The Gradient and the Pattern of Crown-Size Reduction in Simple Hypodontia

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Agenesis of one or more permanent teeth, resulting in a decrease in tooth number, has long been a subject for comparative studies. Considerable information has been amassed on the prevalence of hypodontia in different populations and it is clear that tooth number reduction is also partially influenced by sex.

More recently, attention has been directed to the individual correlates of hypodontia. Here, the generation of new information has been considerable. Even the minimal degree of hypodontia (agenesis of one or more mandibular third molars) is associated with a 13-fold increase in the prevalence of other missing teeth[8,14] and with reductions in cusp number and other alterations in crown morphology.[5,24,28] Third molar agenesis, moreover, is associated with crown-size reduction in the remaining teeth[13,21,23] and with delayed somatic development and developmental immaturity at birth.[2,10,25]

Under these circumstances we have explored three possibilities. The first is that hypodontia has a progressive or incremental effect upon crown-size reduction in all of the remaining teeth. The second is that there is a gradient of crown-size reduction in hypodontia, from the most posterior teeth to the midline. The third possibility is that hypodontia is associated with a distinctive alteration in the crown-size profile pattern of the remaining teeth, such that even minimal hypodontia is reflected in a systematic departure from the usual.

These possibilities have been explored for twenty-eight permanent teeth in the largest single series so far considered in the odontometric literature, and including increasing degrees of hypodontia involving M_3, I^2, P^2 and even M^2.

Methods and Materials

This study is based upon vernier-caliper measurements of mesiodistal crown diameters of 658 subjects from southwestern Ohio.[15] Most of the subjects were born in Ohio and the majority were of Northwest European ancestry. Crown-size diameters of this group have been the subject of extensive studies, since it is the largest single group of its kind.

Of the total of 658 subjects, 82 were shown to have radiographically-confirmed agenesis of one or more third molar teeth. Furthermore, there was an additional subgrouping of 19 subjects with agenesis of multiple teeth, usually lateral incisors or second premolars. These three groupings are here described as (1) the reference population, (2) the agenesis group and (3) the multiple agenesis group.

Since the purpose of the study transcended sex, group and morphological class, it was necessary to put all crown-size measurements on a uniform basis. This was done by converting raw mesiodistal crown-size diameters into normalized T-scores,[6,19,22] using McCall's method[27,28] but employing a computer approach designed by C. A. Black.[3] Since

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a given T-score then indicated a comparable position in the distribution of tooth sizes, after correction for sex and morphological class, it was possible to combine the two sexes for final data analysis.

Furthermore, conversion of raw mesiodistal crown-size diameters into normalized sex-specific T-scores made possible both the graphical and the mathematical representation of the "crown-size profile pattern" for the reference population, the agenesis group and the multiple agenesis group.[6,16-18] Finally, the statistic r_T made possible the comparison of these crown-size profile patterns to each other using the familiar product moment correlation (r) as a measure of similarity.[16-18] In this way it was practicable to measure the extent to which agenesis of M_3, or multiple agenesis, affects the crown-size profile pattern and causes it to deviate from that of the reference population.[17,18]

For further details on the crown-size profile pattern and the statistic r_T, the reader is referred to previous papers in the *Archives of Oral Biology,* the *Journal of Dental Research,* and the *American Anthropologist.*[16-19]

Findings

The first step in the data analysis involved confirmation of the hypothesis that tooth number reduction (hypodontia) is simply associated with crown-size reduction. To do this, mesiodistal crown-size measurements for 658 individuals in the total or comparison population were compared to similar measurements for 82 subjects with radiographically-verified third molar agenesis and measurements of 19 subjects with multiple dental agenesis. All measurements were converted into normalized T-scores, in terms of the reference or comparison population as previously described. [15-18]

As shown in Table I, the results are quite unequivocal. As a group, individuals with third molar agenesis evidence smaller permanent teeth than do individuals with a full dental complement. This is shown for the majority of permanent teeth in male subjects with third molar agenesis (excluding tied values of T for P^2 and P_2). This is further shown for all fourteen permanent teeth in female subjects with radiographically confirmed agenesis of M_3. Combining the sexes, all fourteen pairs of teeth considered are smaller in the third molar agenesis group than in the reference population without exception. In all, males are smaller by 1T (0.1 standard deviation) and females are smaller by 3T (0.3 SD). By sign test, both the female values and the combined-sex values of T are significantly smaller than the reference population ($\chi^2 > 10.0$ and 10.0 respectively).

Furthermore, the multiple agenesis group (lacking M_3 and other teeth) extends the crown-size diminution trend set by the simple M_3 agenesis group. Combining sexes because of the small size of this latter sample, the following generalizations may be made. First, crown size is generally reduced in this multiple agenesis group. Second, the reduction of crown size exceeds that in simple third molar agenesis. So tooth number reduction is associated with crown-size reduction, more so in multiple agenesis than in simple third molar agenesis, and more so in females than males.

The reduction in crown size associated with hypodontia could be simple, involving a downward shift of the size distributions, or it could be complex, involving a change in the size distributions. To explore these possibilities we have compared tooth size variance in the groups in question, again using T scores throughout for simple comparison. The data in Table II indicate a

TABLE I

Progressive Size Reduction of the Remaining Teeth in Agenesis

Tooth	Reference Population		Third Molar Agenesis Group						Multiple Agenesis	
			Males		Females		Combined		Combined Sex	
	N*	T	N	T	N	T	N	T	N	T
			Maxillary Teeth							
I1	645	49.9	36	48.5	46	46.8	82	47.5	36	44.2
I2	626	50.0	31	49.7	42	44.7	73	46.8	21	41.3
C	576	50.0	34	46.7	44	45.1	78	45.8	36	45.1
P1	583	49.8	34	48.6	45	47.9	79	48.2	36	47.7
P2	564	49.7	31	49.7	43	47.1	74	48.2	28	47.7
M1	533	49.8	35	50.2	46	48.3	81	49.1	36	50.5
M2	455	49.7	28	50.4	36	49.0	64	49.6	31	50.4
			Mandibular Teeth							
I1	638	50.0	35	49.4	43	46.7	78	47.9	30	46.4
I2	644	50.0	36	50.5	46	47.3	82	48.7	35	44.4
C	614	50.0	34	49.4	45	46.4	79	47.7	36	46.8
P1	596	49.9	35	49.2	44	48.3	79	48.7	35	47.7
P2	538	49.8	23	49.8	42	47.3	65	48.2	20	46.2
M1	605	49.9	36	46.3	45	48.5	81	47.5	36	47.0
M2	389	50.1	26	50.8	36	48.0	62	49.2	28	49.6
Mean T	8106	49.9	454	49.2	603	47.2	978	48.1	444	46.8

* No. of persons, left side primarily, except for multiple agenesis group.

TABLE II

Effect of Hypodontia on Crown-Size Variance (σ^2)

Tooth	Tooth Size Variance (σ^2)			F Test*		
	1. Reference Population	2. M_3 Agenesis	3. Multiple Agenesis	1 vs 2	1 vs 3	2 vs 3
		Maxillary Teeth				
I1	100	117	136	1.17	1.36	1.16
I2	100	115	121	1.15	1.21	1.06
C	100	94	141	1.06	1.47	1.55
P1	100	89	90	1.13	1.11	1.01
P2	100	95	161	1.05	1.61*	1.68
M1	100	101	108	1.01	1.08	1.07
M2	100	89	177	1.12	1.77*	1.99*
		Mandibular Teeth				
I1	100	115	128	1.15	1.28	1.11
I2	100	113	151	1.13	1.51	1.34
C	100	112	172	1.12	1.72*	1.54
P1	100	83	100	1.20	1.00	1.20
P2	100	78	93	1.28*	1.08	1.19
M1	100	99	149	1.01	1.49	1.51
M2	100	70	83	1.43*	1.21	1.18

* Values of F based on number of subjects.

TABLE III
The Molar-Incisor Gradient of Crown-Size Reduction in Hypodontia

Tooth Class	Reference Population* Mean T	M_3 Agenesis* Mean T	Multiple Agenesis* Mean T
Incisors	50.0	48.6	44.1
Canines	50.0	47.1	45.8
Premolars	49.8	49.2	47.4
Molars	49.9	49.6	49.5

* Sample sizes 658, 82 and 19 respectively. See reference 20 for other aspects of patterning.

substantial alteration in the size variance of the remaining teeth in both third molar agenesis and in multiple tooth agenesis. The results given in Table III clearly attest to the alteration in crown-size variance in agenesis, particularly for P^2-P_2 and M^2-M_2. Thus, when M_3 or other permanent teeth are congenitally missing, the size variance of the remaining teeth is altered. So, agenesis and multiple agenesis are characterized first by size reduction of the remaining teeth and second, by variations in size variance of the teeth that are still present and erupted. The more teeth missing, the greater the size reduction and the greater the disturbance in the size distributions.

Now the next question is whether crown-size reduction in agenesis is uniform, from I_1 through M_2, or whether there is a *gradient* of size reduction, from M_2, in decreasing fashion. This can not be ascertained from the raw scores (actual millimeter values) but can be ascertained from the T-scored values where all teeth are transformed on a uniform basis. When this is done, as in the third table, the trend is then clear. Anterior teeth (I and C) are more reduced, relatively, than posterior teeth (P and M). Particularly for the multiple agenesis group, lacking M_3 and other permanent teeth, there is a simple gradient of relative size reduction starting at the anterior and diminishing in a mesial-to-distal fashion. The incisors are most reduced (T 44.1), the canines next reduced (T 45.8), the premolars somewhat less reduced (T 47.4) and the molars reduced least of all (T 49.5). Hence the data confirm the existence of a gradient of size reduction in hypodontia, such that the anterior teeth are most reduced and the posterior teeth least reduced. Alternatively, this gradient of size reduction may be described as a "field" of size reduction centering about the incisors and diminishing toward the molars, even though the key tooth missing (M_3) is at the opposite end of the gradient.

Having established the crown-size reduction, gradient of crown-size reduction and the alteration in crown-size variance associated with hypodontia, it is then possible to explore the effect of agenesis on the crown-size pattern as a whole. Since the combined-sex values for the reference population, the agenesis group and the multiple agenesis group are in the form of normalized T-scores throughout, crown-size profile patterns can then be compared by the familiar product moment correlation or Pearsonian r. As with r itself, the values of r_T range from -1.0 (indicating a perfect reciprocal relationship) to $+1.0$, indicating a perfect positive relationship.

Within these familiar limits therefore, it is important to observe in Table IV that both the M_3 agenesis group and the multiple agenesis group show negative values of r_T with respect to the comparison population ($r_T = -0.34$ and -0.38 respectively). At the same time, the crown-size profile patterns of the two agenesis groups significantly resemble each other ($r = 0.71$). It follows then that any degree of hypodontia profoundly alters the crown-size profile pattern, and brings about a new patterned relationship within the perma-

TABLE IV
The Effect of Agenesis on the Crown-Size Profile Pattern

Comparison	r_T*
3rd Molar Agenesis vs Reference Population	—0.34
Multiple Agenesis vs Reference Population	—0.38
3rd Molar Agenesis vs Multiple Agenesis	+0.71

* Based on 14 pairs of teeth, mean values of T as in Table I, for details of r_T see references 6 and 16-18.

nent dentition. Agenesis then is responsible for a qualitative as well as a quantitative alteration in crown size throughout the dentition.

Discussion

It is now more than evident that reduction in tooth number (hypodontia) is associated with a wide variety of alterations in the size, morphology and developmental timing of the remaining teeth and with alterations in the rates of extraoral development and the size of the body in the perinatal period. If we exclude those C, D and G group chromosomal reduplications, deletions, and translocations in which tooth-number reductions are the rule and confine ourselves to third molar agenesis in the putatively normal population alone, the following generalizations may be made. Third molar agenesis is associated with delayed formation timing of all of the remaining teeth, especially so for the most posterior teeth and for the distal tooth of each class.[1,10,11] Third molar agenesis, therefore, is characterized by a gradient of delay in formation timing, a distinctly different pattern of (relative) formation timing[10] and, by virtue of differential delay of M_2, the P_2M_2 formation sequence in contrast to the M_2P_2 order of formation.[10]

Third molar agenesis, moreover, is associated with reductions in the cusp number of the molars and therefore with the relative number of cusps on M_1 and M_2,[5,12] an alteration of considerable taxonomic significance. In addition to these changes in crown morphology, third molar agenesis is associated with crown-size reduction, particularly crown-size reduction of the lateral incisors, the second premolars and the second molars and, inevitably, with hypoplastic or "peg-shaped" lateral incisors, particularly so in the female.[13,22]

Further, the developmental concomitants of third molar agenesis extend beyond the teeth and postnatal development. There is evidence of reduced body size and an increased incidence of prematurity, suggesting a reduction of prenatal growth rates in affected individuals.[2,22,25] Thus a relatively common sex-influenced developmental anomaly proves to have multiple dental and many somatic correlates. Either alone, or in combination with other genes affecting growth, size and development, third molar number polymorphism may be indicative of multiple developmental delays. Indeed, it is even possible that the lesser incidence of third molar agenesis observed in the male may be due to selective prenatal loss of the XY or other Y-bearing chromosomal combinations rather than to a simple influence of two X chromosomes.

Early in our studies we postulated the existence of a gradient of diminished tooth size in the presence of third molar agenesis, based upon the direct evidence of a gradient of timing delay extending (in diminishing fashion) from the most distal teeth towards the midline. Our findings here do support the postulate of a gradient of size reduction but in the *opposite* direction from what we had originally anticipated. The anterior teeth, not the posterior, are relatively most reduced in the presence of third molar agenesis. The diminishing gradient of size reduction therefore operates in a mesiodistal direction.

So third molar hypodontia manifests itself as two different gradients. There is the posterior-to-anterior, distal-to-mesial gradient of formation delay and there is the anterior-to-posterior, mesial-to-distal gradient of relative size reduction. The general population, therefore, consists of two phenotypic groups. One is the hypodontic group with a timing gradient in one direction and the size-reduction gradient in the other direction. The second group is the "normal" group, lacking both of these gradients of reduction. Since third molar agenesis varies in its frequency from population to population, from near zero in some African groups to ten to thirty per cent in various reported groups of European origin (to as much as one-half in some groups of Asiatics), the conventional total-population comparisons of crown size may well be misleading. It may be that norms for tooth formation timing and standards for crown size should both be revised. With affected subjects tabulated separately from unaffected subjects, with third molar agenesis handled separate from size and development of unaffected subjects, population differences in crown size and formation timing might then be more clearly delineated.

Third molar agenesis is further associated with a marked alteration in the crown-size profile pattern.[9] Even with the minimal degree of hypodontia in the form of agenesis of one or more mandibular third molars, the entire crown-size profile pattern becomes altered and the normal dimensional relationship no longer apply. Further, the crown-size profile patterns of individuals with any degree of hypodontia resemble each other and no longer resemble those of the general population. Tooth number reduction again proves to be no simple and isolated anomaly but rather the key to altered patterned relationships within the dentition.

The fact that the least degree of hypodontia is associated with a gradient of size reduction and with a distinctly different crown-size profile pattern, and the fact that more extensive degrees of hypodontia extend and exaggerate these departures has further bearing on the behavior of the teeth in congenital abnormalities (birth defects) and with abnormalities of chromosomal number or balance. Demonstrably in Downs' syndrome (trisomy G or "Mongolism") there is hypodontia, crown-size reduction and a patterned departure from the population normal.[4] It is particularly important, therefore, to ascertain whether the temporal, dimensional and patterned alterations associated with reduplications of the 21st chromosome or with balanced translocations involving the 21st chromosome extend and exaggerate the departures demonstrated in third molar agenesis and multiple agenesis, or whether the extra G-group chromosome introduces a new pattern of its own. This would have diagnostic value, since not all cases of Downs' disease can be diagnosed from the karyotype alone and it would be further appropriate to ascertain the extent of patterned crown-size reduction in the parents and siblings of children with trisomy G. Exactly the same principle obtains for other autosomal reduplications such as Edward's syndrome, the cri-du-chat syndrome, Wolff's syndrome, etc. Moreover, the known alterations of facial development exhibited in parents and siblings of children with cleft palate and harelip coupled with tooth-number variations in the affected cases would suggest the value of investigating crown size and the crown-size profile pattern in the unaffected parents and siblings as well. Since both tooth-number reduction and tooth-number increases have been reported in cleft palate, a variety of crown-size profile-pattern alterations might be expected in the families of individuals with this multivariate condition.

In previous work we have established the genetic nature of the crown-size profile pattern as demonstrated in monozygotic twins, siblings, cousins and parent-child parents.[16,18] We have shown that the crown-size profile pattern has taxonomic value, affording a simple numerical expression of resemblance between different populations.[16,17] We have shown that the crown-size profile pattern helps to explain phylogenetic relationships.[16] Now it is apparent that the crown-size profile pattern has value within the population responding as it does to single-gene substitutions and providing an indication as to how a single polymorphism can affect total patterned relationships. Finally, the crown-size profile pattern may have diagnostic value, useful in detecting the recessive carriers of some genetic disease and the carriers of balanced translocations and other chromosomal irregularities.

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