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Original Research Article

Facial anthropometry in an adult male with Sotos syndrome

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Abstract

Introduction: Sotos Syndrome is a dominant autossomic disease caused by a mutation in NSD1 gene localized in chromosome 5. The craniofacial phenotype of Sotos Syndrome is quite distinctive, especially in the young child, and includes macrocephaly, widely-spaced eyes, prominent chin and mandible, high and curved forehead, palpebral slits oblique and downward, long and narrow face. This phenotype plays an important role in the identification of this syndrome. **Objective:** The aim of this study was to analyze the craniofacial anthropometric landmarks of a young adult male with medical diagnosis of Sotos Syndrome. **Material and methods:** Using noninvasive method of craniofacial anthropometry, twenty five anthropometric measurements were taken of the individual and compared with the facial pattern of non-syndromic individuals, matched in gender and age. The findings were standards and converted to Z-scores. **Results:** the data analysis showed that the majority of variables were in supernormal range (greater than +2 standard deviation (SD). None none of them was in the subnormal range (less than –2SD). **Conclusion:** Anthropometric analysis of Sotos Syndrome demonstrated the usefulness of craniofacial analysis in defining abnormal craniofacial dimensions.

Introduction

Sotos Syndrome (SS) is a dominant autossomic disease caused by a mutation in NSD1 gene localized in chromosome 5 and was first described by Sotos *et al.* [12]. The majority of patients (80%-90%) have a point mutation or deletion on NSD1 gene, being more common find partial or total deletions of this gene in the Japanese population [4]. The non-efficiency of this gene prevents the synthesis of NSD1 protein, a nuclear receptor that plays a role in cell growth and differentiation [15].

This Syndrome is association with neonatal icterus, scoliosis, apoplexy, strabismus, conductive hearing loss, congenital heart anomalies and renal abnormalities. Also is characterized by mental retardation, ranging from mild to severe and cognitive deficits that can be variable. Delay in child development and language acquisition are common [2, 9].

The disorder is characterized by a distinctive facial appearance, overgrowth in childhood and includes widely-spaced eyes, prominent chin and mandible, high and curved forehead, palpebral slits oblique and downward, long and narrow face and macrocephaly [2, 4, 9]. Especially the macrocephaly plays an important role in the identification of this syndrome once the height and cephalic perimeter varies of one to two standard deviation (SD) above average, being perceptible mainly in childhood. Based in these evidences, the aim of this study was to describe the facial anthropometry of a Brazilian adult male with Sotos Syndrome.

Material and methods

This research is an observational study of a caucasian male, aged 22 years, who had been diagnosed with SS and was assisted in the clinic of Dentistry for Patients with Special Needs at Pontifical Catholic University of Paraná, Curitiba, Brazil. Data about medical and dental history was obtained. The subject was in a good health status, without any major systemic disease and no previous history of craniofacial surgery or trauma. His legal guardian gave written, informed consent to his participation in the investigation.

After clinical examination, frontal and lateral photographs were taken with help of a digital lens Sony® camera positioned 1.0 meter away from the face, using ambient lighting conditions. The photos were then taken in natural head posture with a backdrop of 1 centimeter scale placed parallel to the mid-sagittal plane of the subject with the help of an adjustable rod for helping set measurements on the photographs. The images were analyzed by researchers for 25 anthropometric facial measurements: three on the skull, nine on the face, four at the orbits, four on the nose, three at the lips and mouth, and two on the ears [7, 8] in Image J® software [11] whose source code is freely available on http://rsb.info.nih.gov/ij. To illustrate the selected number of measurements, a 3D human head model was purchased from TurboSquid (http://www.turbosquid.com) and created with the anthropometric landmarks, as shown in figure 1.

The findings were compared to normal standards and converted to Z-scores. The Z-score system are used to express anthropometric values as several standard deviations (SDs) and how many SD a particular score is from the reference mean. Z-score pattern profiles were produced using age and sex matched normal standards as detailed by Deutsch and Farkas [5]. The average measurements were compared with standard using the anthropometric norms of the face established for adult white North Americans males (18–25 years old) [6]. Based on anthropometric category and Z-score range, the Z-scores were classified into descriptive categories as follows [5]. In this methodology, Z-scores within the range of −1 to +1 are considered as optimal, from −2 to +2 are normal, less than −2 as subnormal, and greater than +2 as supernormal. An abnormality is considered severe if the Z-score is less than −3 or greater than +3.

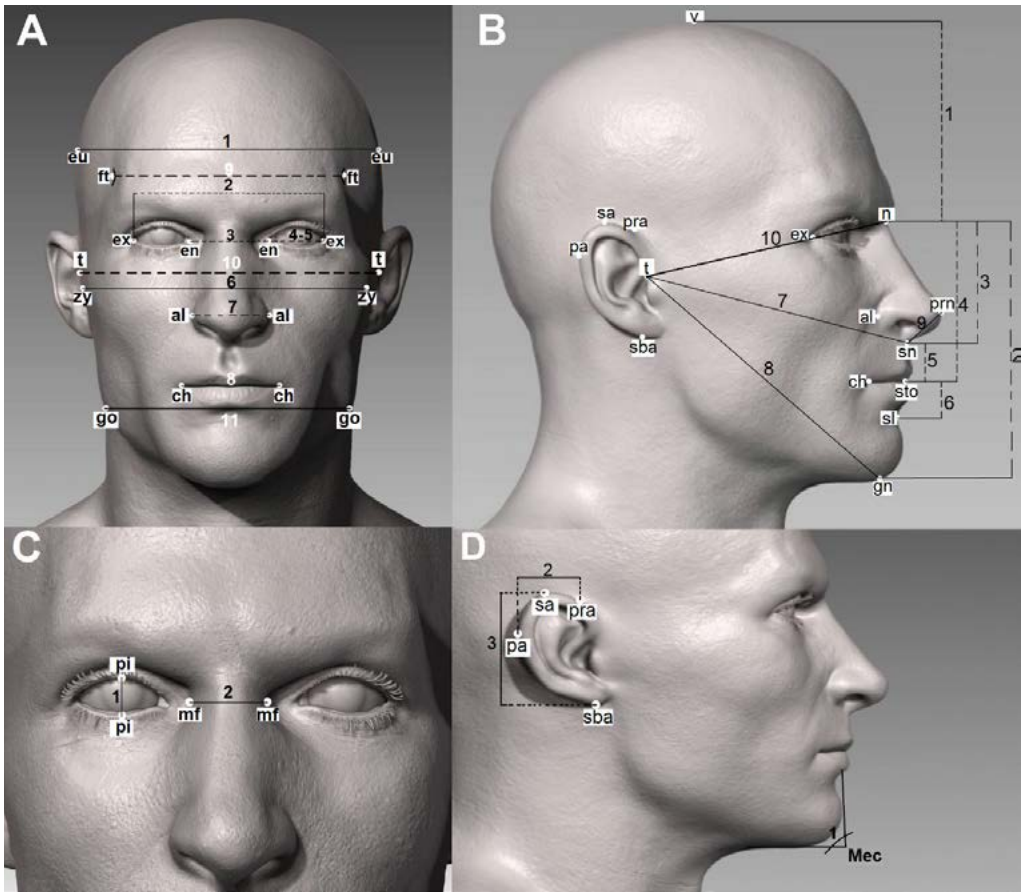

Figure 1 – Measurements used in the study. A: 1) eu-eu, head width; 2) ex-ex, biorbital width; 3) en-en, intercanthal width; 4-5) en-ex, palpebral fissure length and its inclination; 6) zy-zy, face width; 7) al-al, nose width; 8) ch-ch, mouth width; 9) ft-ft, forehead width; 10) t-t, skull base width; 11) go-go, lower face width. B: 1) v-n, head height; 2) n-gn, face height; 3) n-sn, nose height; 4) n-sto, upper face height; 5) sn-sto, upper lip height; 6) sto-ls, lower lip height; 7) t-sn, middle face depth; 8) t-gn, lower face depth; 9) sn-prn, nasal tip protrusion; 10) t-n, upper facial depth. C: 1) ps-pi, palpebral fissure height; 2) mf-mf, nasal root width. D: 1) Mentocervical angle (MeC); 2) pra-pa, ear width; 3) sa-sba, ear length

Results

The raw measurements were transformed into Z-scores (table I). Craniofacial pattern profile of the subject based on the 25 Z-scores is plotted in figure 2. Most of the dimensions showed significative difference when compared with the mean, except by ten of them (t-t, t-sn, t-gn, MeC, v-n, sn-prn, sn-sto, ch-ch, pra-pa e go-go). Within the differenced measurements, all of them were in supernormal range (above +2SD) which means that these variables that are in supernormal range (eu-eu, ft-ft, n-gn, n-sto, zy-zy, t-n, go-go en-en, ex-ex, ex--en, ps-pi, n-sn, al-al, mf-mf, sto-sl, sa-sba) are abnormally big when compared to the adult North Americans white males (18–25 years old) (table I). None of the dimensions were in the subnormal range (less than −2D). Seven measurements were considered as severe abnormality with Z-score greater than +3SD (eu-eu, ft-ft, n-gn, n-sto, zy-zy, t-n, en-en, ex-ex, mf-mf, sa-sba).

Table I – Comparison between the anthropometric measurements of the head and face from Sotos syndrome (SS) and North American White Males (NAWM)

Region	Landmark	SS mean (mm) ± SD	NAWM mean (mm) ± SD	Z-score for SS
Head	Head width (eu-eu)	177,6 (±0,7)	151,1 (±5,7)	**4,3**
	Forehead width (ft-ft)	151,0 (±0,8)	115,9 (±5,2)	**5,6**
	Head height (v-n)	90,1 (±1,0)	111,3 (±6,9)	**-1,9**
Face	Face height (n-gn)	167,7 (±0,8)	124,7 (±5,7)	**7,5**
	Skull base width (t-t)	152,1 (±0,6)	146,8 (±5,6)	**1,3**
	Upper face height (n-sto)	89,0 (±0,1)	76,6 (±4,0)	**3,1**
	Face width (zy-zy)	158,9 (±0,1)	139,1 (±5,3)	**3,3**
	Middle face depth (t-sn)	135,1 (±0,3)	133 (±4,6)	**0,9**
	Upper face depth (t-n)	148,5 (±0,7)	126,6 (±4,2)	**5,2**
	Lower face depth (t-gn)	168,7 (±0,4)	170,4 (±6,4)	**-0,3**
	Lower face width (go-go)	119,0(±1,2)	105,6 (±6,7)	**2,0**
	Mentocervical angle (MeC)*	91,5 (±0,3)	78,3 (±7,9)	**1,7**
Orbits	Intercanthal width (en-en)	45,6 (±0,7)	33,3 (±2,7)	**4,6**
	Biocular width (ex-ex)	116,9 (±0,4)	91,2 (±3,0)	**8,6**
	Palpebral fissure length (ex-en)	37,5 (±0,6)	31,3 (±1,2)	**2,1**
	Palpebral fissure height (ps-pi)	13,4 (±0,2)	10,8 (±0,9)	**2,7**
Nose	Nose height (n-sn)	65,7 (±0,4)	54,8 (±3,3)	**2,1**
	Nose width (al-al)	38,6 (±0,2)	34,9 (±2,1)	**2,2**
	Nasal root width (mf-mf)	31,1 (±0,2)	19,6 (±1,9)	**6,0**
	Nasal tip protrusion (sn-prn)	21,6 (±0,3)	19,5 (±1,9)	**1,1**
Labio_oral	Upper lip height (sn-sto)	23,1 (±0,1)	22,3 (±2,1)	**0,4**
	Lower lip height (sto-sl)	26,5 (±0,2)	19,7 (±2,1)	**2,8**
	Mouth width (ch-ch)	59,6 (±1,0)	54,5 (±3,0)	**1,1**
Ears	Ear length (sa-sba)	74,3 (±0,6)	62,7 (±3,6)	**3,2**
	Ear width (pra-pa)	37,6 (±0,3)	36,9 (±2,5)	**0,3**

(SS) Sotos individual anthropometric measurements of the head and face; (NAWM) North American data values obtained from Farkas *et al.* [6]; Z-score system to express the anthropometric values for SS individual

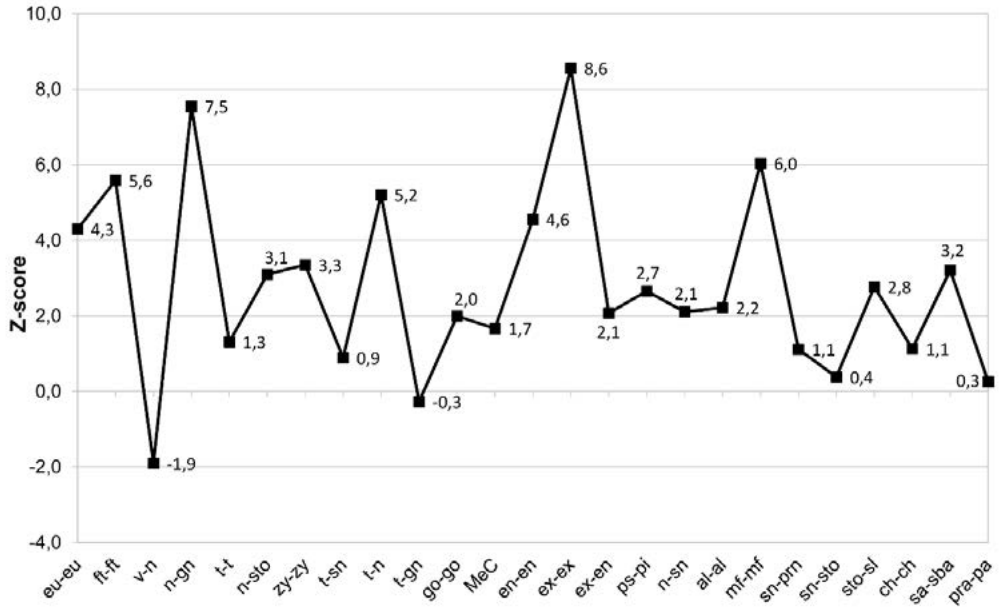

Figure 2 – Craniofacial pattern profile of young adult male patient with Sotos Syndrome

Discussion

To achieve a data base about the Syndrome, we reported the measurements of a patient with SS from Curitiba, Brazil. The results of this study indicate that the individual with SS show bigger craniofacial proportions than non-syndromic individuals in same age and gender. The analysis of the images led to the conclusion that the measurements were significantly different from the population pattern of caucasian North American males observed by Farkas *et al.* [6].

Alterations were observed in almost all analyzed measurements, except for the skull base width (t-t, z-score = 1,3), head height (v-n, z-score = -1,9), midface depth (t-sn, z-score = 0,9), lower face depth (t-gn, z-score = -0,3), mentocervical angle (MeC, z-score = 1,7), nasal tip protrusion (sn-prn, z-score = 1,1), upper lip height (sn-sto, z-score = 0,4), mouth width (ch-ch, z-score = 1,1), ear width (pra-pa, z-score = 0,3) and lower facial width (go-go, z-score = 2,0).

Agreeing with the data obtained by Takei *et al.* [13], we observed that the patient had maxillary protrusion with mandibular retrusion. Other feature includes an increase in the head width (eu-eu, z-score = 4,3) and in the forehead width (ft-ft, z-score = 5,6), aspects that give individuals with Sotos Syndrome a characteristic wide and prominent forehead [1].

We also noticed that the individual's head is dolichocephalic [3] and has a typical format, being narrower in the base, but the skull base width (t-t) has a normal value, not following the forehead's exacerbated growth pattern. The individual's palpebral fissures characteristically point downward [10], and the intercanthal width (en-en, z-score = 4,6) and the biocular width (ex-ex, z-score = 8,6) values deviated significantly from the standard values for caucasian North American males. Furthermore, it is possible to observe that the inner corner of the patient's eye is situated higher than the external corner, giving the palpebral fissure an antimongoloid appearance [3]. In addition, the patient has a prominent chin (n-gn, z-score = 7,5), which is also agreeing with literature data [3, 14].

This analysis allowed us to observe that the individual shows the Sotos Syndrome typical phenotype, in which the main alterations are macrocephaly, antimongoloid palpebral fissures and exacerbated growth of the forehead and jaw. As a rare disease, the individuals present a phenotype that can be a challenge to be precisely diagnosed and new studies are needed to achieve a database of Soto's Syndrome individuals. In this way, the anthropometric values can finally be used as a precise diagnostic.

Conclusion

The measurements corroborated with the literature as anthropometric values were abnormally big in the forehead and the eyes were widely-spaced.

Conflict of interest

The authors declare no conflicts of interest.

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