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The effect of ancient population bottlenecks on human phenotypic variation

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Abstract

The origin and patterns of dispersal of anatomically modern humans are the focus of considerable debate¹⁻³. Global genetic analyses have argued for one single origin, placed somewhere in Africa⁴⁻⁷. This scenario implies a rapid expansion, with a series of bottlenecks of small amplitude, which would have led to the observed smooth loss of genetic diversity with increasing distance from Africa. Analyses of cranial data, on the other hand, have given mixed results⁸⁻¹², and have been argued to support multiple origins of modern humans^{2, 9, 12}. Using a large dataset of skull measurements and an analytical framework equivalent to the one used for genetic data, we show that the loss in genetic diversity has been mirrored by a loss in phenotypic variability. We find evidence for an African origin, placed somewhere in the central/southern part of the continent, which harbours the highest intra-population diversity in phenotypic traits. We failed to find evidence for a second origin and confirm these results on a large genetic dataset. Distance from Africa accounts for an average 19% - 25% of heritable variation in craniometric traits, a remarkably strong effect for phenotypic traits known to be under selection.

The origin of anatomically modern humans has been the focus of much heated debate^{1, 3}. Recent large scale genetic analyses⁴⁻⁷ seem to support the idea that all modern humans originated from a single location (single origin hypothesis, SO). More specifically, all studies point to Africa as the putative cradle of modern humans. If rapid, the expansion out of Africa would imply progressive loss of genetic diversity through a series of founder events (bottlenecks), a prediction that has recently received empirical support⁴⁻⁶. Heterozygosity declines monotonically with distance from east Africa, with South American populations carrying 64% of the neutral variability (as measured from microsatellites) found in African populations. This view is further supported by some archaeological and anthropological evidence¹. However, studies of craniometric data have yielded mixed results⁸⁻¹², and the presence of archaic human-like traits in skulls that would be otherwise classified as *H. sapiens* in several continents has been interpreted as evidence for multiple origins (multiregional hypothesis, MR)^{2, 12}.

An important step towards an univocal answer regarding the number of origins of modern humans would be to analyse the phenotypic (cranial) traits using the same approach used for genetic traits. The alternative models (SO and MR) make clear predictions about how craniometric diversity should be distributed. Under SO, we expect to find a monotonic decrease in phenotypic variability analogous to that seen for genetic traits (unless the sampling process is so strong as to destabilise canalisation through the loss of genetic diversity)^{13, 14}. In contrast, multiple origins should lead to several clines, the magnitude of each cline being determined by the relative contribution of its origin.

To test these predictions, we used an exceptional dataset of 4666 male skulls measured for 37 morphometric traits (Table S1) and drawn from 105 populations (Fig.1; Table S2)^{15, 16}. A minimum sample size of 15 individuals was enforced (median size: 36) and skulls older than 2,000 years were excluded to avoid any bias in the quality of the material. It is well known that some skull traits correlate with climate, implying natural selection^{17, 18}. Consequently, before considering the effect of ancient demography, we investigated the effect of three key climatic variables on the within-population cranial variability: maximum and minimum temperature, and average annual precipitation. For each population, we estimated the mean standardised phenotypic variance¹⁹ and fitted it in a linear model with climate variables (maximum temperature, minimum temperature and precipitation, with all possible interactions) as predictors (see Methods). Backwards stepwise elimination selected the interaction between maximum temperature and precipitation ($\Delta\text{BIC}=-2.2$) as the best predictors of cranial variability. The minimal model including this interaction was used as the starting point for the investigation of any effect of ancient demography, effectively assuming that climate was the most parsimonious explanation for any global pattern, and that ancient demography had to explain variance that had not already been accounted for by climate. This is arguably a very conservative approach, given that Relethford¹⁸ found a strong pattern of isolation by distance in craniometric inter-population differences and argued that selection through climate is insufficient to erase ancient demographic signals.

We next searched the globe for the putative origin giving the strongest relationship between within-population phenotypic variability (corrected for climate) and distance on land^{5, 20} (see Methods). This strongest cline originates in central / southern Africa and could be either a single origin or the main origin in an MR scenario (Fig. 2a & Fig. 3; effect of distance from the centroid of the likely origins after correcting for climate: $\Delta\text{BIC}=-12.5$; distance $R^2=14.0$). A similar analysis on the 789 autosomal neutral microsatellites from the 54 populations of the HGDP-CEPH panel^{21, 22}, using heterozygosity as a measure of genetic variability, gives almost identical results (Fig. 2b; showing patterns similar to those obtained by Ramachandran et al⁶ and Ray et al⁷, who used previous versions of the HGDP-CEPH dataset and somewhat different analytical approaches). The only noticeable difference between the estimates based on phenotypic and genetic traits is that the latter does not include south Africa amongst the most likely origins.

To test the MR hypothesis, we sought a second, non-African origin capable of increasing the explanatory power of the model (see Methods). Adding distances from other non-African origins did not improve our models (neither for phenotypic nor for genetic traits), supporting Ray et al⁷, who used a spatially explicit stochastic population model and also failed to find evidence for the multiregional hypothesis. Our approach therefore suggests a multiple origin is unlikely. However, we cannot distinguish between single vs multiple exoduses from Africa, because both scenarios would lead to a major cline from Africa. Depending on the exact timing and extent of the multiple exoduses, we could expect several subtly different patterns, and neither the genetic nor phenotypic datasets are currently large enough to investigate this level of detail. Also, very localised episodes of admixture between anatomically modern and archaic humans might go undetected if they left no signature in present day modern humans².

How strong are the patterns for individual cranial traits? Since we could not identify a precise location for the African origin of humans, we chose a centroid of the likely craniometric origins, and the possible influence of outliers was minimised by using robust regression²³ (see Methods). We considered both a model with distance as the only predictor, and one with a correction for climate. Out of 37 cranial traits, 34 showed a decline in variability with distance from Africa (binomial test, $p<0.001$; Table S3), and 12 of these (18 if we did not correct for climate) were significant after correction for multiple testing

with a false discovery rate (FDR) procedure²⁴. Although mean R^2 was 6.3% (7.0% if we did not correct for climate), some traits showed a strong demographic signal (Fig. 4; Table S3). A further test of how reliable these results are is to repeat the analysis on an equivalent but smaller dataset of female skulls, composed of 1579 individuals from 39 populations (Table S2). The results are very similar to the ones found in males (Table S4), with a mean R^2 of 9.1% for distance (8.9% without correcting for climate). Furthermore, slopes of trait CV over distance for females are almost identical to those obtained for males (best regression line: $[\text{female_slope_trait_x}] = 1.00 * [\text{male_slope_trait_x}]$, $R^2 = 0.77$, $F_{1,36} = 124.9$, $p < 0.001$).

Given that distance from Africa explains over 87% of variance in heterozygosity at neutral microsatellite markers⁵, the equivalent values for morphometric traits might seem disappointing. However, phenotypes are only partially determined by genotypes, as the environment is also playing an important role. Heritability, h^2 , defines the fraction of variance in a trait affected by genetics, and this represents an upper ceiling for the size of the demographic signal that can be detected. Estimates of heritability for cranial traits are rare, but Carson²⁵ recently derived values for 19 of the traits included in our analysis and these correlate significantly with the proportion of variance explained by distance from Africa (males $r_s = 0.56$, $p = 0.012$). On average, $R^2/h^2 = 0.20$ (s.e. = 0.06) for males and $R^2/h^2 = 0.20$ (s.e. = 0.06) for females (0.24 ± 0.06 and 0.25 ± 0.06 respectively if we did not correct for climate), indicating that the proportion of explained variance is at least a fifth of the heritability. Interestingly, this figure is similar to the 17 - 35% of variance explained by distance from Africa for class I MHC genes which are under selection by infectious diseases²⁶, just as climatic factors select for skull shape. Thus, after allowing for the impact of heritability and selection, the signal of ancient demography in human skull variability should properly be seen as remarkably strong.

Methods Summary

Thirty-seven morphometric cranial traits (Table S1) were measured in 4666 male skulls drawn from 105 populations (Fig. 1; Table S2) 15, 16. After correcting for climate, we looked for the likely origin of human diversity by investigating the relationship between phenotypic diversity (scored as mean standardised phenotypic variance¹⁹) and distances on land from locations across the globe. We then tested for the presence of a second origin by testing whether adding distances to putative locations improved the single origin model. We also assessed the strength of the signal from ancient demography on variability in individual traits for both male skulls and an additional dataset of 1579 female skulls from 39 populations, and compared patterns found in the two sexes. Finally, we investigated the magnitude of the ancient demographic signal in the context of the heritability of individual traits, since heritability provides an upper limit to any signature left by genetic factors.

Methods

Datasets

Thirty-seven morphometric cranial traits (Table S1) were measured in 6245 skulls (4666 male and 1579 female), drawn from 105 and 39 populations for males and females respectively (Fig. 1; Table S2). Details on the measurements are provided elsewhere^{15, 16}. Mid-oceanic populations were excluded because their origins are often unclear. Also excluded were samples over 2,000 years old, as deterioration might lead to biased estimates of phenotypic variability. Only the male dataset was large enough to discriminate among potential origins of diversity. Consequently, the female dataset was used for comparison when estimating the strength of the clines detected using male skulls. Genetic data come from the latest version of the HGDP-CEPH panel^{21, 22}, which includes 971 individuals

belonging to 54 populations and typed for 789 neutral autosomal microsatellites. Climate data (minimum and maximum temperature, and average precipitation) were obtained from WORDCLIM27, as sets of global climatic GIS layers with a 30 arc-seconds resolution.

Statistical analysis

Total within-population phenotypic variability was computed as the mean standardised phenotypic variance over all traits, following Relethford and Blangero¹⁹. Variability of individual traits within each population was computed as the Coefficient of Variation (CV, the ratio of the standard deviation to the mean). This dimensionless measure allows comparisons between different traits. Realistic geographic distances between locations were computed as the shortest route through landmasses that avoid areas with a mean altitude over 2,000 m and assuming the following land bridges: a single connection between Africa and Eurasia via a route through the Sinai to the Levant, the Bering Strait between Eurasia and the Americas, and connections between the Malaysian Peninsula to Melanesia and Oceania^{5, 20}.

To model the effect of climate on craniometric traits (male skulls only), we fitted a linear model with mean standardised phenotypic variance as the response and three climatic variables and all their possible interactions as predictors. Starting from this full model, we then found a minimal model for climate by backwards stepwise elimination using the Bayesian Information criterion (BIC) ²⁸.

The presence of a primary cline in diversity was tested by fitting as an additional predictor to the minimal climate model, distance from a range of potential origins distributed at intervals of 5 degrees latitude / longitude across the whole of Africa, Eurasia and Australia. As we effectively had to compare hundreds of similar models with only a slight difference in the values of the predictor variable (distances from different locations), we used BIC to select origins that gave similarly good fits. Models within 4 units of the best model have “considerable support”²⁹, thus providing a suitable envelope for the likely real origin. Having identified an African origin, we searched for a second origin by fitting distances from origins outside Africa as an additional predictor to the best African model. This approach was then repeated using the genetic dataset, with heterozygosity as the response variable in a linear model.

The strength of the relationship between variability of individual traits and distance from Africa was explored by considering individual traits in both males and females. Distances from a centroid of likely origins were fitted on top of the minimal climate model with the CV of traits as individual responses. Visual inspection of the relationship between CV and geographic distance revealed outliers in several traits. To account for heteroskedasticity without resorting to ad-hoc removal of populations, we used robust regression with MM-estimators²³ fitted in R30 using the robustbase package. This technique allows the estimation of linear models that are not affected by the outliers. We fitted models both with and without correcting for climate. The proportion of variance explained by distance from Africa when correcting for climate was estimated by subtracting the R^2 of the model including distance and climate from the R^2 of the climate model alone. Due to the large number of nested tests, it is difficult to formulate exact p-values. To provide a measure of goodness of fit, we computed Local False Discovery Rates²⁴ using the fdrtools package in R30.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Map of locations of populations from which male (blue) and female (red) skulls were collected. Locations from which skulls of both sexes were collected are marked in purple.

Fig. 2. Maps showing the likely location of a single origin for (a) phenotypic and (b) genetic data. Lighter colours represent better fits of models of variability as predicted by distance from a location. The area containing the most likely origins are marked by a dashed blue line. Areas of the world not investigated as possible origins (such as Iceland and Madagascar, which would require substantial land bridges to the main continents) are shown in grey.

Fig. 3.
Relationship between mean phenotypic variability (corrected for climate) for male skulls and distance from the putative African origin (represented by the centroid of likely origins)

Fig. 4.

Relationships between phenotypic variability for four traits (expressed as CV, corrected for climate) from male skulls and distance from the putative African origin (represented by the centroid of locations of origins). The traits are: (a) Lambda-opisthion chord (OCC), (b) Nasion prosthion height (NPH), (c) Nasal height (NLH), and (d) Zygomaxillary subtense (SSS).