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Statistical Genetic Comparison of Two Techniques for Assessing Molar Crown Size in Pedigreed Baboons

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ABSTRACT Dental anthropologists and paleoanthropologists commonly use an estimated molar crown area (mesiodistal length multiplied by buccolingual width) to describe and compare individuals, populations, and species. Advances in digital imaging now allow researchers to measure the actual crown area of a molar in an occlusal two-dimensional plane. Because error is reduced by this more accurate measurement, actual crown area is thought to be a better representation of the mechanisms that determine tooth crown size, meriting the additional time required to collect it. We tested this assumption by estimating the heritability of both these measurements for the second left mandibular molar from a sample of individuals (n = 332) from a captive breeding colony of baboons.

Heritability estimates of both the actual and estimated crown areas of molars are approximately 0.83. Therefore, both measurements are informative as population descriptors, with no significant difference between the accuracy of either to reflect additive genetic contributions to molar crown size. This is fortunate, because genetic studies and inference can be based on estimated areas rather than actual crown area.

The heritability estimates for mesiodistal length and buccolingual width are both substantial but lower: ~0.67 and ~0.73, respectively. The best fitting models in these analyses show that sex, body size, and subspecific affinity differentially affect molar length and width. We interpret these results to suggest that potentially some of the genetics underlying these covariates also underlie tooth size. As such, measurements designed to describe molar crown size are useful for general descriptive purposes, but do not conform to the assumption of independence inherent in phylogenetic analyses, such as cladistics (Hennig [1966] Phylogenetic Systematics. Urbana: University of Illinois Press). Therefore, if variables like actual crown area and estimated crown area are to be used in phylogenetic parsimony analyses, we suggest that researchers account for the effects of covariates such as sex and body size in their analyses. Am J Phys Anthropol 117:182–189, 2002.

The outer surface of tooth crowns is comprised of enamel. Because enamel is made of mostly inorganic material, teeth are robust to postmortem decay. Therefore, they are usually the most abundant, and sometimes the only, morphology known for primate taxa. Since teeth are critical to mastication and also function in social interactions, they play a large role in our understanding of adaptation and evolution within primates. Tooth size has been one of the most important variables used in odontological research, having applications in hominid paleontology (e.g., Broom et al., 1950; White et al., 1981; Wood, 1991), modern human origins (e.g., Wolpoff, 1971), modern human population variation (reviewed in Scott and Turner, 1997), nonhuman primate paleontology (e.g., Pilbeam et al., 1977; Delson, 1979; Benefit and Pickford, 1986; Kay, 1990), extant primate variation and intraspecies relationships (e.g., Phillips-Conroy and Jolly, 1981; Hayes et al., 1990), and studies of tooth development (e.g., Osborn, 1979).

All of the above-mentioned articles estimate tooth size as the product of mesiodistal length and buccolingual width. This estimated crown area is a commonly used and practical variable because length and width measurements are relatively quick to collect. Researchers can also include damaged teeth in their data sets, since estimated crown area does not require the entire tooth crown. The implicit assumption is that molar size, calculated via the estimated crown area, is a reflection of the genetic and developmental mechanisms that underlie molar crown size variation. This measure has been used to interpret phylogeny, adaption, and dental development (such as field vs. clone theories).

Forty years ago, odontologists started to develop more accurate methods for capturing molar crown

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size (e.g., Hannihara et al., 1961; Erdbrink, 1965, 1967). These publications suggested that crown area is more informative than the product of length and width. Following these studies, the more accurate actual crown area became the molar crown size descriptor of choice (Wood and Abbott, 1983; Wood et al., 1983; Suwa et al., 1994). The use of area measurements has been expanded to include relative cusp proportions (Hills et al., 1983; Kanazawa et al., 1985; Reid et al., 1991; Suwa et al., 1994; Uchida, 1998a,b; Wood et al., 1983).

Generally, it is assumed that a more accurate technique is better for investigations of population, species, and/or evolutionary relationships because it reduces measurement error. Because the estimated crown area is merely a rough estimate of what is a rather complicated shape, the actual crown area will usually be a significantly more accurate representation of molar size. One of the drawbacks to using actual crown area instead of estimated crown area is that broken and partial molars cannot be used. As Wood and Abbott (1983:197) explained, . . . "the choice is whether to use relatively simple measurements, and thus maximize the sample size, or whether to make more detailed observations and measurements, which may be taxonomically more meaningful, on fewer specimens." Wood and Abbott (1983) proceeded to demonstrate that actual crown area is between 8–40% more accurate than estimated crown area. Though molar crown size alone is by no means a comprehensive trait for phylogenetic and taxonomic assessments, actual crown area is preferable because it is assumed to be a more accurate representation of the underlying biology. This assumption has yet to be tested.

The heritability of an anatomical trait is an estimate of the proportion of the phenotypic variance of that trait in a sample that can be accounted for by genetic factors (including additivity, dominance, and epistatic interactions) as opposed to nongenetic factors (such as environmental effects, measurement error, or unidentified covariates). Heritability in the narrow sense estimates the amount of phenotypic variance accounted for by additive genetic factors alone.

Heritability estimates have two important applications in studies of continuously varying traits like odontometrics. First, the magnitude of the heritability estimate is a major determinant of the statistical power to detect and localize specific genes responsible for the genetic effects on variation in a quantitative trait (Almasy and Blangero, 1998; Rogers et al., 1999), i.e., the greater the heritability estimate, the greater the power to detect linkage with a chromosomal region that contains a gene (or genes) that contributes substantially to the variance. Second, the proportion of the variance in a continuously varying trait due to the additive effects of genes has been employed extensively in studies of animal and human populations. The amount of variance in a trait due to the additive effects of genes provides an estimate of a trait's potential responsiveness to selection—both natural and artificial. Consequently, narrow-sense heritability estimates have implications for finding genes for complex traits like molar crown size, and they also contribute to our understanding of the sensitivity of molar crown size to selective pressures.

Any nongenetic factor that increases phenotypic variance reduces heritability estimates, because heritability is the proportion of variance due to only additive genetic effects. Both imprecise and inaccurate measures on a phenotype can increase the random (unmeasured) environmental component to the variance in a trait. Imprecision in measurements may be due to unreliable measurement techniques, and can be reduced by careful and repeated measurements. The accuracy of a measure, i.e., how closely it approximates or describes the actual trait of interest, is another issue. First and foremost in importance is the selection of the trait for study; second, is the measurement protocol employed to collect the data. While direct measurement of the trait of interest is usually preferred, indirect assessments are occasionally necessary or more convenient. This is the case with molar crown area.

It is possible that proxy measures for crown area, such as estimated crown area, would be so imprecise and inaccurate that they would undermine our ability to detect and characterize the effects of genes and other important factors on tooth size variation within and between species. We report a study to determine if proxy measures for, or indirect estimates of, molar crown size are less useful for detecting and measuring the effects of genes on variance in molar crown size in a nonhuman primate species. We expect that a less accurate measure (i.e., one that does not reflect the actual variation in molar crown size upon which genes, environment, and selection may act) will return smaller heritability estimates with larger standard errors.

MATERIALS AND METHODS

Data for this study were obtained from 332 pedigreed baboons, *Papio hamadryas* (following the taxonomy of Jolly, 1993), who are part of a much larger breeding colony at the Southwest Foundation for Biomedical Research (SFBR) in San Antonio, Texas. These 332 individuals comprise five subsets of the pedigreed breeding colony (300 were still living at the SFBR as of June 1999, and the skulls of 32 dead animals were curated by Dr. J.M. Cheverud at Washington University, St. Louis, MO). The pedigree sample studied consisted mainly of olive baboons (*Papio hamadryas anubis*), yellow baboons (*Papio hamadryas cynocephalus*), and their hybrids (Williams-Blangero et al., 1990; Jolly, 1993), with a female to male sex ratio approximating 2:1, and ranging in age from 4.6–30 years. While strict genetic management was (and is) employed to prevent inbreeding, all nonfounder animals in this study were the result of matings that were random with respect to phenotype. Since birth or, in the case of some of the oldest of the founders, arrival at the

SFBR colony, all animals have been housed out of doors in social group cages and maintained on monkey chow diets to which they have ad libitum access. Animal care personnel and staff veterinarians provide daily maintenance as well as healthcare to all animals throughout their stay at SFBR, in accordance with the *Guide for the Care and Use of Laboratory Animals* (National Research Council, 1996). All procedures related to their treatment during the conduct of this study were approved by the SFBR and University of Illinois Animal Care and Use Committees, in accordance with the established guidelines.

Impressions of the living animals' dentitions were made while they were anesthetized intramuscularly with ketamine followed by intravenous "RAAK" (rompun, atropine, acepromazine, and ketamine) to affect relaxation. Each animal's mouth was held open, using a mouth splint. The animal's teeth were brushed clean with a toothbrush prior to molding when necessary, and wiped dry using gauze. Both the maxillary and mandibular postcanine dentition and incisors were molded using a rapidly setting impression material commonly used by dentists (Coltene President© gel). This procedure is approved by the SFBR and University of Illinois Animal Care and Use Committees, in accordance with established guidelines. Positive casts were poured with high-resolution dental plaster within 1 week of the mold being made. Casts were used for assessment of variation. The dentitions of the skulls at Washington University were molded and cast following the same protocol.

Digital images were made of the molar casts using a digital camera (Pixera© Professional, Pixera Corporation, Los Gatos, CA) and an 18–108-mm F2.5 zoom lens (D.O. Industries©, Navitar, Inc., Rochester, NY). The camera was positioned vertically over the molar, with the lens about 30 cm above the surface of the tooth. In living monkeys, the gumline obscures the cervix and forms the outer visual boundary of the tooth. The outline of each tooth was chosen to be 1 mm below the lowest point of the mesial and distal foveae. This was measured by sinking the tooth into a pool of titanium beads of approximately 0.15 mm diameter. These beads acted like a liquid, filling in around the tooth at a certain level. The level was defined and checked using a mounted ruler (Fig. 1). Buccolingual level was set so as to maximize the view of the tooth occlusally. Following this protocol, the outer line of the tooth was standardized and could be used in all further measurements taken. Scale (pixel aspect ratio) was set, using a ruler mounted at the level of the titanium beads in each picture. Replicability of the digitizing protocol was tested for 14 molars. Measurement error between the duplicated images was between 1.5–1.7% of the total measurement.

Mesiodistal length was measured as the maximal length of the molar. Interproximal wear was not accounted for because of the large amount of variation in the mesial and distal marginal ridges. We decided that it is better to work with interstitially worn teeth instead of introducing an unknown amount of error by reconstructing these highly variable regions of the molars. Buccolingual distance was measured as the maximal width of the tooth oriented through the two mesial cusps (see Fig. 2 for diagram of measurements). Note that the orientation of this latter measurement is not always directly perpendicular to the mesiodistal axis of the tooth. Measurements were not taken from teeth that were worn below the landmark defined by the mesial/distal foveal depth. Working from these digital images of second left mandibular molars, molar actual crown area (n = 280), mesiodistal length (n = 262), buccolingual width (n = 260), and estimated crown area (n = 260) were collected using Optimas© software. Intraobserver error for collecting these measurements was between 0.8–2.6% for the linear measurements, and 1% for the area measurement.

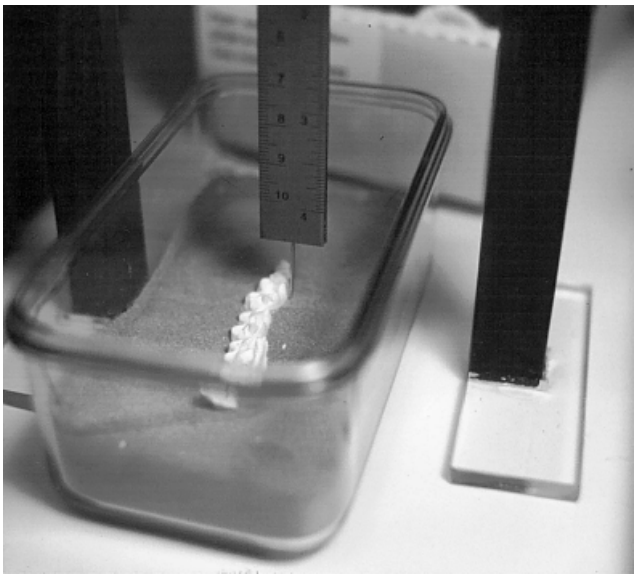

Fig. 1. Digitizing protocol. Right mandibular postcanine tooth row cast is sunk into titanium beads for digitizing of right third molar. Each tooth was oriented individually. Digital camera is positioned ~30 cm directly above occlusal surface of the tooth. The mounted ruler was used to check level prior to digitizing. See text for further explanation.

ANALYTICAL METHODS

All pedigree data management and preparation were accomplished using the routines implemented in the computer package PEDSYS (Dyke, 1996). For the purposes of the analyses presented in this paper, the animals were organized into five extended pedigrees. An additional 79 baboons for whom dental data were not collected were used to facilitate reconstruction of these pedigrees, which ranged in size from 13–205 members, with a mean size of 80 animals. The largest of the five pedigrees is three generations deep, and the smallest is two generations deep.

Statistical genetic analyses were conducted by means of a maximum likelihood-based variance de-

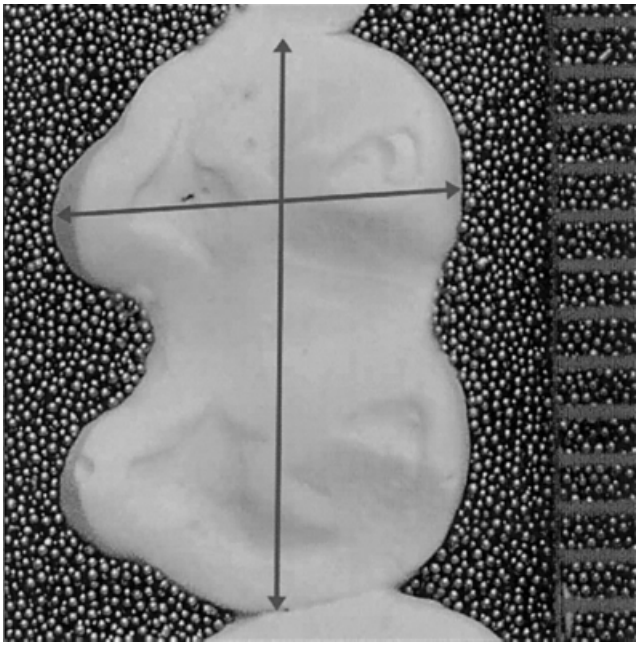

Fig. 2. Digital image of second left mandibular molar. Lines indicate orientation of mesiodistal length and mesial buccolingual width measurements. Actual crown area was defined as a line drawn around the entire tooth crown, defined as the edge between the tooth crown and the titanium balls. Scale is in millimeters. Buccal is to the left.

composition approach implemented in the computer package SOLAR (Almasy and Blangero, 1998). This approach, developed following methodology originally proposed by Hopper and Mathews (1982) and Boehnke et al. (1987), was described in detail elsewhere (Wang et al., 1997). In short, we use this approach to partition the phenotypic variance (σ_P^2) into components corresponding to the additive genetic (σ_G^2) and nongenetic (i.e., environmental) (σ_E^2) effects. Because these components are additive, such that $\sigma_P^2 = \sigma_G^2 + \sigma_E^2$, we estimated the heritability, or proportion of the phenotypic variance attributable to additive genetic effects, as $h^2 = \sigma_G^2/\sigma_P^2$. We estimated the proportion of the phenotypic variance attributable to non-genetic factors as $e^2 = 1 - h^2$. In addition to these terms, we simultaneously estimated the mean effects of sex, age, body weight, crown-rump length, and genetic affinity to "pure" *Papio hamadryas cynocephalus* on crown size for each molar studied. Degree of subspecific affinity to a founder *P. h. cynocephalus* individual is estimated as the kinship coefficient.

Significance of the maximum likelihood estimates for heritability and other parameters was assessed by means of likelihood ratio tests (Edwards, 1992), in which the maximum likelihood for the general model where all parameters were estimated was compared to that for restricted models in which the value of the parameter to be tested was held constant at some value (usually zero). The log likelihood of the constrained model was subtracted from the log likelihood of the general model. This difference was then multiplied by −2. Under broadly applicable conditions, this value, twice the difference in the log likelihoods of the two models compared, is known to be distributed asymptotically approximately as either a ½:½ mixture of χ^2 with a point mass at zero for tests of parameters like h^2 (for which a fixed value of zero in a restricted model is at a boundary of the parameter space), or a χ^2 variate for tests of covariates (for which zero is not a boundary value) (Hopper and Mathews, 1982). In both cases, degrees of freedom are obtained as the difference in the number of estimated parameters in the two models (Hopper and Mathews, 1982). However, in tests of parameters like h^2, whose values may be fixed at a boundary of their parameter space in the null model, the appropriate significance level is obtained by halving the *P*-value (Boehnke et al., 1987).

The analyses performed here decompose the total phenotypic variance into two basic categories: variance that can be accounted for by the identified covariates (sex, age, weight, crown-rump length, and percent ancestry from *Papio h. cynocephalus*), and variation not accounted for by the covariates. This latter, residual category is then decomposed further into variation that is attributable to genetic factors (the residual heritability, h_r^2) and variation due to nongenetic factors. Total phenotypic heritability is the proportion of the total phenotypic variance accounted for by additive genetic effects.

We used a multivariate extension (Blangero and Konigsberg, 1991) to the quantitative genetic analysis methods described earlier to determine the extent to which normal variation in both actual crown area and estimated crown area is attributable to the effects of the same genes or suite of genes. Described in detail elsewhere (Mahaney et al., 1995), this approach models the multivariate phenotype of an individual as a linear function of the measurements on the two crown measures (i.e., actual and estimated crown areas), the population means of these measures, any covariates and their regression coefficients, plus the additive genetic values and random environmental deviations. By maximizing the likelihood of this model on the data from these pedigreed baboons, we also can estimate the additive genetic correlation, ρ_G, between the two measures. This correlation is an estimate of the shared additive effects of genes (i.e., pleiotropy) on the phenotypic variance of the two measures.

RESULTS

All four left second mandibular molar phenotypes are found to be highly and significantly heritable: a major fraction of all variation in the traits is due to additive genetic effects rather than environmental variation in these pedigrees (see Table 1). Estimated crown area and actual crown area are found to have almost equal heritability estimates $h^2_{ECA} = 0.848 \pm 0.210$ and $h^2_{ACA} = 0.834 \pm 0.16$. However, the standard error is higher for estimated crown area compared to actual crown area. Mesiodistal length heritability is estimated to be 0.67 ± 0.192, a surprisingly high estimate given the potential error

TABLE 1. Heritability estimates for second left mandibular molar[1]

	Actual crown area (N = 280)		Mesiodistal length (N = 227)	
	MLE	*P*-value	MLE	*P*-value
Age	0.182	0.123	0.031	0.756
Sex	−15.942	<0.001	−0.018	0.987
Weight	0.069	0.575	0.15	0.12
C-R length	0.038	0.824	0.585	<0.001
% P. h. cyno.	−0.059	0.121	−0.085	0.004
	Variance due to covariates = 0.344		Variance due to covariates = 0.417	
e^2	0.166		0.33	
h_r^2	0.834 ± 0.16	<0.001	0.67 ± 0.192	<0.001
	Estimated crown area (N = 225)		Buccolingual width (N = 260)	
	MLE	*P*-value	MLE	*P*-value
Age	0.141	0.397	0.096	0.213
Sex	−18.153	<0.001	−6.533	<0.001
Weight	0.098	0.576	0.036	0.668
C-R length	0.24	0.315	0.143	0.203
% P. h. cyno.	−0.093	0.071	−0.029	0.183
	Variance due to covariates = 0.418		Variance due to covariates = 0.365	
e^2	0.152		0.266	
h_r^2	0.848 ± 0.21	<0.001	0.734 ± 0.178	<0.001

[1] C-R length, crown-rump length; *% P. h. cyno.,* degree of relatedness to a *Papio hamadryas cynocephalus* founder animal; MLE, maximum likelihood estimate; e^2, variance due to nongenetic affects; h_r^2, variance due to additive effects of genes (heritability) ± standard error of the estimate; buccolingual width was measured through the mesial cusps.

introduced by not accounting for interstitial wear. Buccolingual width heritability is estimated to be 0.734 ± 0.178.

The heritabilities reported in Table 1 are the residual heritabilities, and estimate the amount of phenotypic variance due to the additive effects of genes, after the variance due to the covariates is removed. Heritability, expressed in terms of total phenotypic variance, was obtained by multiplying the noncovariate variance by the estimated heritability reported in Table 1.

Actual crown area was the molar crown size measure with the greatest proportion of phenotypic variance being due to the additive effects of genes, i.e., 55%; covariates and unmeasured, nongenetic factors accounted for 34% and 11%, respectively. Estimated crown area is next, with 49% of its total phenotypic variance attributable to the additive effects of genes, 42% due to the mean effects of covariates, and 9% to unmeasured, nongenetic effects.

The two most commonly used measures of molar crown size follow. When expressed in terms of total phenotypic variance in mesial buccolingual width, the additive effects of genes account for 42%, covariates 37%, and unmeasured, nongenetic factors 17%. The additive effects of genes account for the smallest proportion of total variance for mesiodistal length, i.e., 39%, with 42% and 19% due to the effects of covariates and unmeasured, nongenetic factors, respectively.

The ultimate models for variation in these four traits included different significant covariates. For actual crown area, the covariate of sex accounted for 34% of total phenotypic variance ($P < 0.001$). Sex was a significant covariate for estimated crown area ($P < 0.009$), as was subspecific affinity to a *P. h. cynocephalus* founder animal ($P < 0.071$). These two covariates accounted for 42% of the total phenotypic variance in estimated crown area. For mesial buccolingual width, the only significant covariate included in the final model was sex, accounting for 37% of variance ($P < 0.004$). Two covariates were found to be significant for mesiodistal length variance, crown-rump length ($P < 0.001$) and subspecific affinity to a *P. h. cynocephalus* founder animal ($P < 0.004$). These two covariates accounted for 42% of the phenotypic variance in mesiodistal length.

The maximum likelihood estimate for the genetic correlation between actual crown area and estimated crown area is $\rho_G = 0.925$. This correlation is significantly different from zero ($\chi^2 = 5.81$, $P = 0.015$, df = 1), but it is not significantly different from 1.0 ($\chi^2 = 0.471$, $P = 0.493$, df = 1).

DISCUSSION

Contrary to our hypothesis that actual crown area would yield a higher, or at least more precise heritability estimate, estimated crown area and actual crown area resulted in highly significant heritability estimates that were almost equal ($h^2_r \sim 0.83$). Only when viewed on the scale of the total phenotypic variance does actual crown area have a higher heritability estimate (55%) than does estimated crown area (49%), both of which are higher than mesial buccolingual width and mesiodistal length. However, when viewed as a proportion of the residual variance, actual crown area and estimated crown area are effectively indistinguishable (~0.83). Therefore, both measures equally capture the same biological "signal." The residual heritability reported here describes the amount of variance attributable to genetic effects *after* the variance due to the covariates is removed. Thus, the biological signal being captured is that which is most relevant to the tooth developmental patterning process rather than

to possible pleiotropic effects of genes underlying body size or sex determination of the animal.

Given the added time and technical difficulty required to collect actual crown area phenotypes, they do not result in a significantly better representation of the genetic contribution to molar crown size. As such, the estimated crown area suffices as a description of the molar crown size of a population. Further studies will be needed to assess whether this phenomenon is found in molars that are less rectangular than cercopithecoid second mandibular molars, such as third mandibular molars. The higher degree of error between estimated crown area and actual crown area for hominid third mandibular molars found in a previous study (Wood and Abbott, 1983) suggests that this extrapolation should be made with caution until investigated more fully.

These results have direct implications for studies of genetic influences on crown size variation and development. There is currently growing interest in trying to identify the genetic basis of tooth size and shape, both for its own sake and to understand variation among present-day species and our evolutionary past. Typically, teeth that are available for study are often damaged, limiting the number of specimens available for measuring actual crown area. Our findings show that estimates of tooth crown size can be used for genetic research into dental patterning, thereby enabling the inclusion of broken teeth and ultimately increasing sample sizes. We are attempting to identify genes responsible for variation in the baboons used in the present study (Hlusko, 2000; Hlusko and Mahaney, 2000). The evidence reported here is part of that larger effort.

Developmental studies of tooth crown morphogenesis typically attempt to demonstrate the role of a known candidate gene by examining the gene's expression pattern in specific areas of the tooth germs during various stages of development (Jernvall et al., 1994; Jernvall and Thesleff, 2000; Keränen et al., 1998; Thomas and Sharpe, 1998; Thomas et al., 1998; Weiss et al., 1998; Zhao et al., 2000). The important stages of development are those when the cusp locations and relationships are just becoming visible. At this stage, the location of the enamel knots (Jernvall et al., 1994) signals the position of the future cusps, and the relative positions of the primary and secondary enamel knots between species appear to indicate their final configuration (Jernvall et al., 1994; Jernvall and Thesleff, 2000; Keränen et al., 1998). This, however, is not possible to determine directly because the tooth germs studied are not living at the time of the investigation: animals are sacrificed in studies of this type, so that gene expression can be observed directly in developing teeth. Consequently, these teeth do not progress to final form because they are no longer living. However, in living tooth germs, once the dynamics of morphogenesis have been completed, the germs mineralize in their final size and shape. Genetic studies of adult tooth characteristics, such as were used here, are a direct reflection of the process of tooth embryogenesis, though they investigate the genetic mechanisms through means of the ultimate morphology rather than at various stages during the process of development. Thus, the results reported here based on adult morphology are relevant and informative for studies of the genetics of dental patterning.

Most developmental genetic studies are based on expression patterns tested for known genes, and usually are able (at most) to detect the effect of a gene's presence or absence in its normal sites and times during development. Studies of natural *variation* are, however, capable of revealing additional genetic factors, because they can allow the mapping of genetic effects of previously unknown genes. Doing that is one objective of our work in the San Antonio baboon colony.

It is important to note that the similar heritabilities of estimated crown area and actual crown area do not automatically imply that one measure is a genetic surrogate for another. However, these two measures are highly correlated in the mature tooth ($r = 0.9$ with $r^2 = 0.82$, data not shown). More importantly, bivariate analysis shows that the genetic correlation between these two dental crown measures is not significantly different from one, suggesting that all or nearly all of the genetic variation in both of these two dental crown measures is attributable to the additive effects of the same gene or suite of genes. Additionally, while not completely identical, the developmental process as seen in experimental animals seems to be essentially the same for the two aspects of the crown. This is all strong circumstantial evidence that these two measures reflect the same phenotype, and that the analysis of either in this pedigreed baboon colony will detect the same genes.

Coupling quantitative genetic analyses, as was done here, with studies of developmental gene products (and candidate genes) is potentially a highly promising technique for unraveling the genetic evolutionary history of primate dental patterning. Expression studies focus on early development and the initial stages of morphogenesis. Perhaps more importantly, such work is usually typological in that it is usually based on genetically invariant (homozygous), and hence in many ways unnatural, strains of laboratory animals. Quantitative genetics enables the study of adult morphology, the result of tooth morphogenesis. Therefore, by studying dental development via both techniques, we will approach the process through opposite ends, and ultimately meet in the middle. This will provide a more complete understanding of the genetics of dentition than either method can achieve on its own.

Our results also have indirect implications for studies relying on genetic assumptions of dental metrics. One argument against the research presented here is that we have identified genetic mechanisms for variation within one population; how do we justify extrapolating these results to variation between populations? Research in developmental

genetics shows a close relationship in gene function between even distantly related taxa. For example, the patterning of the vertebral column is coded for by the same gene family in both mice and humans, Hox (Condie and Capecchi, 1993, Kessel and Gruss, 1991), and functions remarkably similar to its fly homologue, HOM-C, responsible for axial formation (Gilbert, 1997). Given that the earliest true primates lived only ~55 million years ago, it is reasonable to assume that the genetic mechanisms that underlie the primate dentition today are at least *generally* the same as those that determined primate dentition in the past. Additional support for this assumption stems from dental developmental research in gene expression, which shows that genes involved in mouse early dental patterning are largely the same as those seen in human early dental patterning (Davideau et al., 1999). Genetic sequencing and hybridization studies also argue for very close genetic similarities between extant primates, and therefore their last common ancestors. For example, baboons and humans are estimated to be ~92–95% genetically similar (Vandeberg and Williams-Blangero, 1997), with an evolutionary divergence approximately ~23.5 million years ago (Goodman et al., 1998; Kumar and Hedges, 1998). Rogers et al. (2000) reported that for seven human chromosomes, the locus order is the same in the baboon homologue. Very few rearrangements differ between the other 15 autosomes (Rogers et al., 2000).

Because of these close genetic relationships and the apparent conservation of developmental mechanisms, applying the knowledge of genetic mechanism gained in one primate to our understanding of other primates is reasonable. There are likely to be some differences, and of course, primates differ in detail in their dental patterns, but studies of natural genetic variation can point to genes that are at least good candidates for playing a similar role in such closely related species (even if their *quantitative* contribution, timing, and so on may differ somewhat). It is important to note, however, that heritability estimates from modern populations are not informative of past selective pressures because these estimates are highly sensitive to the sample population structure and nongenetic covariates that contribute to variation (such as household effects, environment, or measurement error). Therefore, it is the revelation of genetic mechanisms that are of particular interest to evolutionary questions, e.g., the assessment of different covariate effects.

The variance components analyses used here confirm that tooth size is determined by many different factors. We find that tooth size is dependent on crown-rump length, sex, or subspecific affinity of the individual. Most importantly, our results show that the effects of these covariates are not the same for length and width of the molar. Sex significantly effects molar width, but not length. Crown-rump length and subspecific affinity contribute to molar length, but not molar width. The proportion of total variance attributable to the covariates is quite high, ranging between 34–42%. Therefore, these covariate differences are not trivial. We suggest that estimated crown area and actual crown area are not accurate representations of the biological mechanisms that determine molar crown size. Rather, these measurements represent numerous genetic mechanisms, such as those that determine crown-rump length and sex of the individual, and not just tooth size-specific mechanisms. To demonstrate this point, note that only sex is found to be a significant covariate for both estimated crown area and actual crown area, whereas crown-rump length, and *not* sex, is a significant covariate for mesiodistal length. As such, measurements designed to describe molar crown size are useful for general descriptive purposes, but are inappropriate for analyses assuming that measures accurately and adequately reflect genetic/developmental processes, such as cladistics (Hennig, 1966). Therefore, if variables like actual crown area and estimated crown area are to be used in phylogenetic parsimony analyses, we suggest that researchers account for the effects of covariates such as sex and body mass and size in their analyses, as was attempted in some studies (e.g., Chamberlain and Wood, 1987).

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