Neanderthal-human Hybrids

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Evidence from studies of nuclear and mitochondrial DNA extracted from Neanderthal fossils and humans points to fascinating hypotheses concerning the types of interbreeding that occurred between these two species. Humans and Neanderthals share a small percentage of nuclear DNA. However, humans and Neanderthals do not possess the same mitochondrial DNA. In mammals, mitochondrial DNA is exclusively maternally inherited. Taking into account an understanding of interspecific hybridity, the available data leads to the hypothesis that only male Neanderthals were able to mate with female humans. If Haldane's Law applied to the progeny of Neanderthals and humans, then female hybrids would survive, but male hybrids would be absent, rare, or sterile. Interbreeding between male Neanderthals and female humans, as the only possible scenario, accounts for the presence of Neanderthal nuclear DNA, the scarcity of Neanderthal Y-linked genes, and the lack of mitochondrial DNA in modern human populations.

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Introduction

Since the discovery of the first recognized Neanderthal remains in 1856, scientists have debated about the relationship between Neanderthals and humans. Neanderthals were not as tall as humans, had shorter limbs, thicker bones, a protruding mid-face, pronounced brow ridges, a receding chin, a morphologically different vocal tract, and a raised larynx. Yet, sufficient similarities have led researchers to ask, "Are Neanderthals an extinct variant of humans, or are they a separate species?"

An average of estimates indicates that Neanderthal and human ancestral populations split approximately 370,000 years ago (1). Over time, Neanderthals genetically diverged. Analyses of mitochondrial DNA (mtDNA) sequences extracted from Neanderthal fossils suggest that their most recent common ancestry dates back to approximately 250,000 years ago (2).

Neanderthals inhabited a vast geographical area extending from Portugal to western Siberia and from northern Europe to the Middle East until approximately 25,000 years ago (3). Recent evidence from DNA extracted from fossil Neanderthal bones reveals geneflow between Neanderthals and anatomically modern humans in the Middle East around 80,000 to 50,000 years ago as humans spread out of Africa and into Europe and Asia (4). Despite morphological and ontogenetic differences to humans (5-8), it appears that Neanderthals did not become extinct without first contributing some of their nuclear DNA to the human gene pool. Indeed, there was chronological overlap and coexistence between Neanderthals and humans (9,10), and hybrid specimens have been found that feature both Neanderthal and modern human features (11-15). It appears that many centuries of hybridization led to mosaic fossils with human cranial and dental features mixed with Neanderthal body proportions.

Studies of nuclear DNA and hybrid fossils offer convincing evidence for interbreeding between Neanderthals and humans, but with a twist. Studies of mtDNA reveal that Neanderthals carried a type of mtDNA distinct from modern humans (16-21). Mitochondria are tiny energy regulating organelles that reproduce asexually and live inside each cell of our bodies. In mammals, mitochondria are exclusively maternally inherited (22). How is it possible that Neanderthals and humans do not possess the same mtDNA, yet share a small percentage of nuclear DNA? This intriguing mix of findings leads us to contemplate the types of interbreeding that occurred between Neanderthals and humans.

Understanding Interspecific Hybridity

Speciation is the process by which new species are formed. If, for example, a species is subdivided into two subpopulations that become geographically separated, then the two groups may accumulate biological differences that reduce hybrid fertility. A clear speciation event between Neanderthals and humans has not been documented to date, but Neanderthals seem to have accrued distinctive characteristics and features along the second half of the Middle Pleistocene (23).

Researchers have long wondered if Neanderthals were an entirely separate species. Recent DNA evidence (4) might suggest that they were not. However, even if Neanderthals were a separate species, speciation without loss of hybrid fertility is possible.

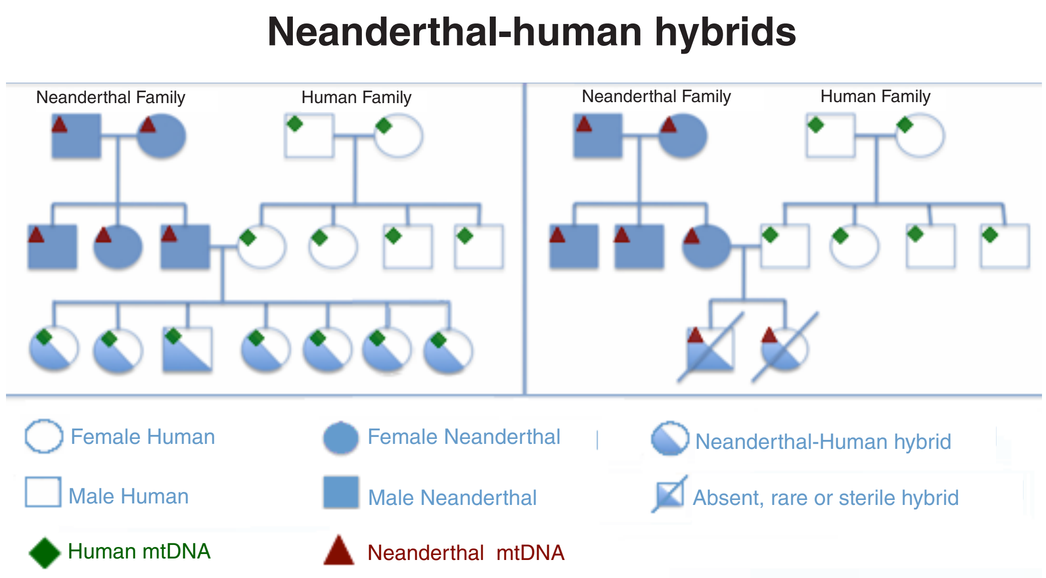

Figure 1 | Possible outcomes of Neanderthal-Human Interbreeding. Mammals contain two different types of DNA: (i) nuclear DNA, which is from both parents and contributes directly to the phenotype, and (ii) mitochondrial DNA, which is involved in energy regulation and is exclusively maternally inherited. Nuclear DNA from Neanderthals has been found in the human genome. Mitochondrial DNA from Neanderthals has not been found in humans. While not conclusive, these findings could indicate that male Neanderthals were able to reproduce with female humans, but that the reciprocal cross was absent, rare or sterile. If Haldane's Law applies to Neanderthals and humans, female offspring were more common.

Take the example of the Camelidae that originated in Florida. The little ones migrated into South America and into the Andes to become the Llama, Alpaca, Vicuna and Guanaco—phenotypically quite different species, but all of which will produce fertile hybrids when crossbred. The bigger ones migrated up the Rockies, across the Bering Strait, through Mongolia and Northern China—where we find the two-humped Bactrian camel—and into India and from there into Persia and Saudi Arabia—where we find the one-humped Dromedary camel. The spread of the Camelidae from the Americas to the Middle East is an example of phenotypic differentiation in a sexually reproducing species as a result of geographical isolation. Researchers have been able to produce Camas by inseminating female Alpacas with Dromedary semen, although the reciprocal cross gave fetuses, but no live-born young (24,25).

As Old World and New World Camelids are some 10 – 12 million years apart, we can be fairly certain, through inference, that Neanderthals were able to hybridize with humans from whom they had diverged by only a few hundred thousand years. Given that mtDNA is exclusively maternally inherited in mammals, the absence of Neanderthal mtDNA in modern humans suggests that perhaps only male Neanderthals and female humans were able to produce fertile offspring.

Incorporating Haldane's Law

Sexual selection in humans and Great apes shows that males are physically bigger and stronger than females, hence allowing them to monopolize reproduction (26). Considering that Neanderthals were robust and humans were in comparison gracile, male Neanderthals may have had *le droit de seigneur* in any matings.

Evidently, hybrid offspring who contained the mtDNA from Neanderthals did not produce a lineage that survived until today. One possibility is that mtDNA from Neanderthals contained detrimental mutations that led to the eventual extinction of carriers.

According to Haldane's law, the heterogametic offspring of interspecific hybrids are likely to be absent, rare or sterile (27). In mammals, the heterogametic sex is the male sex with two different sex chromosomes, X and Y. In 1922, J.B.S. Haldane wrote a key paper on "Sex ratio and unisexual sterility in hybrid animals", where he showed that fertile XY progeny are unlikely (28). The high mutation rate of male sex-determining genes on the Y chromosome may account for why nature rarely permits heterogametic offspring from interspecific hybrids (27).

Haldane's law has been shown in a number of different hybrid crosses from the Camelidae, Equidae, and Anatidae. If Haldane's Law applies to the offspring of Neanderthals and humans, we would expect to find female hybrids quite commonly, but male hybrids much more rarely. Any male hybrids who survived, would have carried a Y chromosome very similar to that of the original hybridizing male.

The lack of Neanderthal mtDNA in humans suggests that initial hybridization involved a Neanderthal male. With a Neanderthal father, there would be no Neanderthal mtDNA in resultant hybrids. If Haldane's law applies, few Neanderthal Y chromosomes would have survived. Nonetheless, the Neanderthal autosomes would have happily mingled and interchanged with human autosomes, eventually losing their identity in the process. In a scenario previously not considered by other researchers (29), if male Neanderthals mated with female humans, Haldane's law would account for the apparent absence of Neanderthal Y-linked genes in the human population.

Neanderthal-human Interbreeding Hypothesis

Any hypothesis about the reproductive potential of Neanderthals and humans must take into account data collected from the nuclear and mtDNA of both species. Humans and Neanderthals share a small percentage of nuclear DNA, but they do not share the same type of mtDNA. The mtDNA recovered from Neanderthal fossils contains sequences not found in present-day humans. How can we reconcile the data from studies of nuclear and mtDNA extracted from Neanderthal fossils and humans?

Evidently, hybrid offspring who contained the mtDNA from Neanderthals did not produce a lineage that survived until today. One possibility is that mtDNA from Neanderthals contained detrimental mutations that led to the eventual extinction of carriers. Another possibility is that hybrid children of Neanderthal mothers may have been raised in Neanderthal groups and eventually became extinct together with the rest of the Neanderthals. A third scenario, which is consistent with our knowledge of interspecific hybridity, is that female Neanderthals were incapable of producing fertile offspring with male humans.

The suggestion that Neanderthals practiced patrilocal mating behavior (30) becomes more nuanced in the light of data indicating that the contribution of nuclear DNA from Neanderthals to humans came uniquely from male Neanderthals. The idea that Neanderthals and humans were able to interbreed is not new (31), but the most recent data, coupled with an understanding of interspecific hybridity, allows us to conjecture that only male Neanderthals were able to mate with female humans.

If Haldane's Law applies to the progeny of Neanderthals and humans then female hybrids would have been much commoner than male hybrids. Interbreeding between male Neanderthals and female humans accounts for the presence of Neanderthal nuclear DNA, the scarcity of Neanderthal Y-linked genes, and the lack of Neanderthal mtDNA in modern human populations. Thus, gene flow from Neanderthals to humans was the product of male Neanderthals mating with female humans to produce fertile female hybrids. H

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Mason performs research into biological and cultural diversity, and teaches Human Evolution and Diversity in the Department of Anthropology at Macquarie University. Roger Short is a Professorial Fellow at Melbourne University, specialising in reproduction, evolution, and population health.

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