the high growth rate of the cranium in the first year of life suggests that this period is a critical period in which the disruption of developmental processes may have long-lasting effects on the morphology of the cranium with a prognostically unfavourable effect of the further growth of the viscerocranium.

Introduction

Modern humans are characterized by a large and complex neurocranium. The primary functions of the cranium are to protect the brain and to provide a platform for craniofacial growth. The morphology of the cranium is associated with brain development, facial orientation, and evolutionary changes such as bipedalism with an upright posture (Adams and Moore, 1975; Zollikofer et al., 2008).

During the postnatal development of the cranium, growth occurs in all three dimensions. Expansion in the sagittal (antero-posterior depth), transverse (width), and vertical (height) directions leads to substantial changes in the size, shape, and proportions of the entire cranium as skeletal maturation progresses.

Understanding the complexity of cranial growth, cranial function, and cranial architecture is important for testing hypotheses concerning many aspects of craniofacial evolution and variations (Lieberman et al., 2002). Therefore, craniometric data have been used to quantify the variations in the cranium and to differentiate morphology from pathomorphology (Roseman and Weaver, 2004). Particularly within the context of increasing neurocranial asymmetries due to positioning, which result in posterior deformational plagiocephaly or brachycephaly, a clear classification system is necessary (Argenta et al., 2004).

To analyse the development and growth of a malformed cranium, longitudinal growth data for normal development are indispensable. The majority of growth studies based on surface measurements of the head in healthy Caucasian subjects are cross-sectional (Farkas and Posnick 1992; Farkas et al., 1992a). Although craniometric data have been used extensively to ascertain variations in head shape and size in deceased individuals, there is little information regarding living humans during development, especially during early years (Vannucci et al., 2011). Moreover, these studies started after the first year of life, thus excluding the time span of maximum growth of the cranium. Therefore, no information on changes in this significant growth phase have been provided to date (Farkas et al., 1992a).

Many studies involving measurements of the human skull have been performed by researchers in different disciplines, such as anthropology and biology (Coquerelle et al., 2011; Ross and Williams, 2010). Different angular and linear anthropometric variables have been established to quantify growth changes (Farkas et al., 1992a). In addition, cephalometric radiography provides the ability
to study the craniofacial complex. Longitudinal growth studies from the last century used metallic implants as markers to determine the magnitude of growth at specific areas of the craniofacial complex (Bjork, 1964, 1968). These data provide two-dimensional information about growth increments (Bjork, 1968).

With the modern technical approaches of magnetic resonance imaging and computed tomography, three-dimensional (3D) data can be generated. Significant disadvantages of using these methods in infants are the need for sedation and the radiation exposure associated with CT scans, respectively (Brenner and Hall, 2007; Schweitzer et al., 2012).

The aim of this study was to generate a 3D longitudinal database of cranial growth using a non-invasive approach. These data might be used as a reference when analysing specific anomalies affecting cranial growth. Moreover, a 3D database of the physiological growth of the cranium can be associated with other clinical parameters such as age, sex, state of health, and total body length. If accurate values for such parameters are available, the proper interpretation of various aspects of cranial morphology, including anomalies in the cranial development, might be possible.

Subjects and Method

Subjects
The analysis of the growth pattern of the calvarium from 6 to 12 month of age was conducted using 52 Caucasian infants (27 females and 25 males). To generate 3D growth data, two acquisition dates, at 6 and 12 months of age, were prospectively established. The infants were recruited from paediatric practices by means of an information brochure. The mean age at the first growth data acquisition (T1) was $6.3 \pm 0.5$ months, and the mean age at the second data acquisition (T2) was $11.5 \pm 0.6$ months. The inclusion criteria were as follows: birth between the 37th and the 42nd week of gestation (birth of the infants: mean, $39.2 \pm SD\ 1.3$ weeks of gestation), a birth weight of more than 3000 grams (weight of the infants: mean $3211.9 \pm SD\ 446.9$ grams), and no visible deformity of the head. No twins were included in the sample. Infants with any type of medical or neurological disorder, regardless of its relevance to head growth, were excluded from the study. Infants that had undergone previous operations or had congenital anomalies or syndromes were excluded from the study as well.

Growth data acquisition
This pilot study was based on a prospective longitudinal design, which was reviewed and approved by the Ethics Committee of the Medical Faculty of the University Wuerzburg (ethics number 143/09). The study was carried out according to the Declaration of Helsinki, and written consent was obtained from each infant’s parents.

For the analysis of the growth of the calvarium, 3D data of the entire head of every infant were generated. The 3D data were generated using a standardized recording protocol as described in the literature (Meyer-Marcotty et al., 2012). The infants were seated in a special chair, where infants could sit, as soon as they can support their own head (bumbo floor seat®, Bumbo International). To avoid artefacts due to hair on the head, each infant was fitted with a tight nylon cap before recording and was centered in the scanner.

The entire head of each infant was recorded circularly with no contact by a specially photo-optical scanner for infant recordings (3dMD®, Atlanta, GA, USA). Using five synchronized cameras, 360 degree data acquisition based on the stereophotogrammetric method could be guaranteed (Figure 1a). Using this procedure, only one scan is required. Therefore the recording time of 1.5 ms allows a fast data acquisition time, which is necessary to prevent artefacts due to movements of the infant. By using this photo-optical scanner no radiation was used. Therefore the whole data acquisition procedure was completely non-invasive.

3D data analysis

After triangulation and editing, the scans were converted to a common 3D data format (.stl) and analysed with Cranioform Analytics 4.0 3D software (Cranioform®, Alpnach, Switzerland). To align the 3D datasets in virtual space, a co-ordinate system was established based on four anatomically defined reference points (tragion left (Tl), tragiion right (Tr), nasion (N) and subnasale (Sn)). The aligning procedure had been performed in a previous study (Meyer-Marcotty et al., 2012). First, the midpoint of the co-ordinate system was defined as the intersection of the tragus connection line. Based in the midpoint (M), a line through the N represents the y-axis. To construct the x-axis, in the first step a sagittal reference plane through the M, N, and Sn was defined. The x-axis is then defined as the line perpendicular to the plane starting at the M of the co-ordinate system. Finally, the z-axis is defined the vertical line perpendicular to the other two axes (also starting at the M).

After the 3D image of the head was virtually orientated, two reference planes were defined for the analysis. The base plane (0-plane) includes all three reference points (Tr, Tl, N). The measurement plane was defined as the plane parallel to the 0-plane at the level of the maximum posterior curvature in the occipital region (Figure 1b).

To quantify the growth of the cranium longitudinally, 10 parameters in all three spatial dimensions were defined. To differentiate the 10 parameters, they were divided into six growth-related variables and four symmetry-related parameters (Figure 2a-c). The growth-related parameters were the following: maximum circumference, maximum width, maximum length, maximum height, ratio of the maximum width to the maximum length (CI index), and
total cranial volume. The following measurements were defined as symmetry-related parameters: the diagonal difference, the ear offset, and the anterior and posterior cranial asymmetry indices (ACAI/PCAI) (Table 1a/1b).

Statistical data analysis

Statistical analysis was performed using the IBM® SPSS® Statistics version 19.0 software for Windows (IBM Germany GmbH, Ehningen, Germany). A descriptive approach was used for all 10 parameters (mean, standard deviation). Distribution-independent, nonparametric analysis was performed using the Wilcoxon test to compare T1 and T2, and using the Mann–Whitney U test to compare the parameters between females and males at T1 and T2. Additionally, the growth increment was calculated as a percentage for each parameter. The level of significance was P < 0.05. To determine the method error, 10 randomly selected 3D datasets were measured again after a 1 week interval.

Results

Reliability of the parameters

Calculation of the Dahlberg coefficients showed good reproducibility for each 3D parameter (Table 2). All parameters
had a clinically irrelevant method error related to the parameters’ absolut value.

Growth-related parameters

The growth-related parameters at T1 and T2 are shown in Table 3. As expected, all growth-related measurements of linear distances in all three dimensions and the total volume of the cranium increased from 6 to 12 months of age. The increment of growth for all infants was statistically significant in relation to the initial values (circumference: $P < 0.001$; width: $P < 0.001$; length: $P < 0.001$; vertex height: $P < 0.001$; total volume: $P < 0.001$). The highest increment of growth was observed in the total volume of the cranium, with an increase of 18.76 per cent. In contrast, the cephalic index, which is a measure of the width-to-length ratio, exhibited a significant decrease over the observation period (CI: $P < 0.001$).

Sex-specific analysis showed a significantly higher circumference and length in male infants at 6 and 12 months of age (circumference: T1: $P = 0.012$; T2: $P = 0.003$; length: T1: $P = 0.049$; T2: $P = 0.017$). However, there were no sex-related differences in the growth increment between T1 and T2 with respect to the circumference or any other two-dimensional parameter. Another sex-specific difference was observed in the total volume at 12 months of age with a higher value in males ($P = 0.013$), leading in a statistical significant higher increment of growth in males ($P = 0.049$).

Symmetry-related parameters

The results of the symmetry-related parameters at T1 and T2 are shown in Table 4. None of the parameters showed a statistically significant difference in the analysis of all infants. The sex-specific analysis showed initially a higher degree of the ear offset in females, which was no longer detectable at T2. The values of the diagonal differences and the ear offset were nearly the same in all infants. In contrast, the PCAI was always higher than the ACAI in all infants at both 6 and 12 months of age.

Discussion

In this prospective clinical study, the morphology of the cranium was measured in healthy infants. To analyse the growth of the cranium from the sixth to the 12th month of age, 451x728]P. MEYER-MARCOTTY ET AL.

Figure 2c  3D growth-related parameter: Total volume—Sum of all anterior (Q1/Q2) and posterior (Q3/Q4) cuboid volumes relative to the 0-plane. 3D symmetry-related parameters: ACAI—Q1/Q2: anterior cuboid volumes; PCAI—Q3/Q4: posterior cuboid volumes

Table 1a  Definition of the growth-related parameters for the 3D-analysis of the cranium.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>unit</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circumference</td>
<td>cm</td>
<td>Maximum distance around the head on the measurement plane</td>
</tr>
<tr>
<td>Width</td>
<td>cm</td>
<td>Maximum width of the head on the measurement plane</td>
</tr>
<tr>
<td>Length</td>
<td>cm</td>
<td>Maximum length of the head on the measurement plane</td>
</tr>
<tr>
<td>CI-Index</td>
<td>%</td>
<td>Cephalic Index—ratio of the maximum width to maximum length on the measurement plane ×100</td>
</tr>
<tr>
<td>Vertex height</td>
<td>cm</td>
<td>Maximum height of the head starting from the midpoint (M); height of the z-axis.</td>
</tr>
<tr>
<td>Total volume</td>
<td>cm$^3$</td>
<td>Sum of all anterior and posterior cuboid volumes relative to the 0-plane.</td>
</tr>
</tbody>
</table>

Figure 3  3D-Growth-related changes of a infant’s head from 6 to 12 months of age. The scale range is from 6.1 mm (blue level) to −7.6 mm (red level).
age, a longitudinal 3D database of the entire head was generated. 3D imaging based on the principles of stereophotogrammetry was used as a non-invasive approach.

In contrast to two-dimensional linear and angular anthropometric measurements, the method used in this study enables additional volumetric calculations of the neurocranium (Farkas et al., 1992a; Schaaf et al., 2010). Furthermore, by generating a virtual model, the data analysis is almost completely independent of patient compliance. This independence ensures the method’s reproducibility, especially when recording infants (McKay et al., 2010; Weinberg et al., 2006). The clinically irrelevant measurement error found in this study demonstrates the high reproducibility of the method.

For the longitudinal analysis of growth the 3D data were aligned on a co-ordinate system defined through four anatomical reference points. Therefore, all measurements were based on this reference plane. A difficult aspect in a longitudinal analysis is that in the infant head all regions are changing their size and shape through growth. This means that there are no unchangable and stable areas for the registration. In future growth studies geometric morphometrics with procrustes registration could be used to avoid the selection of one reference plane to compare multiple forms and to separate size from shape (Krey and Dannhauer, 2008).

Table 1b Definition of the symmetry-related parameters for the 3D-analysis of the cranium.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 Diagonal difference cm</td>
<td>Compares the right side of the skull to the left side of the skull by measuring the difference of the longest diagonal from the anterior left to the posterior right and the longest diagonal from the anterior right to the posterior left on the measurement plane.</td>
</tr>
<tr>
<td>8 Ear offset cm</td>
<td>Offset of the tragus points on the 0-plane in the sagittal direction</td>
</tr>
</tbody>
</table>
| 9 ACAI—Anterior Cranial Asymmetry Index % | The ratio of the two anterior cuboid volumes: \[
\frac{\text{larger cuboid volume} - \text{smaller cuboid volume}}{\text{smaller cuboid volume}} \times 100
\] |
| 10 PCAI—Posterior Cranial Asymmetry Index % | The ratio of the two posterior cuboid volumes: \[
\frac{\text{larger cuboid volume} - \text{smaller cuboid volume}}{\text{smaller cuboid volume}} \times 100
\] |

Table 2 Method errors according to Dahlberg (1940).

<table>
<thead>
<tr>
<th>Growth-related parameters</th>
<th>unit</th>
<th>Reproducibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Circumference cm</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>2 Width cm</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>3 Length cm</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>4 CI-index %</td>
<td></td>
<td>0.11</td>
</tr>
<tr>
<td>5 Vertex height cm</td>
<td></td>
<td>0.08</td>
</tr>
<tr>
<td>6 Total volume cm'</td>
<td></td>
<td>7.93</td>
</tr>
<tr>
<td>Symmetry-related parameters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 Diagonal difference cm</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>8 Ear offset cm</td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>9 ACAI %</td>
<td></td>
<td>2.12</td>
</tr>
<tr>
<td>10 PCAI %</td>
<td></td>
<td>1.93</td>
</tr>
</tbody>
</table>

As expected, the growth-related parameters exhibited significant increases in all three dimensions of the cranium. The expanding brain exerts separating tensional forces upon the cranium. In this context, the brain acts as a ‘functional matrix’ by determining the extent of neurocranial bone growth (Sperber, 2001). Unfortunately, most data regarding the anthropometric growth of the head have been gathered starting after the first year of life with a cross-sectional study design (Farkas and Posnick, 1992; Farkas et al., 1992a, 1992b). Up to now there are no longitudinal data in the literature about the 3D growth of the infant’s head in the first year of life. Therefore, this pilot study could give first longitudinal data about the physiological growth of the infant’s cranium from 6 to 12 months of age.

As total brain volume increases by approximately 101 per cent in the first year life, the present study has made available detailed 3D information on this most dynamic phase of postnatal growth of the cranium (Knickmeyer et al., 2008). The highly dynamic nature of this phase is reflected in the increase in the circumference of approximately 6.51 per cent in all infants from 6 to 12 months of age in this study. Related to brain expansion, the rapidly enlarging circumference of the head is a good two-dimensional indicator of brain
Table 3
Analysis of the growth-related parameters of the infants at 6 months of age (T1) and 12 months of age (T2). Mean and standard deviation (SD); significant (S) for *P < 0.05; **P < 0.01; ***P < 0.001.

<table>
<thead>
<tr>
<th>Growth-related parameters</th>
<th>T1</th>
<th>T2</th>
<th>Δ(T2-T1)</th>
<th>F (M versus F)</th>
<th>P (M versus T1)</th>
<th>P (F versus T1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Circumference (cm)</td>
<td>43.50 (1.25)</td>
<td>44.00 (1.03)</td>
<td>43.04 (1.27)</td>
<td>0.012*</td>
<td>46.33 (1.30)</td>
<td>46.91 (1.15)</td>
</tr>
<tr>
<td>2 Width (cm)</td>
<td>12.50 (0.52)</td>
<td>12.62 (0.53)</td>
<td>12.40 (0.51)</td>
<td>0.116</td>
<td>13.02 (0.54)</td>
<td>13.12 (0.47)</td>
</tr>
<tr>
<td>3 Length (cm)</td>
<td>8.35 (0.47)</td>
<td>8.76 (0.43)</td>
<td>8.12 (0.41)</td>
<td>0.098</td>
<td>8.67 (0.42)</td>
<td>8.77 (0.41)</td>
</tr>
<tr>
<td>4 CI (%)</td>
<td>83.87 (4.92)</td>
<td>83.76 (5.15)</td>
<td>83.98 (4.83)</td>
<td>0.885</td>
<td>83.76 (4.43)</td>
<td>83.50 (4.38)</td>
</tr>
<tr>
<td>5 Vertex-height (cm)</td>
<td>10.94 (0.41)</td>
<td>11.32 (0.40)</td>
<td>10.97 (0.49)</td>
<td>0.032</td>
<td>11.01 (0.41)</td>
<td>10.97 (0.49)</td>
</tr>
<tr>
<td>6 Total volume (cm³)</td>
<td>1299.01 (100.32)</td>
<td>1327.30 (100.6)</td>
<td>28.29 (100.03)</td>
<td>0.009</td>
<td>1362.87 (100.6)</td>
<td>1327.30 (100.6)</td>
</tr>
</tbody>
</table>

Increment of growth (IG) in percent (Wilcoxon test to compare T1 and T2). Increment of growth (IG) in percent (Wilcoxon test to compare T1 and T2).

The significantly greater circumference and length in males at 6 and 12 months of age could be related to a greater brain and head size as the result of the sexual dimorphism (Bulygina et al., 2006).

Analysis of the width and length measurements showed that the head grows 2.84 per cent more in length than in width in the first year of life in all infants. This greater growth in length is responsible for the decrease in the cephalic index over the observation period. The cephalic index is frequently used when analysing malformed head shapes (Schaa et al., 2010). Unfortunately, there is little information on the cephalic index of the normal head shape. In the 1970s, a cephalic index of 76.7 per cent in infants at 12 months of age was reported (Dekaban, 1977). More recent publications suggest that the cranial index has risen to 80–85 per cent since 1992 in response to the supine sleeping position of infants (Graham et al., 2005; Hutchison et al., 2004; Kane et al., 1996). This increase is supported by the results of the present study, which showed a CI of 81.76 per cent at 12 months of age.

Of all cranial dimensions, the head height is the least frequently analysed. Only one cross-sectional study has published data regarding head height by direct measurement of the infant’s head (Dekaban 1977). The data from that cross-sectional study (head height: 11.0 mm in males and 10.4 mm in females at 6 months of age; 11.3 mm in males and 11.0 mm in females at 12 months of age) are consistent with the data from the present longitudinal study (Dekaban 1977). Therefore, these data could be used as references to differentiate normal and abnormal growth patterns. Clinically, this differentiation could be helpful in the treatment of infants with craniosynostosis.

The total volume of the cranium exhibited the most growth, with an increase of 18.76 per cent over the 6 month observation period. This increase is in accordance with previously published data obtained using invasive computed tomography. In a retrospective analysis, head computed tomography scans showed an increase of almost 19.5 per cent from 6 to 12 months of age (Kamdar et al., 2009). Therefore, similar values for the 3D growth rate can be obtained using a non-invasive approach.

Despite the large number of studies about cranial asymmetries published in recent years, there is no information about the symmetry of the cranium in healthy infants. There are no standard definitions of ‘normal’ baseline infantile head symmetry and normal variances. Moreover, the ideal head shape is not yet known (Lipira et al., 2010). The two-dimensional symmetry-related parameters used in this study revealed an almost symmetric shape of the cranium in healthy infants with a physiologically formed head. Only the ear offset was initially higher in females. But this difference was not detectable at 12 months of age anymore.

The mean diagonal difference was 0.37 cm and the ear offset was 0.24 cm at 6 months of age, and these values remained stable over the observation period. These results
Table 4 Analysis of the symmetry-related parameters of the infants at 6 months of age (T1) and 12 months of age (T2). Mean and standard deviation (SD); significant (S) for \( P < 0.05 \); Increment of growth (IG) in per cent (Wilcoxon test to compare T1 and T2. and Mann–Whitney \( U \)-test to compare females and males at T1 and T2).

<table>
<thead>
<tr>
<th>Symmetry-related parameters</th>
<th>T1 Mean (SD)</th>
<th>T2 Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (n = 52)</td>
<td>M (n = 25)</td>
</tr>
<tr>
<td>1 Diagonal difference (cm)</td>
<td>0.37 (0.23)</td>
<td>0.36 (0.24)</td>
</tr>
<tr>
<td>2 Ear offset (cm)</td>
<td>0.24 (0.18)</td>
<td>0.20 (0.19)</td>
</tr>
<tr>
<td>3 ACAI (%)</td>
<td>4.78 (3.03)</td>
<td>4.48 (3.30)</td>
</tr>
<tr>
<td>4 PCAI (%)</td>
<td>6.52 (5.01)</td>
<td>6.46 (4.34)</td>
</tr>
</tbody>
</table>

\* \( P < 0.05 \).

support the findings of Moss et al., who classified asymmetries of the cranium as severe if the deformity of the cranium was greater than 1.2 cm (Moss, 1997). Therefore, the data from the present study could be used as a reference based on healthy infants when analysing anomalies affecting cranial growth.

The 3D data of the symmetry analysis confirm the 2D findings of a symmetric shape of the cranium in healthy infants during the first year of life.

The difference in size between the left and right anterior cuboid volumes was 4.78 per cent at 6 months of age, respectively 5.19 per cent at 12 month of age. The difference in size of the left and right posterior cuboid volumes differed by 6.52 per cent, respectively 5.29 per cent, from each other. An interesting finding was that the per cent difference of the posterior cuboid volumes was always higher than that of the anterior cuboid volumes. This difference in magnitude might be associated with a mild position-induced growth inhibition of the occipital region caused by the supine sleeping position.

A limitation of the study lies in the fact that data before the 6th month of life were not analysed. But this is due to the weak neuromotorical development as well as the poor head control in the first months of life; therefore, data were analysed in the second half of the first year of life. Secondly, the sample size does not allow a calculation of the infant’s head growth curve. Although future studies on cranial development might include the first months of life with an increase in the number of infants, up to now there is no study reporting longitudinal data on cranial growth neither in the first nor in the second half of the first year of life. Therefore our reported findings should provide valuable information on physiological growth and development of the infant’s cranium.

Conclusion

The 3D data generated in this study for the entire heads of healthy infants could be used for diagnostic evaluation and to analyse the growth of the cranium from 6 to 12 months of age. Moreover, these normative data are clinically helpful in the correction of cranial asymmetries induced by craniosynostosis or positional plagiocephaly.

The high growth rate of the cranium in the first year of life suggests that this is a critical period in which the disruption of developmental processes may have long-lasting or permanent effects on the morphology of the cranium, with a prognostically unfavourable effect on the later growth of the viscerocranium.

Acknowledgements

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