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Quantitative genetic variation and selection on skull shape in humans Neus Martínez-Abadías^{1,2}, Mireia Esparza¹, Torstein Sjøvold³, Miquel Hernández¹ and Christian Peter Klingenberg⁴

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Quantitative genetics of human shape

The genetic basis of shape variation has been investigated for some time by combining the methods of geometric morphometrics with the multivariate theory of quantitative genetics. This combined approach has been applied extensively in studies of animals (e.g., Klingenberg and Leamy 2001; Mezey and Houle 2005; Willmore et al. 2005; Klingenberg et al. 2010), plants (Gómez et al. 2009), and humans (Martínez-Abadías et al. 2009b; Martínez-Abadías et al. 2012).

The key requirement for quantitative genetic studies of shape is a dataset containing morphometric data and information on the genealogical relationships among the individuals. From this information, biologically relevant parameters such as the genetic covariance matrix can be estimated using individual-based statistical models (e.g., Wilson et al. 2010). The data for our study were from the population of Hallstatt (Austria), where identified skulls and records of genealogical relationships are available. This population has been used for quantitative genetic studies of traditional morphometric traits (Carson 2006; Martínez-Abadías et al. 2009a) and also with geometric morphometrics (Martínez-Abadías et al. 2009b; Martínez-Abadías et al. 2012). Alternative data sources are large-scale medical surveys, which also have been used in analyses of traditional morphometric traits (Sherwood et al. 2008).

Predicted response to selection

The response to selection was predicted with the multivariate breeders' equation (Lande 1979), using the genetic covariance matrix and selection gradients obtained for the Hallstatt population.



Estimates of selection on shape can be obtained by regression of fitness measures on shape. Such studies have been done in plants (e.g., Herrera 1993; Gómez et al. 2006), but not yet in animals or humans.

Here, we use the estimate of the genetic covariance matrix and estimated selection on skull shape to predict the expected response to selection, and we compare this prediction to the observed secular change over the approximately 150-year period covered by the data.

The data

The skulls from Hallstatt (Austria) provide a unique opportunity for studying the genetics of cranial variation. Our sample includes 390 individuals buried on the Catholic churchyard of the town. As a tradition, the skeletal remains were exhumed and various decorations were painted on the skulls. Most decorations include the name of the deceased, so that the skulls can be linked to church records.



correspond to those in the selection gradients.





Secular change of cranial shape

The pattern of secular change was estimated by a regression of shape on birth year (Drake and Klingenberg 2008; Weisensee and Jantz 2011)

This pattern is quite different from the patterns of predicted response to selection. There can be several possible reasons for this discrepancy. First, it is likely that selection not only affects skull shape, but also other variables that are not included in our estimate of selection. Second, environmental factors such as nutrition, care for children and medical provision may have changed during the period covered by our data. Third, processes such as population turnover also might produce changes that are different from those induced by selection.



For each skull, 29 anatomical landmarks were digitized in three dimensions with a MicroScribe digitizer (full details in Martínez-Abadías et al. 2012).

Shape information was extracted with a Procrustes superimposition. All geometric morphometric analyses were carried out in MorphoJ (Klingenberg 2011).

The genetic covariance matrix was estimated for the first 32 principal components of the shape variation in the sample using the Wombat software (Meyer 2007). The resulting matrix was rotated back into the coordinate system of the landmark coordinates (full details in Martínez-Abadías et al. 2012).

Estimating selection on skull shape

Selection was estimated using four different fitness measures: (1) a composite measure of fitness, lambda, taking into account the number of children and the parental age at birth of the children, (2) fertility, the total number of children, (3) lifetime reproductive success, the number of children surviving to adulthood, and (4) longevity. For each fitness measure, linear and nonlinear selection was estimated (Blows and Brooks 2003) and statistical significance was tested with a permutation approach.

Conclusions and outlook

Quantitative genetic analyses of shape variation in humans hold considerable promise for research in evolutionary anthropology. They can supply crucial information in various contexts, such as inferences of past selection or neutral variation, adaptation, and population structure. Using the complete information from geometric morphometric analyses is feasible with currently available methods, as published studies have shown (Martínez-Abadías et al. 2009b; Martínez-Abadías et al. 2012).

Analyses of selection are feasible whenever data on shape and a measure of fitness are available. Such analyses can provide valuable extra information that supplement indirect inferences of past selection or genetic drift or genomic analyses of selection.

Fully multivariate methods for mapping quantitative trait loci (QTL) of shape are also available (Klingenberg et al. 2001; Workman et al. 2002; Klingenberg et al. 2004), but are yet to be applied to human populations. In humans, QTL analyses of craniofacial traits have been conducted based on traditional morphometrics (Sherwood et al. 2011), but studies using geometric morphometrics are yet to be done.

References

- Blows, M. W., and R. Brooks. 2003. Measuring nonlinear selection. American Naturalist 162:815–820.
- Carson, E. A. 2006. Maximum likelihood estimation of human craniometric heritabilities. American Journal of Physical Anthropology 131:169–180.
- Drake, A. G., and C. P. Klingenberg. 2008. The pace of morphological change: historical transformation of skull shape in St. Bernard dogs. Proceedings of the Royal Society of London, B Biological Sciences 275:71–76.
- Gómez, J. M., M. Abdelaziz, J. Muñoz-Pajares, and F. Perfectti. 2009. Heritability and genetic correlation of corolla shape and size in *Erysimum mediohispanicum*. Evolution 63:1820-1831
- Gómez, J. M., F. Perfectti, and J. P. M. Camacho. 2006. Natural selection on *Erysimum mediohispanicum* flower shape: insights into the evolution of zygomorphy. American Naturalist 168:531–545.
- Herrera, C. M. 1993. Selection on floral morphology and environmental determinants of fecundity in a hawk moth-pollinated violet. Ecological Monographs 63:251–275.
- Klingenberg, C. P. 2011. MorphoJ: an integrated software package for geometric morphometrics. Molecular Ecology Resources 11:353–357.
- Klingenberg, C. P., V. Debat, and D. A. Roff. 2010. Quantitative genetics of shape in cricket wings: developmental integration in a functional structure. Evolution 64:2935-2951.
- Klingenberg, C. P., and L. J. Leamy. 2001. Quantitative genetics of geometric shape in the mouse mandible. Evolution 55:2342–2352.
- Klingenberg, C. P., L. J. Leamy, and J. M. Cheverud. 2004. Integration and modularity of quantitative trait locus effects on geometric shape in the mouse mandible. Genetics 166:1909-1921

Nonlinear selection was not statistically significant for any of the fitness measures, indicating that there is no stabilizing selection.

Significant linear selection was found and the shape features favoured by selection (selection gradients) were similar for all four fitness measures.





Klingenberg, C. P., L. J. Leamy, E. J. Routman, and J. M. Cheverud. 2001. Genetic architecture of mandible shape in mice: effects of quantitative trait loci analyzed by geometric morphometrics. Genetics 157:785–802.

Lande, R. 1979. Quantitative genetic analysis of multivariate evolution, applied to brain:body size allometry. Evolution 33:402–416.

Martínez-Abadías, N., M. Esparza, T. Sjøvold, R. González-José, M. Santos, and M. Hernández. 2009a. Heritability of human cranial dimensions: comparing the evolvability of different cranial regions. Journal of Anatomy 214:19–35.

Martínez-Abadías, N., M. Esparza, T. Sjøvold, R. González-José, M. Santos, M. Hernández, and C. P. Klingenberg. 2012. Pervasive genetic integration directs the evolution of human skull shape. Evolution 66:1010–1023.

Martínez-Abadías, N., C. Paschetta, S. de Azevedo, M. Esparza, and R. González-José. 2009b. Developmental and genetic constraints on neurocranial globularity: insights from analyses of deformed skulls and quantitative genetics. Evolutionary Biology 36:37–56.

Meyer, K. 2007. WOMBAT—A tool for mixed model analyses in quantitative genetics by restricted maximum likelihood (REML). Journal of Zhejiang University Science B 8:815-821.

Mezey, J. G., and D. Houle. 2005. The dimensionality of genetic variation for wing shape in *Drosophila melanogaster*. Evolution 59:1027–1038.

Sherwood, R. J., D. L. Duren, E. W. Demerath, S. A. Czerwinski, R. M. Siervogel, and B. Towne. 2008. Quantitative genetics of modern human cranial variation. Journal of Human Evolution 54:909–914.

Sherwood, R. J., D. L. Duren, M. C. Mahaney, J. Blangero, T. D. Dyer, S. A. Cole, S. A. Czerwinski et al. 2011. A genome-wide linkage scan for quantitative trait loci infuencing the craniofacial complex in humans (Homo sapiens sapiens). Anatomical Record 294:664–675.

Weisensee, K. E., and R. L. Jantz. 2011. Secular change in craniofacial morphology of the Portuguese using geometric morphometrics. American Journal of Physical Anthropology 145:548-559.

Willmore, K. E., C. P. Klingenberg, and B. Hallgrímsson. 2005. The relationship between fluctuating asymmetry and environmental variance in rhesus macague skulls. Evolution 59:898–909.

Wilson, A. J., D. Réale, M. N. Clements, M. M. Morrissey, E. Postma, C. A. Walling, L. E. B. Kruuk et al. 2010. An ecologist's guide to the animal model. Journal of Animal Ecology 79:13-26.

Workman, M. S., L. J. Leamy, E. J. Routman, and J. M. Cheverud. 2002. Analysis of guantitative trait locus effects on the size and shape of mandibular molars in mice. Genetics 160:1573-1586.