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Photoanthropometric Study of Craniofacial Traits of Individuals With Prader-Willi Syndrome

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Abstract

A photoanthropometric method, which enables an objective description of facial structures, was used to better delineate the craniofacial characteristics of 37 individuals with Prader-Willi syndrome (PWS; 21 males and 16 females; 22 with 15q11q13 deletions and 15 with normal-appearing chromosome 15s) between the ages of 0 to 12 years. Facial parameters were measured from strict frontal and profile photographic 35 mm slides and compared with other facial measurements from the same face (e.g., palpebral fissure width to bizygomatic diameter). We studied 16 photoanthropometric craniofacial indices following the protocols established by Stengel-Rutkowski et al. [1984: Hum Genet 67:272–295] and Butler et al. [1988: Am J Med Genet 30:165–168]. Based on our measurements of 37 Prader-Willi syndrome individuals, none of the parameters were consistently outside of the normal range when compared with photoanthropometric index standards for age established from white control children [Stengel-Rutkowski et al., 1984]. However, several suggestive findings were documented by our analysis including: narrow palpebral fissure width [particularly in older children (6–12 years)], high midface, broad interalar distance, short back of the nose, prominent high chin, and broad low-set ears. No significant differences were found in craniofacial parameters between deletion or nondeletion Prader-Willi syndrome patients with this methodology. These craniofacial parameters (many not previously evaluated in PWS patients) may become useful for early detection, and aid in the diagnosis and the study of the development of the characteristic face seen in Prader-Willi patients.

Keywords

Prader-Willi syndrome; photoanthropometric parameters; craniofacial indices

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INTRODUCTION

Common manifestations in Prader-Willi syndrome (PWS) include obesity, hypotonia, hypogonadism, minor facial anomalies, small hands/feet and learning/behavioral problems. While 60% have an interstitial deletion of the proximal long arm of chromosome 15, 10–15% have submicroscopic deletions, 20–25% have maternal disomy of chromosome 15 and 5–10% have biparental inheritance of normal appearing chromosome 15s [Mascari et al., 1992], although the clinically typical PWS patient has either a deletion or maternal disomy of chromosome 15 [Lai et al., 1993]. Although consensual diagnostic criteria have been established for Prader-Willi syndrome and several minor craniofacial anomalies (including narrow bifrontal diameter, almond-shaped palpebral fissures and down-turned mouth) have been reported, there is a paucity of anthropometric data on craniofacial traits in this syndrome. Thus, to better characterize craniofacial characteristics and to further delineate the phenotypic findings of the face in PWS patients, we have undertaken a photoanthropometric analysis of PWS patients from 0 to 12 years and compared the data with normative standards.

MATERIALS AND METHODS

The photoanthropometric method used in the study followed the protocol established by Stengel-Rutkowski et al. [1984] and utilized by Butler et al. [1988] in the study of fragile X syndrome patients. This methodology enables an objective description of facial structure and allows a comparison with normative standards for age and race.

We studied 18 facial parameters including inner canthal distance; palpebral fissure width; bizygomatic diameter; midface height; mouth width; nose length; interalar distance; tragion-subnasale, tragion-ophryon and tragion-chin distances; ear length and width; conchae length and width; nasolabial distance, chin and total face heights; and ear position. Facial parameters were measured to the nearest 0.1 mm with a vernier caliper from frontal and profile facial views of the patients without restraining or supporting the subject’s head, using colored photographic 35 mm slides. The photographs were taken from a distance of over 1.5 m from the subject and projected onto a viewing screen. Several photographic exposures were taken for each patient in order to obtain the best suitable frontal and profile views for analysis. Thirty-seven Caucasian individuals (21 males and 16 females and age range from 0 to 12 years) with PWS were analyzed; they were diagnosed by at least two clinical geneticists. Twenty-two of the PWS patients showed the 15q11q13 deletion with high resolution chromosome analysis while the remaining 15 patients had normal appearing chromosomes (DNA data are not available). The measurements were compared with other facial measurements from the same face to develop indices (e.g., mouth width to bizygomatic diameter). Sixteen indices were developed from the 20 measurements (3 from frontal face [total face height, midface height, bizygomatic diameters], 2 from eye region [inner canthal distance, palpebral fissure width], 3 from nose region [length of back of nose, inclination of nasal base, interalar distance], 2 from mouth region [nasolabial distance, mouth width], 4 from profile face [tragion-ophryon, tragion-subnasale, chin height, tragion-chin], and 6 from ear region [ear position, inclination of ear insertion, ear length, ear width, conchae length, conchae width]). References used in calculating the ratios or indices in this

study were the bizygomatic diameter as the horizontal reference, the midface or total face height as vertical references, and the tragion-ophryon as the sagittal reference.

To test for inter- and intraobserver reliability and for measurement errors, the measurements were obtained by at least two observers and repeated measurements were taken by the same observer over time. Generally, intra- and interobserver variability was less than 10%, which is similar to other reported anthropometric studies [Stengel-Rutkowski et al., 1984; Brandt et al., 1991; Butler and Meaney, 1991]. Pearson product moment correlation coefficients with age, chi-square with Yates' correction and Z score or standard deviation units were calculated for each of the individual photoanthropometric indices from the PWS patients. Normative data from Stengel-Rutkowski et al. [1984] were used for comparison purposes throughout this study. The coefficient of variation (i.e., the standard deviation expressed as a percentage of the mean) ranged from 4.5% (for tragion-subnasale to tragion-ophyron) to 29.1% (for ear position to midface height) with the latter index being the only index with the coefficient of variation greater than 25%. According to standards of reliability and precision described elsewhere [National Center for Health Statistics, 1973; Brandt et al., 1991; Butler and Meaney, 1991], the coefficient of variation should preferably be less than 25%. Thus, we would conclude that measurement errors did not interfere sufficiently with the development of the indices or lessen the value of using the indices in the study of the PWS children.

RESULTS

The data from 16 (5 frontals, 11 profiles) craniofacial photoanthropometric indices are shown in Table I. Based on our measurements of 37 Caucasian PWS patients (21 males, 16 females) between the ages of 0–12 years, none of the Z score mean index measurements were consistently outside of the normal range (e.g., the calculated overall Z score for each index ranged from −1.2 for nose length to midface height index to 1.3 for ear position to midface height index) when compared with photoanthropometric index standards for age and race established from control children [Stengel-Rutkowski et al., 1984]. However, the following differences were noted: narrow palpebral fissure width (palpebral fissure width to bizygomatic diameter [30% of PWS patients were equal to or less than 3rd percentile], correlation coefficient with age = −0.10 [$P > 0.05$], chi-square = 16.99 [$P = 0.00004$]); prominence of the chin (tragion-tip of the chin to tragion-ophryon [44% of PWS patients were greater than or equal to 97th centile], correlation coefficient with age = 0.71 [$P < 0.001$], chi-square = 26.29 [$P = 0.0000003$]); increased chin height (height of the chin to total face height [33% of PWS patients were greater than or equal to 97th centile], correlation coefficient with age = 0.45 [$P > 0.05$], chi-square = 14.15 [$P=0.0002$]); high midface height (midface height [ophryon-stomion] to bizygomatic diameter [24% of PWS patients were equal to or greater than 97th centile], correlation coefficient with age = 0.06 [$P > 0.05$], chi-square = 11.60 [$P = 0.0008$]); broad interalar distance (interalar distance to bizygomatic diameter [20% of PWS patients were equal to or greater than 97th centile], correlation coefficient with age = 0.09 [$P>0.05$], chi-square = 8.59 [$P = 0.003$]), short length of back of nose (length of the back of the nose [deepest point of the nose root-tip of the nose] to midface height [ophryon-stomion; 22% of PWS patients were equal to or less than 3rd centile], correlation coefficient with age = 0.76 [$P < 0.001$], chi-square = 6.95 [$P = 0.008$]), broad ears (width of ears to tragion-subnasale [27% of PWS patients were equal to

or greater than 97th centile], correlation coefficient with age = 0.15 [$P > 0.05$], chi-square = 8.98 [$P = 0.003$]), low-set ears (position of the ears [distance from the outer canthus to the vertical of the profile line, ophryon-subnasale, through the tragion] to midface height [ophryon-stomion; 36% of PWS patients were equal to or greater than 97th centile], correlation coefficient with age = −0.67 [$P < 0.01$], chi-square = 15.44 [$P = 0.00008$]). No significant differences were noted in craniofacial parameters between deletion or nondeletion PWS patients or between males and females. Figures 1–4 show the photoanthropometric data for the 16 indices grouped by craniofacial regions.

In comparing correlation coefficient with age between normative and PWS data, discrepancies with five indices (midface height to bizygomatic diameter, palpebral fissure width to bizygomatic diameter, ear width to tragion-subnasale, chin height to total face height and inclination of ear insertion) were found. For example, a distinct positive age effect (r=0.30) was reported for midface height to bizygomatic diameter for the normative data [Stengel-Rutkowski et al., 1984] while the correlation coefficient for our PWS data for this index was only 0.06. Similarly, the palpebral fissure width to bizygomatic diameter correlation coefficient was 0.40 for normative data and r = −0.10 for our PWS data and conversely a distinct negative age effect (r = −0.49) was observed for ear width to tragion-subnasale for the normative data while the correlation coefficient for our PWS data for this index was positive (r = 0.15) but not significant ($P > 0.05$). The chin height to total face height correlation coefficient with age was − 0.01 for normative data and 0.45 for our PWS data while the inclination of ear insertion correlation coefficient with age was 0.11 for normative data and −0.59 for our PWS data. The remaining indices showed nearly identical correlations between the normative data and our PWS data ([e.g., a distinct positive age effect for tragion-subnasale to tragion-ophryon for both the normative data [r=0.48] and our PWS data [r = 0.50]). Significant correlations with age were found in our PWS patients for four indices (nose length to mid-face height, tragion-subnasale to tragion-ophyron, tragion-tip of chin to tragion-ophyron, and ear position). Correlation and chi-square values for the individual indices for PWS and correlation values for the normative group are shown in Table I.

DISCUSSION

Our photoanthropometric analysis of 16 craniofacial indices in PWS patients indicated that several parameters were significantly different (chi-square values [$P < 0.05$]) when compared with normative photoanthropometric index standards for age and race reported by Stengel-Rutkowski et al. [1984]. Our data supported a narrow palpebral fissure width, high midface height, broad interalar distance, short length of back of nose, broad low-set ears, a prominent chin with an increased height. The small palpebral fissure width to bizygomatic diameter index in our PWS patients indicates that the face is either wide with an increased bizygomatic diameter or the palpebral fissure width is narrow. The comparison of the bizygomatic diameter with other measurements (e.g., inner canthal distance to bizygomatic diameter) did indeed support a narrow palpebral fissure width in PWS patients. Interestingly, the palpebral fissure width to bizygomatic diameter index did not increase with age (r = −0.10) compared with a significant positive correlation coefficient of 0.40 reported by Stengel-Rutkowski et al. [1984] for their normative data. Therefore, the appearance of

"almond-shaped" eyes reported in patients with PWS is supported by our photoanthropometric study. Our data also indicate that the palpebral fissure width is relatively narrower as the child grows older, particularly between 6 to 12 years of age.

Similarly, an abnormal chin (prominent chin with an increased chin height in PWS patients) was suggested by our data (e.g., 44% of our PWS patients showed the tragion-chin to tragion-ophryon index to be greater than or equal to the 97th centile when compared with normative data). In addition, there was a distinct positive correlation with age for the tragion-chin to tragion-ophryon distances both in our PWS patients ($r = 0.71$) and in the normative data ($r = 0.52$). Although there was no correlation ($r = -0.01$) with chin height to total face height in the reported normative data, the calculated correlation coefficient was 0.45 ($P > 0.05$) for our PWS patients.

Our photoanthropometric analysis supports the clinical impression of almond-shaped eyes and/or narrow appearing palpebral fissure width as well as other minor craniofacial anomalies. The palpebral fissure finding has been reported previously (almond-shaped eyes have been reported in 20–80% of PWS patients in published surveys) [Butler et al., 1986; Butler, 1990], but the observations of a prominent chin with an increased chin height, broad interalar distance, short back of nose and broad low-set ears were previously unrecognized traits of individuals with PWS. These craniofacial parameters (many not previously evaluated in PWS patients) may become useful in the early detection of PWS patients, although more research is needed to better define the craniofacial structures and features in individuals with PWS.

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TABLE I

Photoanthropometric Data of Craniofacial Traits in Individuals With Prader-Willi Syndrome

Index[a]	No. of PWS subjects	Mean	Standard deviation	Overall Z score for PWS compared with normative data	% of PWS outside normal range		Chi-square value	Chi-square probability (2-tailed)	Correlation with age for normative group[b]	Correlation with age for PWS group
					≥97%	≤3%				
ICD/BD	32	25.69	1.83	0.72	9.4	0	1.04	0.31	−0.02	−0.05
MHF/BD	34	61.06	4.60	0.62	23.5	5.9	11.60	0.0008	0.30**	0.06
PFW/BD	30	18.21	1.38	−0.33	13.3	30.0	16.99	0.00004	0.40***	−0.10
IAD/BD	35	25.39	2.50	0.45	20.0	5.7	8.59	0.003	0.06	0.09
WM/BD	31	31.94	5.62	−0.23	12.9	3.2	2.84	0.09	0.07	−0.05
NL/MHP	18	38.80	6.66	−1.18	5.6	22.2	6.95	0.008	0.71***	0.76***
TS/TO	18	95.05	4.28	0.73	16.7	0	3.41	0.06	0.48***	0.50*
TC/TO	18	105.32	11.29	1.20	44.4	5.6	26.29	0.0000003	0.52***	0.71***
EL/MHP	15	77.08	6.98	0.06	6.7	6.7	0	0.97	−0.42***	−0.22
EW/TS	15	35.25	4.01	0.50	26.7	6.7	8.98	0.003	−0.49***	0.15
WC/LC	13	77.59	13.99	−0.64	7.7	15.4	1.76	0.18	−0.35***	−0.38
ND/MHP	20	18.14	2.42	0.37	5.0	0	0.05	0.82	−0.09	−0.25
CH/TFH	15	27.08	2.80	0.95	33.3	0	14.15	0.0002	−0.01	0.45
INB	16	63.93	7.54	−0.25	0	6.3	0.01	0.94	0.27**	0.31
EP/MHP	14	34.20	9.96	1.27	35.7	0	15.44	0.00008	−0.42***	−0.67**
IEI	10	82.50	5.25	−0.29	10.0	10.0	0.06	0.81	0.11	−0.59

[a]Explanation of indices: ICD/BD, inner canthal distance to bizygomatic diameter; MHF/BD, midface height (frontal) to bizygomatic diameter; PFW/BD, palpebral fissure width to bizygomatic diameter; IAD/BD, interalar distance to bizygomatic diameter; WM/BD, width of mouth to bizygomatic diameter; NL/MHP, length of back of nose to midface height (profile); TS/TO, prominence of the upper jaw (tragion-subnasal) to tragion-ophryon; TC/TO, prominence of the chin (tragion-tip of the chin) to tragion-ophryon; EL/MHP, ear length to midface height (profile); EW/TS, ear width to tragion-subnasal; WC/LC, width of concha to length of concha; ND/MHP, nasolabial distance to midface height (profile); CH/TFH, chin height to total face height; INB, inclination of nasal base; EP/MHP, ear position to midface height (profile); IEI, inclination of ear insertion.

[b]From Stengel-Rutkowski et al. [1984].

*$P < 0.05$ (2-tailed).

**$P < 0.01$ (2-tailed).

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***$P < 0.001$ (2-tailed).