Mandibular Dysmorphology in Unicoronal Synostosis and Plagiocephaly without Synostosis

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Patients with unicoronal synostosis (UCS) or plagiocephaly without synostosis (PWS) have distinctive skull dysmorphologies. Associated mandibular dymorphologies have been suspected but not quantified. This study was performed to test the hypothesis that discrete mandibular dysmorphology exists in both UCS and PWS. All patients at a tertiary referral center at a medical school-affiliated children's hospital with confirmed diagnosis of UCS or PWS with adequate pretreatment CT data were included in the study population, which population was comprised of 20 UCS, 23 PWS, and 8 normal infants. Each patient had a head CT scan using 2-mm slices. 3-D images were created using Analyze™, a biomedical imaging program. The mandibles were isolated, and the coordinates of 8 landmarks were sampled from each mandible by a single investigator: a single volume value was measured, and 9 linear distances and 4 angles were calculated. Corresponding measurements from each hemimandible were expressed as ratios of ipsilateral/contralateral side. In UCS, the affected side was defined as the side ipsilateral to the synostosis; in PWS, the affected side was defined as the side ipsilateral to the occipital flattening. The results from both groups were *t* tested for statistical significance. For UCS, statistically significant ($p < .001$) findings included: ipsilateral hemimandibular volume 5% smaller than contralateral; affected hemimandibular body length 1.9% shorter; affected gonial angle 2.6% more acute; affected coronoid process tilted anteriorly 2.5%; and distances from condylion and tip of the coronoid process to the chin landmarks 4% shorter on the affected side. For PWS, significant findings included: affected hemimandibular volume 3.8% larger; ramal height 3.5% shorter; mandibular body length 3% longer; and coronoid process tilted anteriorly by 2.3% on the affected side. In the UCS/PWS comparison, findings included: affected hemimandibular volume in UCS 8.7% less; affected gonial angle in UCS 3% more acute; affected mandibular corpus length in UCS 5% shorter; distances from the condylion and the tip of the coronoid process to the chin landmarks 4% shorter on the affected side in UCS. The hypothesized presence of diagnosis specific mandibular dysmorphology in UCS and PWS is confirmed. This analysis forms the baseline for study of the effects of unperturbed growth or therapeutic interventions upon the dentoskeletal dysmorphology of these anomalies.

KEY WORDS: *plagiocephaly, mandibular dysmorphology, unilateral coronal synostosis*

The term "plagiocephaly" literally means "twisted head." This combination of Greek roots, plagios and kephale, refers to the morphology but not the etiology of the condition. Plagiocephaly is commonly used either inclusively to describe asymmetric crania with somewhat similar phenotypes resulting from several different etiologies, or exclusively to indicate craniosynostosis of one coronal suture. Plagiocephaly may result from or be associated with: (1) unilateral craniosynostosis of a paired suture (e.g., unilateral coronal or unilateral lambdoid synostosis); (2) cranial deformation, which may begin either

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in utero [gestational deformation (Clarren, 1981)] or postnatally; or (3) other craniofacial anomalies [e.g., torticollis and hemifacial microsomia (Padwa et al., 1993)]. While several authors have attempted to clarify terminology so that it will reflect the different etiologies of the calvarial asymmetry (Bruneteau and Mulliken, 1992; Lo et al., 1995), consensus on a standard nomenclature has not been reached. Nonetheless, plagiocephalic patients have generally been divided into two subclasses, depending on the presence or absence of synostosis. At our craniofacial center, patients with plagiocephaly secondary to craniosynostosis are designated by the affected suture: unilateral coronal synostosis (UCS) or unilateral lambdoid synostosis. We refer to the subset of patients with cranial asymmetry without premature sutural fusion or any other discernible cause for the asymmetry as having "plagiocephaly without synostosis" (PWS)(Marsh and Vannier, 1985).

The comparative literature of plagiocephaly has tended to focus on calvarial dysmorphology. Nonetheless, different etiologies of plagiocephaly are associated with variable degrees of facial dysmorphology. While orbital dysmorphology is recognizable in infants (Marsh et al., 1986), dentoskeletal dysmorphology may not be perceived until later (Kreiborg, 1981). It is unclear, regardless of the etiology of the plagiocephaly, whether this dentoskeletal dysmorphology: (1) is part of the primary process or a secondary deformation; (2) is etiology specific; or (3) changes with time and/or intervention. Answers to these questions might, in turn, provide insight into the relationship between anomalous calvarial anatomy and dentoskeletal dysmorphology.

The most frequently encountered etiologies of plagiocephaly are PWS and UCS (Lo et al., 1995). As these two plagiocephalies can be distinguished on physical examination of the calvaria by a sophisticated observer, so do their facial appearances differ (Fig. 1). In their study based on clinical photographs and physical examinations of 24 patients with UCS and 33 patients with PWS, Bruneteau and Mulliken (1992) were able to assemble composite qualitative descriptions of each anomaly based on observations of the supraorbital rims, nasal root, ears, malar eminences, chin, palpebral fissures, and

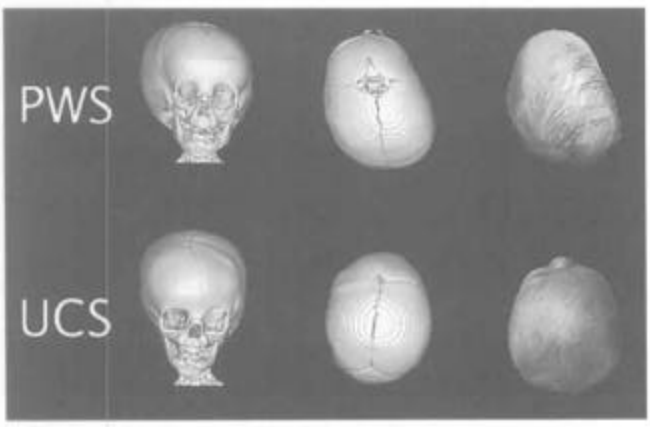

FIGURE 1 Typical 3-D CT osseous frontal and vertex images and vertex photographic appearances of PWS and UCS patients.

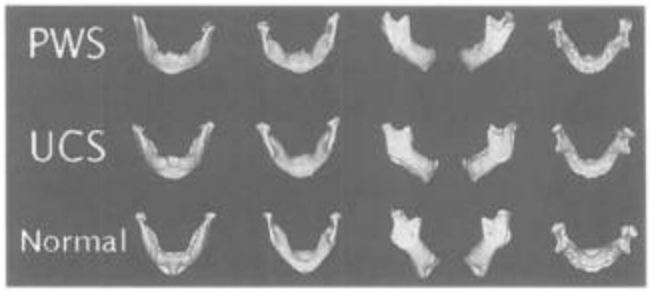

FIGURE 2 Typical 3-D CT osseous images of isolated mandibles from PWS, UCS, and normal patients. Asymmetry is overt in PWS, subtle in UCS, and negligible in normal images.

facial height. Interestingly, the differences between these two dysmorphologies seem discernible at sites anatomically distant from the affected calvarial suture, such as the mandible (Fig. 2). Therefore, we undertook the following retrospective, cross-sectional analysis of computerized tomography (CT) data to test the hypothesis that discrete, measurable, and etiology-specific mandibular dysmorphology exists in untreated infants having either UCS or PWS. If validated, this hypothesis will encourage study of the change over time of those dysmorphologies, with and without therapeutic intervention.

METHOD

Study Population

The records of all patients with the diagnosis of UCS or PWS, presenting to our craniofacial center for evaluation over the decade spanning 1981–1991, were reviewed to confirm the diagnosis and to establish whether or not adequate pretreatment CT data existed for mandibular morphologic analysis. Of 44 patients with UCS and 106 with PWS, 44 UCS and 39 PWS patients had undergone CT scans. Whereas CT scanning was, and continues to be, performed preoperatively for all patients with UCS, preintervention CT scans were only obtained for patients with PWS between 1983 and 1991, because CT scanning is part of the routine preoperative evaluation and planning for UCS at our center, while it was only performed for PWS patients during a study of their cranial dysmorphology.

CT scans with incomplete or corrupted mandibular images were excluded from study, leaving 20 UCS and 23 PWS scans for analysis. The excluded patients had an age and gender distribution similar to that of the included patients. The demographics of the study populations are summarized in Table 1. In the UCS population, the median age at scan was 3.4 months; the range of ages spanned from 2 weeks to 3.5 years; the male-to-female ratio was 3:4; the group was entirely Caucasian with the exception of one African-American; and the right side was affected 50% of the time. In the PWS population, the median age at scan was 4.7 months; the range of ages spanned from 6 weeks to 6.75 years; the male-to-female ratio was nearly equal; the group was entirely Caucasian with the exception of one African-American and one Asian; and the right side was

TABLE 1 Demographics of Study Population

Diagnosis	n	Median Age at CT Scan (mo)	Male/Female	Affected Side	
				Right (%)	Left (%)
UCS	20	3.4	8/12	10 (50)	10 (50)
PWS	23	4.7	12/11	15 (65)	8 (35)
Normals	8	3.7	4/4	N.A.	N.A.

UCS = unilateral coronal synostosis; PWS = plagiocephaly without synostosis.

affected 65% of the time. In addition, comparable head CT data were available for inclusion as "normals" from 8 children, aged 3 to 18 months, who had no significant craniofacial dysmorphology on either physical examination or inspection of their CT scan: 2 had minor extracranial scalp soft-tissue masses, and none had neurologic disorders.

Preparation of Study Data

Scans were obtained on Siemens equipment according to a standardized protocol (Marsh et al., 1986). Axial slices were taken at 2-mm increments from the vertex to the most inferior chin, in a plane parallel to an axial reference plane passing through the most inferior point on the orbit and the external acoustic meatus. Patients who were unable to remain motionless for the procedure were sedated.

Each axial slice was archived as a 512 × 512 pixel image. The actual pixel dimensions varied according to patient size, and the data were resampled using trilinear interpolation to create isotropic voxels with dimensions of 0.6 × 0.6 × 0.6 mm. All work was performed on a Hewlett Packard 7000 series graphics workstation, using ANALYZE™ biomedic-imaging software.

Once each set of CT images had been assembled into a 3-D volume in the above fashion, soft tissues were removed using a standard thresholding technique. The mandibles were electronically disarticulated from the rest of the skull. Each mandible was then segmented into two hemimandibles at the mental symphysis.

Data Analysis

The coordinates of eight cephalometric landmarks were recorded for each mandible: the pogonion (PG) and the infradentale (ID) on the frontal image (Fig. 3); the condylion (CO), the tip of the coronoid process (CP), and the gonion (GO) on the right and left lateral images (Fig. 3). Thirteen distances and angles (Table 2, Figs. 4 and 5) were calculated in three dimensions using these landmarks. Hemimandibular volumes were measured, using a facility within the software that counts the number of voxels within the segmented hemimandibles, and multiplies this number by the volume of a unit voxel. All measurements were performed twice by the same person to estimate intrarater variability.

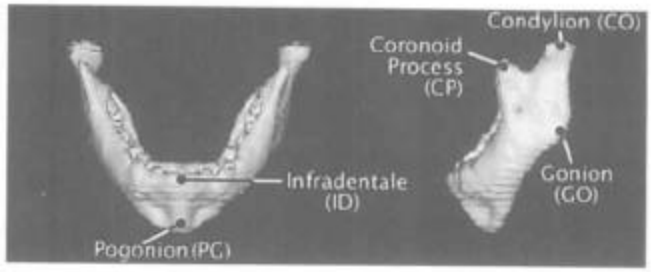

FIGURE 3 Landmarks sampled on each patient's mandible in the frontal and lateral images.

Since the subjects in this study were of differing ages and body parameters (e.g., weight and length), right:left hemimandible ratios were calculated to allow a comparison among individuals. Each hemimandible was designated as either "affected" or "unaffected" based on the calvarial dysmorphology so that the unilaterality of the primary process could be standardized. For UCS, the affected side was defined as the side ipsilateral to the synostosis; for PWS, the affected side was defined as that of the occipital flattening that characterizes these patients. The terms "affected" and "unaffected" are used in this context to differentiate the site of the synostosis, for UCS, or the type of asymmetry, for PWS. These terms have no relationship to normalcy: both hemicrania are abnormal in UCS and PWS.

The landmark coordinates were transferred to a spreadsheet, on which 13 distances and angles were calculated between combinations of landmarks for both the affected and unaffected sides (see Table 2, Figs. 4 and 5). For each patient, corresponding hemimandibular measurements were expressed as a ratio of affected:unaffected side. An average ratio was calculated for each measurement in all three patient populations.

TABLE 2 Entities Measured and Calculated for the Affected and Unaffected Sides (Associated Abbreviations)

Volumes Measured	Linear Distances Calculated	Angles Calculated
Hemimandibular Volume (HV)	Coronoid to condylion (CP–C0)	Coronoid–condylion–gonion (CP–CO–GO)
	Coronoid to gonion (CP–GO)	Condylion–gonion–pogonion (CO–GO–PG)
	Coronoid to pogonion (CP–PG)	Gonion–pogonion–infradentale (GO–PG–ID)
	Coronoid to infradentale (CP–ID)	Coronoid–gonion–pogonion (CP–GO–PG)
	Condylion to gonion (CO–GO)	
	Condylion to pogonion (CO–PG)	
	Condylion to infradentale (CO–ID)	
	Gonion to pogonion (GO–PG)	
	Gonion to infradentale (GO–ID)	

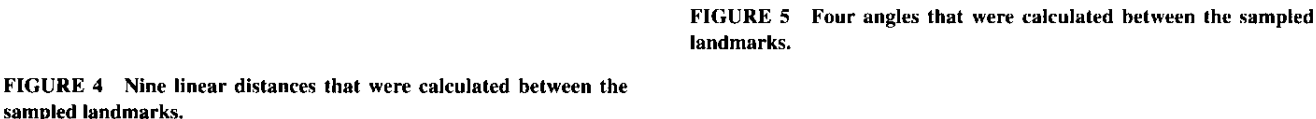

FIGURE 4 Nine linear distances that were calculated between the sampled landmarks.

FIGURE 5 Four angles that were calculated between the sampled landmarks.

These average ratios were tested for significance within each population using a two-tailed *t* test. Finally, the UCS and PWS average ratios were compared, also using a two-tailed *t* test. Statistical significance was assumed at a p value of < .05.

RESULTS

Repeatability of Measurements

The coordinates of each landmark were recorded twice. The average difference between the original and the repeat coordinates was less than 2 mm. In the repeat data set, all of the results were the same in terms of statistical significance; that is, no measurement that reached statistical significance in the original data set was insignificant in the repeat data set, and vice-versa.

UCS Mandibles

The results of the analysis of the UCS mandibles are presented in Table 3. The hemimandibular volume ipsilateral to the synostosis is 5% smaller than the contralateral side (HV). The length of the mandibular body is approximately 2% shorter on the affected side (GO–PG, GO–ID). The gonial angle (CO–GO–PG) is 2.6% more acute on the affected side. The coronoid process is tilted anteriorly 2.5% on the affected side (CP–GO–PG). Distances from the condylion and the tip of the coronoid process to the chin landmarks are approximately 4% shorter on the affected side (CP–PG, CP–ID, CO–PG, CO–ID). No statistically significant differences in ramal height were noted (CO–GO, CP–GO).

PWS Mandibles

The results of the analysis of the PWS mandibles are presented in Table 4. The affected hemimandibular volume is 3.8% larger than the unaffected side (HV). Ramal height (CP–GO,CO–GO) is approximately 3.5% shorter, mandibular body length (GO–PG, GO–ID) is approximately 3% longer, and the coronoid process is tilted anteriorly by 2.3% (CP–GO–PG) on the affected side compared to the unaffected side. There was no significant difference between the gonial angles on each side (CO–GO–PG).

Comparison of UCS and PWS Mandibles

The data comparing the UCS and PWS mandibles are displayed in Table 5 and in graphic format in Figure 6. When comparing the average ratio of affected:unaffected hemimandibles, the volume of the affected hemimandible in UCS is 8.7% less. The average gonial angle is 3% more acute on the affected side in UCS than in PWS (CO–GO–PG). Mandibular corpus length on the affected side is proportionately shorter in UCS by approximately 5% (GO–PG, GO–ID). Distances from the condylion and the tip of the coronoid process to the chin landmarks are approximately 4% shorter on the affected side in UCS (CP–PG, CP–ID, CO–PG, CO–ID). Ramal height ratios are not significantly different in the two disorders (CP–GO,CO–GO). The polar plot graphic display (see Fig. 1) allows comparison of a number of variables shared among

TABLE 3 Affected:Unaffected UCS Measurements

Significant Measurements				*Other Measurements*			
Measure	*Aff:Unaff Ratio*	*% Difference*	*p Value*	*Measure*	*Aff:Unaff Ratio*	*% Difference*	*p Value*
CP–PG	.964	3.6	<.001	CP–CO	.979	2.1	.30
CP–ID	.957	4.3	<.001	CP–GO	.983	1.7	.11
CO–PG	.965	3.5	<.001	CO–GO	.971	2.9	.14
CO–ID	.959	4.0	<.001	CP–CO–GO	1.015	−1.5	.42
GO–PG	.981	1.9	<.001	GO–PG–ID	.992	0.8	.31
GO–ID	.979	2.1	< .001				
CO–GO–PG	.974	2.6	<.001				
CP–GO–PG	.975	2.5	<.001				
HV	.950	5.0	<.05				

TABLE 4 Affected:Unaffected PWS Measurements

Significant Measurements				*Other Measurements*			
Measure	*Aff:Unaff Ratio*	*% Difference*	*p Value*	*Measure*	*Aff:Unaff Ratio*	*% Difference*	*p Value*
CP–GO	.970	3.0	<.01	CP–CO	.968	3.2	.16
CO–GO	.957	4.3	<.05	CP–PG	.997	2.6	.63
GO–PG	1.028	–2.8	<.05	CP–ID	1.004	–0.4	.55
GO–ID	1.031	–3.1	<.001	CO–PG	1.006	–0.6	.32
CP–GO–PG	.977	2.3	<.05	CO–ID	1.011	–1.1	.10
HV	1.038	–3.8	<.001	CP–CO–GO	1.019	–1.9	.31
				CO–GO–PG	1.004	–0.4	.53
				GO–PG–ID	1.010	–1.0	.29

datasets. The noncongruence of the normal, UCS, and PWS mandibles is overt.

Discussion

The findings of this investigation document statistically significant differences among mandibles in infants who are either normal or have untreated UCS or PWS. While these findings cannot distinguish among a primary anomaly (malformation) of the mandible, a secondary deformation of the mandible, or a combination of both, they do clearly demonstrate that what becomes overt with subsequent growth was present, at least, shortly after birth. Having established the baseline, additional studies can now be conducted to determine the effects of unperturbed growth or of intervention—cranio-orbital surgery for UCS and molding helmet therapy for PWS—on the nature and magnitude of these differences. The outcomes of these studies, currently in progress at our center, should help distinguish among the malformation versus deformation possibilities. If deformation is the primary, or even secondary contributing, factor for mandibular asymmetry in UCS and/or PWS, then consideration of the mechanism whereby cranial asymmetry induces mandibular asymmetry is in order.

It is of some interest that the mandibles of normals are not perfectly symmetric. This should not be surprising, since photographers have long known that two different faces can be produced by splitting a negative of the face along the midsagittal line and then reversing each hemiface respectively to generate two new images that usually differ visibly. This natural asymmetry of the normal head may reflect unilateral, cerebral, hemispheric dominance, which is present even in the fetal stage of development (Strauss et al., 1983).

Asymmetry of the mandible *per se*, then, is not abnormal; it is the magnitude of the asymmetry that indicates abnormality. Statistical analysis separates deviations within the normal range from those beyond it. In the case of this study, hemimandible ratios for most of the parameters assessed were beyond the normal range for UCS and PWS infants: these deviations were small but consistent.

A limitation of this study is the use of a few anatomic-landmark data points to describe a complex three-dimensional structure. Such an approach, of course, is the basis of widely used cephalometric analyses for research and treatment purposes. The current study differs from lateral-skull cephalometry in that the anatomic landmarks are placed in three-dimensional space, the distances are true three-dimensional linear distances, and there is no ambiguity of distinguishing right from left due to overlapping structures.

Other methodologies have been used to overcome the limitations of biplanar analysis of three-dimensional structures [i.e., cephalometry, such as finite element scaling (Richtsmeier et al., 1992), three-dimensional cephalography (Grayson et al.,

TABLE 5 Comparison of UCS and PWS Ratios

Significant Measurements			*Other Measurements*		
Measure	*% Difference UCS:PWS*	*p Value*	*Measure*	*% Difference UCS:PWS*	*p Value*
CP–PG	–3.3	<.001	CP–CO	1.1	.72
CP–ID	–4.7	<.001	CP–GO	1.2	.42
CO–PG	–4.1	<.001	CO–GO	1.5	.61
CO–ID	–5.1	<.001	CP–CO–GO	–0.4	.88
GO–PG	–4.7	<.001	GO–PG–ID	–1.8	.15
GO–ID	–5.1	<.001	CP–GO–PG	–0.2	.90
CO–GO–PG	–3.0	<.01			
HV	–8.7	<.001			

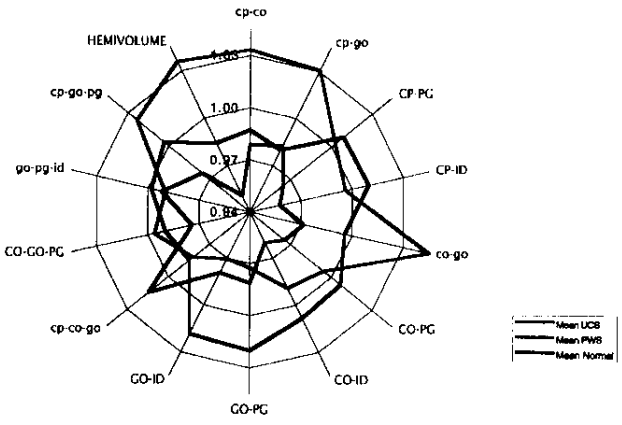

FIGURE 6 Polar plot comparison of UCS (medium gray line), PWS (light gray line), and normal mandibles (black line). Each radius is specific measurement, linear, angular, or volumetric. If all the right:left ratios for normals were 1.00, the "normal" line (black) would coincide with the 1.00 circumference.

1988), and deformable textbook atlases (Christensen et al., 1995)]. To date, however, none of these methodologies have replaced cephalometry as the *lingua franca* of the craniofacial morphometric world. Further development of these or novel solutions to spatial analysis are necessary to process the large magnitude of anatomic data now available through CT and MR imaging.

Conclusion

This analysis demonstrates that discrete, measurable, and etiology-specific mandibular dysmorphology exists in untreated infants having either UCS or PWS.

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