ISSUES

Concocting a Divisive Theory

The phenomenal recovery of an mtDNA segment from the arm of the Feldhofer Cave Neandertal was greeted with the enthusiasm and yes, even with the hoopla it deserved.[1] It was a truly significant breakthrough, and from a laboratory that as recently as a year before had predicted it couldn't be done. The supporters of the theory that Neandertals are a different species were beyond exuberance (few others were quoted on the issue). And then, in a crescendo of exhilaration, Stringer and McKie[2] delivered their coup de grâce in a New York Times op-ed discussing the significance of the Neandertal mtDNA findings:

> The implications for the idea of race are profound. If modern humanity is made up of people who are all recent descendants of a few African pioneers, it is equally clear that *Homo sapiens* must be a startlingly homogenous species. We simply have not had time to diverge genetically in any meaningful manner.
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> Nevertheless, some scientists and those with narrow political agendas have put forward arguments to sustain the idea that races exist with fundamental biological differences.
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> Instead of concocting divisive theories, we would be better served to recognize the importance of recent data that will help us find the attributes that separated *Homo sapiens* from other early humans like the Neanderthals.

Is this more opera or is it all over? Have the ancient DNA studies brought us a real breakthrough and ended the Neandertal controversy so thoroughly that the lone holdouts should stop concocting their divisive theories because they can only disagree if they have a political agenda about race?

Tattersall[3] believes it is all over. He interprets the mtDNA results as showing that the Neandertals were a distinct species for 600,000 years. For this interpretation, one must assume that the history of the Neandertal mtDNA lineage segment is a population history, that constantly accumulating mutations are the sole cause of mtDNA evolution, and that the mutation rate of mtDNA is known with sufficient accuracy to date the putative split. Belief in the Eve theory of modern human origins is the most important prerequisite for these assumptions because it ties mtDNA history to population history through the explanation that low mtDNA diversity in humans comes from a recent population-size bottleneck (in this case, a new species). It is no surprise that Eve theorists reacted to the news with joy.

But perhaps the most surprising finding was that several of the humans were found to differ from each other more than the Neandertal differs from some humans.

It is not that I want to rain on anybody's parade, but there are some nagging details. Let's look at what was actually done. Krings and coworkers[1] reported that the 379 base-pair segment of mtDNA found in the Feldhofer specimen has 27 differences from the reference human sequence and, significantly, that 25 of these differences were at positions that varied in at least one of their comparative human samples of 2,051 individuals. When the Neandertal sequence was compared with 994 contemporary human lineages of known geographic origin, the number of differences was more than three times greater than the mean number of differences between the humans. But perhaps the most surprising finding was that several of the humans were found to differ from each other more than the Neandertal differs from some humans. Lineages in the human sample have between 1 and 24 pairwise differences reflecting mutations, while the Neandertal differed from these humans by between 22 and 36 mutations.

Taking the difference in ages into account, as well as the fact that any particular mtDNA line from that time had only a small chance of persisting until today, this pattern of variation is to be expected, given that an ancient Neandertal is being compared with contemporary humans. In such a comparison, the pairwise differences must always be greater than they would be for the ancestors of the contemporary humans in the analysis who were living at the same time as the Neandertal. This is because the contemporary human mtDNA lines have had a longer time to mutate.

Whether the magnitude of variation is to be expected is a different question. The answer could depend on the mtDNA mutation rate. Here, too, there have been surprising discoveries. Until recently, the rate of change for human mtDNA was determined phylogenetically. Dates for mtDNA coalescence were estimated by comparing the maximum pairwise difference among humans to the number of differences separating human and chimpanzee sequences. Dates for human and chimpanzee divergence were then used to estimate the rate of change. The Neandertal divergence date estimated by Krings coworkers assumes a mutation rate at about the middle of the

range for phylogenetic determinations: 0.01 to 0.2 substitution sites each million years.

But, in fact, even the fastest of these rates may be incorrect. When Czar Nicholas II and his family were exhumed in 1991, their identifications were based on matching their mtDNA with that of other descendents of the Czar's mother. These analyses unexpectedly revealed vastly more mutational changes than the phylogenetic rates predicted.[4] Subsequent calculations of mutation rates between generations proved to be dramatically higher than had been assumed from the longer-range phylogenetic considerations. In two different studies, hundreds of base pairs from the mtDNA control region (more than in the Neandertal analysis) were sequenced and intergenerational mutation rates of 1.2–4.0 substitutions per myr were derived.[5,6]

The Eve theory posits that a recent population-size bottleneck took place at the time of mtDNA coalescence in humans. But if mtDNA mutation rates are indeed as high as the intergenerational analyses indicate, the "Eve" of these studies could well have been a Biblical figure because she would have lived only about 6,500 years ago. Of course, a population-size bottleneck this recent is highly unlikely because "it remains enigmatic how the known distribution of human populations and genes could have arisen in the past few thousand years."[6]

A much more probable explanation for today's mitochondrial diversity is that there was no recent population bottleneck, but that the mtDNA has limited variation because of selection. It is known that the evolution of human mtDNA departs from neutrality. Selection can explain this and the limited variation in human mtDNA by, for example, long-term background selection against slightly deleterious mutations,[7] or by episodes of directional selection, or, perhaps a selective sweep.[8] Selection is an important element in mtDNA evolution because mtDNA does not recombine. Therefore, selection against any portion reduces variability in the entire genome.[9] Even on the same chromosome, nonrecombining portions have much lower variation than do recombining portions. One divisive theory is that selection has reduced mtDNA variation in humans since the Neandertal lived.

A final detail is related to the claim of Krings and coworkers[1] that the Neandertal is equally related to all living people. This contributes to the perception that he was genetically isolated from them. But these authors only presented their comparisons for broad continental groups (Africans, Europeans, and so on). A more appropriate analysis is populational. A comparison of the Feldhofer Neandertal with gene-bank data for 14 worldwide populations resulted in an average pairwise difference of 27.3, the same mean difference as in the study by Krings and coworkers.[1] But in this case, pairwise differences for specific populations could be directly examined. These ranged from 21.3 to 33.2: the smallest mean difference was between the Neandertal and a sample from Finland. One can imagine the divisive theory that might be concocted from these findings.

So what does it mean? The ancient DNA findings are compatible with both phylogenetic interpretations of Neandertals: separate species or human race.

There are others, mostly geneticists, who also have been busy concocting divisive theories about modern human ancestry agree on one point: The Eve theory is wrong.[9,11] The problem they all address is that a population bottleneck severe enough to reset mtDNA variation to zero would reset nuclear variation as well. Mitochondrial genes should recover their variation and return to equilibrium much more quickly because of their higher mutation rate and smaller effective population size. But it is just the opposite. MtDNA is out of equilibrium and has little variation, whereas all neutral nuclear gene systems studied so far are in equilibrium and have more variation.[7,8,12] This alone rules out a severe population-size bottleneck.

One recently supported theory is that modern humans are not a new species but descend from a small ancestral group that lived in Africa for at least a million years.[13] Others are based on analyses of the beta-globin genes[14] and the Y chromosome,[15] each of which reveals evidence for significant genic exchanges both out of Africa and into Africa much earlier than the period of mtDNA coalescence, even when the phylogenetic mutation rate estimates are used. A population-size bottleneck would have erased this older variation.

But if the Eve theory is wrong, there is no reason to limit explanations of the Neandertal mtDNA to past species divergence; nothing to disprove the contention that the Neandertal reflects a greater magnitude of mtDNA variation in the past than in the present; and nothing to detract from the notion that mtDNA can differ dramatically between segments of the same species. Human variation with and without Neandertals is similar to the difference between chimpanzee subspecies. In that comparison, *Pan troglodytes verus* has much more mtDNA variation than does *Pan troglodytes schweinfurthii.*[12]

So what does the ancient DNA mean with respect to the place of Neandertals in human evolution? The implications are inconclusive. It seems that fossil anatomy still provides key data about human evolution. Many Neandertal features persist in much later post-Neandertal Europeans.[16] Moreover, it is normal to find mixtures of various Neandertal features in Europeans today. One recent analysis of Neandertal and early Upper Paleolithic European nonmetric traits indicates that their variation requires Neandertal admixture of at least 25%.[17] Further study of these data estimated an approximately 6% Neandertal genetic input in modern European gene pools, a finding that is in line with the pairwise difference analysis (but does not require ancient mtDNA).

And what does this mean for the Multiregional theory of evolution? Here, the answer is clearly nothing because multiregionalism means evolution in more than one region, but not necessarily in every region.[18] It could be a valid explanation for human evolution even if every single

Neandertal became extinct without issue. Human populations do not persist endlessly or continuously through time. All of them either become extinct without issue or merge with other populations.

So what does it mean? The ancient DNA findings are compatible with both phylogenetic interpretations of Neandertals: separate species or human race. But there are other, independent reasons for rejecting the notion that Neandertals are a different species. Tattersall and I have discussed some of these in previous debates in *Evolutionary Anthropology*. The fact remains that "the genetic variation between the modern and Neandertal sequences is within the range of other species of primates."[19] If Neandertals are not a separate species and the Feldhofer Neandertal data prove valid, they give us two important pieces of information. First, they indicate that if a selective sweep in human mtDNA led to its currently low level of variation, it was more recent than at least some of the European Neandertals. This could provide independent support for generational clock rates, but additional ancient DNA analysis is necessary to examine this possibility. Second, they remind us that calculation of average effective population size in the past from coalescence theory has no relation to the actual number of breeding females living then.[9,13] Although the sample made up of the Neandertal plus living humans has a much larger effective mitochondrial population size than living humans do, it is unreasonable to conclude that there were more people alive during Neandertal times than there are today. Ironically, even as the new data raise the Neandertal debate to a higher and more interesting intellectual level and exemplify how genetic and paleontological data can be wed, the political level of debate sinks to a new low.

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