

Discussion

On the Diffusion-Wave Model for the Spread of Modern Humans

OSBJORN M. PEARSON AND ANNE C. STONE
Department of Anthropology, University of New Mexico, Albuquerque, N.M. 87131, U.S.A.
(ompear@unm.edu). 19 III 03

Eswaran (CA 43:749–74) provides a demonstration of how genes and morphological traits of archaic Eurasian hominids could have existed in a fairly high frequency in the earliest modern humans outside of Africa and yet be virtually absent in living populations. He proposes that several genes could have been responsible for a single advantageous trait, such as the size of full-term fetus's face, that would have conferred a selective advantage on individuals who possessed all of the required alleles. His model predicts that the favorable alleles would have increased gradually in frequency, eventually reaching fixation. For the model to fit the available genetic data, one must assume that all the genes linked with the advantageous loci also increased in frequency, eventually "modernizing" the entire nuclear genome. Variation in neonatal facial size may not account for a major selective advantage (Rosenberg 2002), but Eswaran's insight is applicable to any morphological trait involving multiple loci and a strong selective advantage.

Although the diffusion-wave model initially seems persuasive, we argue that it works only if the amount of archaic admixture was very small. Four major difficulties confront the model. First, because of the number of genetic loci that would have to be involved to "modernize" the archaic genome completely, any version of the model that incorporates extensive admixture between early modern humans and archaic Eurasian hominids is unlikely, given the existing genetic data. If, for example, 5–10 genes on different chromosomes underlie a single morphological change needed to produce modern morphology, then 13–18 chromosomes would be unaffected by selection for the favorable genes. A minimum of 23 loci—and probably more—would be required for linkage disequilibrium to "modernize" the entire genome. It seems highly unlikely that any of the comparatively minor morphological changes that accompanied the origin of modern humans would have been based on so many genetic loci. Given a high amount of admixture in Eswaran's model, one would expect the human genome to have regions of very low variance around the advantageous loci and more (and regionally patterned) variance

elsewhere. This pattern would produce quite different F_{st} values for different parts of the genome. Additional simulation studies incorporating varying numbers of advantageous alleles and proportions of admixture would be an interesting way to explore these possibilities and to test their ability to explain present-day genomewide patterns of variation.

Second, the fossil evidence used by multiregionalists to argue for continuity in Europe (e.g., Frayer 1992a, b) suggests that substantial initial admixture occurred and that Neanderthal traits (and presumably genes) persisted for at least 20,000 years, providing ample time to intermix the selectively neutral haplotype blocks of chromosomes derived from Neanderthals and modern humans. However, studies of worldwide distributions of nuclear DNA short tandem repeats (Tishkoff et al. 1996), single-nucleotide polymorphisms and Alu insertion polymorphisms (Watkins et al. 2001, Jorde et al. 2000), and chromosomal haplotype blocks (Reich et al. 2001, Gabriel et al. 2002) have failed to find the clearly ancient, region-specific patterns of genetic variation that should have arisen as the result of admixture with archaic humans.

Third, the data from several "neutral" genetic loci—such as the MHC genes—cited as genetic evidence for continuity in Eurasia are flawed because the loci are under selective pressure to maintain variation (Hughes and Nei 1988). Considering such loci to be selectively neutral gives a false impression of ancient, separate population histories. Similar problems pertain to beta-globin genes (Harding et al. 1997, 2000). Lastly, data from mitochondrial DNA (mtDNA) and Y chromosomes argue against any version of the model that incorporates a large amount of initial admixture. Nordborg (1998) calculated that, given various assumptions, there could be a 10% chance that even 25% Neanderthal admixture would leave no trace in the mtDNA gene pool of living Europeans. However, the worldwide pattern of human variation, not just that of Europe, must be considered. If one extends Nordborg's simulation of mtDNA and Y chromosomes in Europe, East Asia, and Indonesia/Australia, there is an approximately one in ten chance for *each* of these genetic systems in *each* region that all archaic alleles would have been lost given 25% original archaic admixture. The overall chance that no archaic mtDNA or Y chromosomes would have survived by chance in three separate regions becomes approximately $(1/10)^6$ or one in one million. Similarly, Manderscheid and Rogers (1996) found that only a very small (10% or less) proportion of archaic admixture in mtDNA could have escaped detection today. In the final analysis, it still appears that a single recent origin of modern humans provides the best explanation for the genetic and fossil data (Cann, Stoneking, and Wilson 1987, Stringer and Andrews 1988).

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Reply

VINAYAK ESWARAN

Department of Mechanical Engineering, Indian
Institute of Technology, Kanpur, India 208016
(eswar@iitk.ac.in). 12 V 03

First, I did not imply that the genes of non-African archaics were “virtually absent” in living populations—for that would be subscribing to the recent-African-origin model. While I did suggest that certain archaic morphological traits had disappeared because of selection, in proposing a childbirth-related modern advantage I meant that a coadapted suite of cranial and pelvic traits, not merely “the size of a full-term fetus’s face,” combined to give a collective advantage to the modern phenotype.

Pearson and Stone argue that the diffusion-wave model confronts four major difficulties. Regarding the first of these, however, their argument is based on the misapprehension that the diffusion-wave model proposes that the human genome was modernized (I prefer “Africanized”) by linkage with the genes carrying the modern advantage. Thus, in their view, at least 23 different advantageous genes, each fortuitously on a separate chromosome, would be needed to explain the “modernization” of the human genome. I make clear (p. 755), however, in defining “African parentage,” that it estimates the fraction of “African” alleles at neutral loci *unlinked* to the genes conferring modernity. Figure 6 in my paper shows that for a modern genotype gene number of, say, 8 the African parentage of modern humans 10,000 km from Africa would still be more than 0.5—implying a fraction greater than 50% in modern Chinese of African neutral alleles unlinked to the “modern” functional alleles (which would presumably be fixed).

A high degree of Africanization is possible when a sufficiently large combination (5–10, say) of unlinked genes gives a *coadapted* advantage that does not accrue to hybrids,¹ as then any hybrids that become fully modern² will likely descend from a largely modern lineage. This means that the unlinked neutral genome of modern humans, initially composed wholly of “African” alleles, could yet be diluted at a rate low enough that even far from Africa it would remain largely African.

In their second point, Pearson and Stone contend that a host of genetic data have failed to detect signs of archaic-modern admixture. I disagree. Indeed, while single-locus studies of short tandem repeat polymorphisms are being offered as strong support for the recent-African-origin model (e.g., Tishkoff et al. 1996), it is not widely recognized that the model has been essentially refuted by multilocus studies of such polymorphisms. The data

1. Which have a mixture of archaic and modern alleles in the functional loci determining modernity. In the model, hybrids are, conservatively, treated as selectively equivalent to “pure” archaics. In reality, they would likely have been disadvantaged compared with both archaics and moderns, their genetic makeup falling, metaphorically, between two stools.

2. In the sense of having the advantageous full gene combination.

are wholly consistent with the diffusion wave but not always so with the recent-African-origin model—as they clearly demonstrate archaic assimilation (for a detailed treatment of these issues see the electronic edition of this issue on the journal’s web page).

Regarding the third point raised by Pearson and Stone, the data cited (MHC, beta-globin, MC1R, etc.) in my paper were of necessity from functional loci, as until recently very few global surveys of autosomal noncoding regions had been published. Now data from separate studies of noncoding autosomal regions (Zhao et al. 2000, Yu et al. 2001) have confirmed the essential features that I used (pp. 761–62) to argue the case for archaic assimilation—no (or mild) signs of bottlenecks in non-Africans at low-mutation-rate loci,³ great non-African time-depths, and sometimes a significant number of unique non-African polymorphisms. These researchers specifically state that their data are inconsistent with the strict version of the recent-African-origin model.

Finally, in their last point, Pearson and Stone argue that data from mtDNA and the Y chromosome reject the possibility of a large amount of archaic assimilation. Apart from ignoring the possibility of selection at these loci, this argument assumes that all extant human mtDNA and Y chromosomes are of recent African origin. In fact, indications are that extant Y chromosomes have considerable time-depth and include variants from pre-modern non-Africans, while mtDNA shows every sign of a selective sweep that coincided with the progress of anatomical modernity, with which it was possibly indirectly linked (for details see the electronic edition of this issue).

Multilocus studies have not supported the case that *all* extant global variation is exclusively derived from *recent* African polymorphisms, which is the direct implication of the recent-African-origin model. For every other genetic pattern (the apparent African primacy and greater genetic diversity, the diversity clines, the signals of expansions, etc.) that supported the recent-African-origin against the multiregional-evolution model, the diffusion-wave model offers a more parsimonious explanation stemming from a single mechanism. For others (the sub-Saharan African/Other split, the bottlenecks, the severity of these bottlenecks, the vastly differing expansion times), the diffusion-wave model offers natural explanations where the recent-African-origin gives none. Finally, certain features of the genetic data (the absence of signs of bottlenecks and/or expansions in many loci) directly refute the recent-African-origin model and suggest that a significant non-African archaic genetic inheritance lives on in present-day populations.⁴

3. I argue that the fact that bottlenecks are not empirically evident at some low-mutation-rate loci (which would otherwise “remember” the bottleneck) is proof of archaic assimilation (p. 761).

4. I am grateful to H. C. Harpending and A. R. Rogers for the discussions we had when I recently visited the University of Utah. I thank the Fulbright Foundation of India for making that visit possible. [Supplementary material appears in the electronic edition of this issue on the journal’s web page (<http://www.journals.uchicago.edu/CA/home.html>).]

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On the Adaptively Biased Offspring Sex Ratios of Hungarian Gypsies: A Possible Proximate Cause

WILLIAM H. JAMES
*The Galton Laboratory, University College London,
 Wolfson House, 4 Stephenson Way, London NW1 2HE,
 England. 2 IV 03*

The project of demonstrating adaptive biases in human sex ratios (proportions male at birth) has been frustrated by a lack of knowledge of the proximate causes of sex-ratio variation. When workers have failed to find a predicted adaptive bias, it has not usually been clear whether this was due to constraints on such variation or to the hypothesis's being false in the given situation. Bereczkei and Dunbar (CA 43:804–9), building on their earlier work (Bereczkei 1993, Bereczkei and Dunbar 1997), have established for Hungarian Gypsy populations both that sex ratios are low and that this has an adaptive advantage. They also offer evidence from which one may infer a proximate cause of the low sex ratios of these Gypsies. They note that the mean lifetime fertility of Gypsies is significantly higher when their first child is female than when it is male. This suggests a very weak form of selection. The probability of a male human birth shows some small measure of Lexis variation (*viz.*, across couples). This variance has been estimated as of the order of 0.0025 (Edwards 1958), though it may be larger (James 2000). It is reasonable to suppose that there is a genetic component to this variance. Hence the proportion of sisters of a female index first-born would be expected to be very slightly higher than that of a male index first-born (James 1975), and therefore the sex ratio at birth of Hungarian Gypsies would be expected to be low.

Thus a form of selective reproduction may be a proximate cause of an adaptive sex ratio. However, I suggest that it is quite different from most other proximate causes of sex-ratio variation. I have proposed that the

sexes of mammalian (including human) offspring at birth are partially dependent on hormone (e.g., estrogen and testosterone) concentrations in both parents around the time of conception (James 1996). But high and low levels of these same hormones are also intimately connected with the health, attractiveness, and behavior of human beings. This, if I am correct, constitutes constraint on the operation of adaptive sex-ratio processes, thus precluding direct testing of hypotheses such as that of Trivers and Willard (1973). With regard to non-human primates (Brown and Silk 2002) and human beings (Lazarus 2002), the many attempts to test this hypothesis have been cumulatively unsuccessful. Confirmed predictions have been interpreted as supporting the hypothesis and falsified predictions as exemplifying "constraints." This state of affairs may be remedied by directly testing the hypothesis that parental hormone levels around the time of conception affect the sex of offspring, *ipso facto* imposing constraint on adaptive processes.

It is worth indicating how this testing might be done. It is known that elements on the mouse H-2 region are associated with steroid hormone production (Ivanyi et al. 1972). Analogously, human leukocyte antigen (HLA) genes are associated with testosterone variation in women (Gerencer et al. 1982) and men (Ollier et al. 1989). For instance, the latter authors reported that men who were positive for HLA B 15 had significantly low testosterone levels. Accordingly, Astolfi, Cuccia, and Martinetti (2001) tested a prediction based on my hypothesis, namely, that men carrying HLA B 15 should sire a high proportion of daughters. The prediction was confirmed, and these researchers wrote: "These results suggest an effect of HLA B 15 on the secondary sex ratio mediated by a low testosterone level." This suggests a wide range of further experimentation. The work of Astolfi et al. needs to be confirmed and extended in human beings. Moreover, such work should be initiated in the mouse. Are the H-2 genes associated (as I would predict) with murine offspring sex ratios? If they are, this might even

prove persuasive to experimentalists and evolutionary biologists.

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