Winter 12-14-2018

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Recommended Citation
Hurley, Erin and Dillian, Carolyn, "Drawing the Line: Ancient Hominins and the Species Question" (2018). *Honors Theses*. 322.
https://digitalcommons.coastal.edu/honors-theses/322

Drawing the Line

Ancient Hominins and the Species Question

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Abstract

The present paper asserts that groups such as Neandertals and Denisovans should be considered subspecies of *H. sapiens*. This contention is based upon the biological species concept and the fact that these groups interbred to create viable offspring. It is also stated that introgression from these groups made several positive contributions to the evolution of *H. sapiens* and their genome that may have served to promote the persistence of *H. sapiens* in Eurasia.

Drawing the Line: Ancient Hominins and the Species Question

Since the first discoveries of fossil hominins, these "other" human-like creatures of the past have captivated the imagination. How similar they are to us, and yet also quite different. The first fossil recognized as a Neandertal, Neandertal 1, was found in 1857 (King, 1864). At the time of its discovery, it was said that several of the individual's features "more closely approximates the Neanderthal fossil to anthropoid apes than to *Homo sapiens*" (King, 1864). These features were described as distinct from those known to be human, and it was said that they closely resembled those of the chimpanzee (King, 1864). To some this suggested that the fossil simply belonged to an idiot, and that the observed skeletal abnormalities should be attributed to that identification. However, King (1864) and others concluded that the fossil bears the strongest resemblance to those of apes, and was therefore lesser than even what they considered to be the most inferior of human races. In fact, to them, it was not a human at all.

Later scholars asserted that the Neandertal was the "missing link" between man and ape. Neandertals were thought to be a key phase in the evolution of *H.* sapiens because "man could not possibly have bridged the gulf from his precursor or anthropoid characteristics to the type of *Homo sapiens* without passing through a phase similar to that of Neanderthal man" (Hrdlička, 1926). This was evidenced by the display of progressive continuity between Neandertal features and those of *H. sapiens* (Hrdlička, 1926). Furthermore, a species as long lasting as the Neandertals could not have simply vanished without leaving any sort of ancestral trace (Hrdlička, 1926). Thus, in the view of this set of scholars, they must have been the intermediate between the ape ancestors and *H. sapiens.*

However, recent research indicates that Neandertals coexisted with *H. sapiens* for a very long period of time (Gibbons, 2001). Given the presence of both species over the same geographic area, interaction must have occurred. Much speculation exists in regards to the nature of these interactions. Some scholars suggest that these may have consisted of violence and aggression, which would have contributed to the eventual extinction and replacement of Neandertals in Eurasia (Roper, 1969). However, new evidence suggests that during these interactions Neandertals may have interbred with *H. sapiens* during this period (Slon et al., 2018). Thus, they are not a precursor to *H. sapiens*, but possibly members of the same species.

Furthermore, archaeologists have recently discovered another, similar group of hominins that may also be members of the same species as *H. sapiens* and Neandertals. These individuals have been called Denisovans, and like Neandertals they are very similar to modern humans. The three types of individuals have relatively similar anatomy and genetics. Furthermore, there is evidence of interbreeding among the three, potentially on a regular basis. As such, anatomical and genetic variation among *H. sapiens*, Neandertals, and Denisovans is not strong enough to warrant classification of these groups into different species; instead, they were members of various subcategories of one species because they were able to reproduce with one another, and create viable offspring.

The term ‘species’ is fundamental to accurately taxonomically classify any lifeform, however the definition of a species is quite ambiguous. There are many different and sometimes conflicting concepts of species, although they all generally focus on some combination of morphology, genetics, and reproduction. To attempt a comprehensive list of these concepts is outside the scope of the present paper. Moreover, the biological species concept is the definition preferred by most zoologists (Jurmain, Kilgore, and Trevathan, 2008), and thus this will be assumed to be the “correct” definition for the purposes of this paper. The biological species concept is defined as “Interbreeding natural populations reproductively isolated from other such groups; all individuals that produce fertile offspring" (Zachos, 2016). In other words, all individuals that can produce viable offspring are members of a single species.

Theodosius Dobzhansky (1935) was among the first proponents of biological species concept. He notes that the separation of any set of organisms into various groups must be based observed differences between the members of the set. Among the most readily observable differences among individuals is that "closely similar individuals habitually interbreed, and those less similar do not" (Dobzhansky, 1935). However, not all individuals that could possibly interbreed regularly do so. Thus, Dobzhansky proposes that "a species is a group of individuals fully fertile inter se, but barred from interbreeding with other similar groups by its physiological properties" (1935). This became the foundation of the biological species concept. The concept was later popularized by Ernst Mayr (Zachos, 2016). He amended this definition of species to "groups of actually or potentially interbreeding natural populations, which are reproductively isolated from other such groups" (Ripley and Mayr, 1943). It is important to note that in this instance reproductive isolation does not mean that reproduction is impossible, rather that the necessary gene flow to produce viable offspring is not present (Zachos, 2016). In other words, a species is comprised of any group of individuals that can produce fertile offspring with one another, but not with other such groups, i.e. they can interbreed.

Hominin Interbreeding

Recent research has made it clear that different groups of hominins did in fact interbreed, at least in the case of Neandertals, Denisovans, and *H. sapiens*. Among the first pieces of evidence to support this conclusion was the finding of Neandertal DNA in modern humans of non-African origin (Vernot and Akey, 2015). Further archaeological studies have revealed individual remains possessing both Neandertal and human traits (Fu et al, 2014; Fu et al, 2015).

Recently, an individual resulting from a first generation interbreeding between a Neandertal and a Denisovan has also been found (Slon et al., 2018). Furthermore, there is evidence to support that these were not isolated occurrences. In fact, interbreeding among these three hominin groups appears to have been quite common (Slon et al., 2018).

The first draft sequence of the Neandertal genome was completed in 2010 using three bones found in Vindija Cave, Croatia. These bones came from three different individuals (Green et al., 2010). A comparison of the Neandertal sequences to those of five modern human individuals originating from different parts of the world revealed that Neandertal sequences, for many genomic regions, are within the parameters of present-day human variation, meaning that single nucleotide polymorphism (SNP) alíeles are often shared between the two (Green et al., 2010). Remarkably, this comparison also found that Neandertals are more closely related to present day humans of non-African origin than to individuals of African descent. Furthermore, the data show that 1 to 4% of the Eurasian genome is derived from Neandertals (Green et al., 2010). This implies that Neandertals interbred with *H. sapiens*, at least enough to leave this small mark on the modern human genome.

Less is known about Denisovan contributions to the modern human genome, given that these hominins were only just discovered in 2010. Furthermore, fossil remnants of these individuals are scarce. However, the genome sequence of Denisovans was able to be extracted from a distal manual phalanx (finger bone) discovered in Denisova Cave in southern Siberia. It was found “that Denisovans have contributed to the genomes of present-day Melanesians, Australian aborigines, and other Southeast Asian islanders” (Meyer et al., 2012). Their contributions to other Eurasian mainland populations is to a lesser extent, but still present (Meyer et al., 2012). Such a presence implies introgression between Denisovans and *H. sapiens*.

The presence of Neandertal and Denisovan DNA in the modern human genome is itself clear evidence that some interbreeding between these hominins and *H. sapiens* did in fact take place. However, even more concrete evidence for interbreeding exists in the remains of specific individuals that are results of recent introgression.

Denisova 11.

The first and thus far only discovery of a first generation hominin hybrid took place earlier this year. Found in Denisova Cave, Denisova 11, also known as Denny, was the product of a Neandertal mother and a Denisovan father. Denny was a girl of at least thirteen years at her death, over 50,000 years ago. DNA sequencing revealed that fragments from Denny's DNA matched Neandertal alleles 38.6% of the time and Denisovan alleles 42.3% of the time, meaning that her ancestry included approximately equal Neandertal and Denisovan ancestry (Slon et al., 2018). This implies that Denny either belonged to a population with mixed Neandertal-Denisovan ancestry, or that her parents were each from one of these groups. However, her mtDNA, which is maternally inherited, expresses an entirely Neandertal origin. Thus, Denny must have had a Neandertal mother and a Denisovan father (Slon et al., 2018).

However, Denny is not an isolated circumstance. In the same study, her Denisovan father is shown to have had at least one Neandertal ancestor. However, "it is likely that there was more than one Neanderthal ancestor in his genealogy, possibly as far back as 300–600 generations before his lifetime" (Slon et al., 2018). Thus, DNA extracted from Denisova 11 reveals at least two specific interbreeding events. Of the individuals found in Denisova Cave, Denny is not the only one to reveal introgression between Neandertals and Denisovans. In fact, "two (Denisova 3 and Denisova 11) show evidence of gene flow between Neanderthals and Denisovans" (Slon et al., 2018).

Oase 1.

The Oase individual, found in Pestera cu Oase, Romania, represents another distinct instance of interbreeding, though between modern humans and Neandertals. Oase 1 lived 37,000 to 41,000 years ago, was, in general, morphologically modern, but retained some archaic characteristics typical of Neandertals. Additionally, this individual seems to have possessed the most Neandertal DNA out of all other humans that have yet been analyzed (Fu et al., 2015). Studies have suggested that this means that the lineage of Oase 1 must have included a Neandertal four to six generations before the birth of this individual (Fu et al., 2015). This means that the introgression would have taken place less than 200 years before he lived. An additional discovery from the same site, Oase 2, appears to have retained some morphologically archaic characteristics that may indicate Neandertal introgression+ (Fu et al., 2015). Further analysis of other individuals suggested to bear Neandertal-like morphological traits could reveal additional evidence of introgression among Neandertals and *H. sapiens*.

Ust'-Ishim

The genome of another individual, recovered from western Siberia, seems to contain unusually long segments of Neandertal DNA. Morphologically, the Ust'-Ishim specimen appears to have derived from modern humans, and the genomic proportion of Neanderthal admixture is similar to that of modern humans. "However, the genomic segments of Neanderthal ancestry are substantially longer than those observed in present-day individuals, indicating that Neanderthal gene flow into the ancestors of this individual occurred 7,000–13,000 years before he lived," (Fu et al., 2014) which is far earlier than admixture was previously thought to have taken place. Additionally, especially long fragments of Neandertal DNA indicate that additional admixture could have occurred after this time as well (Fu et al., 2014). This indicates that multiple interbreeding events between modern humans and Neandertals may have occurred.

How Normal was Interbreeding?

Recently, genomic sequences have been recovered from the period in which Neandertals, Denisovans, and modern humans coexisted. However, many of these individual sequences have shown signs of admixture. This prevalence “suggests that mixing among archaic and modern hominin groups may have been frequent when they met” (Slon et al., 2018). It has been hypothesized that there were at least two, and possibly more, major interbreeding events between humans and Neandertals. Admixture between Denisovans and humans is thought to have occurred in two pulses as well.

The first introgression event is suspected to be the cause of the presence of Neandertal DNA in all Eurasian populations. This pulse occurred 50,000 to 60,000 years ago, probably while *H. sapiens* were migrating out of Africa (Taskent et al., 2017). The event would have had to have taken place prior to the dispersion of this group of humans across Eurasia. Therefore, it must have been somewhere in the Middle East (Ko, 2016). This explains the fact that all present-day humans of non-African origin have a small percentage of Neandertal DNA (Taskent et al., 2017). After this first introgression event, the group must have split into at least two groups, one that would become the ancestors of European populations, and one that would become the ancestor of Asian populations (Ko, 2016). At this point, *H. sapiens* began to spread throughout Eurasia.

However, after this first interbreeding event, a second pulse had to have occurred among Neandertals and East Asians. This is because “recent reports show that East Asians have, on average, inherited ~20% more Neandertal ancestry than Europeans” (Vernot and Akey, 2015).

This suggests that "the ancestors of East Asians interbred again with Neanderthals after the split" (Ko, 2016). This marks the second major instance of interbreeding among Neandertals and modern humans.

Until recently, the second introgression event was thought to have been the last. However, it has recently been discovered that introgression likely took place on smaller, regional scales as well, and that these did introgression events were not exclusive to Neandertals (Taskent et al., 2017). It is very likely that there are many other introgression events such as these that we are currently unaware of.

Less is known about Denisovan admixture with modern humans, but a significant portion of the current population bears Denisovan DNA. In particular, 4 to 6% of the Melanesian genome appears to have been derived from that of Denisovans (Vattathil and Akey, 2015). Denisovan ancestry can also be found in East and South Asians, as well as Papuans. In fact, Papua New Guineans seem to possess the most Denisovan DNA out of all populations analyzed (Vattathil and Akey, 2015). Two differing components of Denisovan ancestry suggest that introgression occurred at least twice (Browning, Browning, Zhou, Tucci and Akey, 2018). This accounts for the different levels of ancestry observed across the affected populations.

It is difficult to determine the chronological order of introgressions of Denisovan DNA into modern human populations. Nonetheless, studies have shown that one pulse of Denisovan introgression came "from a population closely related to the Altai Denisovan individual" (Browning et al., 2018). This component of introgression is primarily seen in East Asians. The other component came from a Denisovan "population more distantly related to the Altai Denisovan" (Browning et al., 2018). This introgression event "forms the major part of the Denisovan ancestry in Papuans and South Asians" (Browning et al., 2018). However, the presence of this second introgression is also observable in East Asians, and this displays the most evidence for two waves of Denisovan introgression (Browning et al., 2018).

Implications for Modern Humans

Regardless of the number of introgression events of either Neandertals or Denisovans, it is clear that all non-African populations carry some degree of Neandertal ancestry (Vattathil and Akey, 2015). In some cases, Denisovan ancestry is also present (Browning et al., 2018). This could not be possible without interbreeding among the various groups of hominins. The presence of Neandertal and Denisovan DNA in current human populations is a clear indication that these groups of hominins produced the viable offspring necessary to contribute to the modern human genome. As such, they should be considered members of the same species as *H. sapiens*, albeit members that are no longer extant.

Obviously, Neandertals and Denisovans are no longer walking among us. But are they necessarily extinct? Yes, and no. By strict definition, there are no living Neandertal or Denisovan individuals, therefore they are extinct. However, a large portion of their genes live on in modern humans, which would suggest that, at least in some cases, they were actually absorbed into the larger population of modern humans that occupied the same geographic area.

The genes left behind by Neandertals and Denisovans have had significant impacts upon modern Eurasian humans. Though negative selection weeded out some archaic traits, some positive and helpful traits were preserved, including some related to immunity and metabolism, as well as some linked to adaptations to environmental conditions, such as temperature sunlight, and altitude (Dannemann and Racimo, 2018). These adaptations developed in Neandertals and Denisovans prior to human occupation of Eurasia, and were passed on to *H. sapiens* because their utility for survival in this geographic area.

Their effect on the modern human immune system is perhaps the greatest genomic legacy of archaic hominins. Infectious disease was one of the most prolific killers of the ancient world. In many cases, derived resistance to these diseases was key to survival. When settling in Eurasia, *H. sapiens* would not have had the necessary immunity to combat novel Eurasian diseases. Recent evidence shows that one way that they obtained this immunity was through introgression. By interbreeding with other ancient hominins, the *H. sapiens* gained beneficial genetic variation associated with immunity to these new diseases (Deschamps et al., 2016). Innate immunity is among the first lines of defense against pathogens, and interestingly, "innate immunity genes present a higher average probability of Neandertal ancestry than the remainder of the coding genome" (Deschamps et al., 2016), probably because of their high adaptive advantage. Specifically, there are "three Toll-like receptors (TLR6-TLR1-TLR10) in modern humans that carries three distinct archaic haplotypes, indicating repeated introgression from archaic humans" (Dannemann, Andres, and Kelso, 2016). Two of these receptors are similar to those of Neandertals, and one to Denisovans. Both are important elements of innate immunity.

Additionally, the oligoadenylate synthetase (OAS) locus possesses a high degree of Neandertal ancestry. The higher probability of archaic ancestry at this locus, "along with the key role OAS genes play in protective immunity against viral infections, raises the possibility that introgressed Neandertal haplotypes at OAS may have been adaptive in modern humans" (Sams et al., 2016). There are also "associations between Neanderthal alleles and several neurological, psychiatric, immunological, and dermatological diseases" (Dannemann and Racimo, 2018). Clearly, the introgression of archaic hominins played a large role in improving the immune systems of modern humans.

There is also evidence to support introgression having had effects on the modern human metabolism. Recent studies have suggested that natural selection related to lipid catabolism has favored Neandertal alleles in Europeans, possibly due to an evolutionary advantage associated with an altered diet (Racimo, Sankararamen, Nielsen, and Huerta-Sanchez, 2015). This was not found in Asians as well. In this case, introgression led to “significant excess of lipid concentration and gene expression divergence in lipid catabolism pathways in Europeans” (Khrameeva et al., 2014). Neandertals in this geographic region evolved sequence variants that conferred this evolutionary advantage related to metabolism; as such, when these variants were introduced into the human population, they were given a selective advantage (Khrameeva et al., 2014).

Archaic hominins also contributed to the ability of modern Eurasian humans to cope with environmental conditions. Having evolved in Eurasia, Neandertals and Denisovans had developed distinctive adaptations to survival in this environment. Through introgression, they improved the modern human response to environmental conditions, such as temperature, sunlight, and altitude.

After migrating out of Africa, modern humans would have experienced far greater temperature extremes in Eurasia than they had previously experienced. Consequently, they would not have been well adapted to cope with this range of temperatures, particularly the cold. On the other hand, Neandertals, and probably Denisovans as well, “display a greater degree of morphological adaptation to the extremes of climate” (Pearson, 2000). Introgression allowed these adaptations to be transferred to modern humans.

Additionally, sunlight exposure differs a great deal between geographic regions of high and low latitudes. As such, populations migrating out of Africa may have experienced difficulties related to this change. Neandertals, conversely, “had inhabited Eurasia for more than 200,000 years, they were most likely adapted to lower UVB levels and wider variation in sunlight duration than the early modern humans who arrived in Eurasia from Africa around 100,000 years ago” (Dannemann and Kelso, 2017). Neandertal adaptations to light exposure include variations in skin and hair color, as well as circadian rhythms. (Dannemann and Kelso, 2017).

Skin and hair pigmentation are among the most strongly represented examples of the effects of Neandertal introgression. Dannemann and Kelso (2017) recently discovered some “strongly associated archaic alleles on two unlinked introgressed haplotypes near BNC2 (MIM: 608669), a gene that has been previously associated with skin pigmentation in Europeans.” Furthermore, a Neandertal haplotype in this region had been previously identified. It was found that “all of the Neanderthal-like SNPs overlapping BNC2 on this haplotype have significant scores in a test for recent positive selection in Europeans, perhaps indicating their importance in recent local adaptation ” (Dannemann and Kelso, 2017).

Archaic haplotypes also affect sleep patterns. It has been observed that individuals possess a wide range of diurnal preferences that are divided into various ‘‘chronotypes.’’ Furthermore, research has shown that there is a genetic component to these chronotypes (Dannemann and Kelso, 2017). This component is found near ASB1, which is “associated with a preference for being an ‘‘evening person’’ and an increased tendency for daytime napping and narcolepsy, respectively” (Dannemann and Kelso, 2017). Interestingly, it was found latitude and frequency of the Neandertal allele near ASB1 exhibit a strong correlation (Dannemann and Kelso, 2017). Populations farther north are more likely to exhibit the Neandertal allele at ASB1 than are populaces nearer to the equator. This is reflective of the influence of sun exposure on the circadian rhythm, however the relationship between this influence and Neandertal-like chronotype characteristics is unknown (Dannemann and Kelso, 2017). Nevertheless, this does imply that daylight exposure may have played a large role in shaping Neandertal phenotypes. Furthermore, the variation found in these traits today is likely still influenced by this gene flow (Dannemann and Kelso, 2017).

Denisovans are celebrated as the source of human adaptation to living at high altitudes. This is especially apparent on the Tibetan plateau because of its inhospitality to human life. This is "because of low atmospheric oxygen pressure (40% lower than at sea level), cold climate, and limited resources (for example, sparse vegetation)" (Huerta-Sanchez et al., 2014). However, Tibetans have successfully settled the area due to specialized adaptations to living at high altitudes, some of which came from the Denisovans. Tibetan individuals carry Denisovan adaptations for lower infant mortality, higher fertility, and lower haemoglobin levels (Huerta-Sanchez et al., 2014). These adaptations create different physiological responses to the environment than are found in lower altitude populations, which help them to cope with problems like hypertension during pregnancy and low levels of oxygen (Huerta-Sanchez et al., 2014).

In response to lower levels of oxygen, most individuals increase their blood haemoglobin levels. Contrarily, in the response of the Tibetan population to low oxygen, "the increase in haemoglobin levels is limited, presumably because high haemoglobin concentrations are associated with increased blood viscosity and increased risk of cardiac events, thus resulting in a net reduction in fitness" (Huerta-Sanchez et al., 2014). The gene that is most responsible for this response is "EPAS1, a transcription factor induced under hypoxic conditions" (Huerta-Sanchez et al., 2014). The haplotype of this gene exhibited by Tibetans is quite distinct from that of the general population. It does, however, match that of the Denisovans. Consequently, it can be concluded “that the haplotype associated with altitude adaptation in Tibetans is likely to be a product of introgression from Denisovan or Denisovan-related populations” (Huerta-Sanchez et al., 2014).

Conclusion

In leaving Africa, it is clear that ancient humans would have had a great many new environmental factors to contend with in Eurasia. These would include new pathogens, different foodstuffs, and an unfamiliar landscape. In order to survive, they would have had to adapt – quickly. Adaptations in the immune system, metabolism, and responses to environmental conditions, such as temperature, sunlight, and altitude, would have been key to survival. New research into archaic and modern genomes have revealed that these adaptations came from the introgression of Neandertal and Denisovan DNA.

The presence of archaic DNA in the modern human genome is clear evidence that interbreeding among these three hominin groups must have taken place in the distant past. Furthermore, the presence of Neandertal ancestry in all populations of non-African descent indicates that there was at least one major interbreeding event between Neandertals and *H. sapiens* shortly after the latter migrated out of Africa. Additionally, increased Neandertal ancestry in East Asian populations implies a second important introgression event between the human ancestors of these populations and Neandertals. There is also evidence to support additional, regional events. Furthermore, it is clear that Denisovan interbreeding with *H. sapiens* also took place. Their DNA is present in East and South Asian populations, as well as Melanesians and Papua New Guineans. Different levels of Denisovan ancestry across these populations suggest that this introgression also occurred in at least two pulses.

Altogether, this means that there were at least four major pulses of archaic introgression into Eurasian populations, suggesting that interbreeding among Neandertals, Denisovans, and *H. sapiens* did not only occur in isolated events. Nevertheless, several individuals resulting from some of these more isolated events have been discovered. Notably, Denisova 11 is the first known discovery of a first generation hybrid. Oase 1 is also significant because this individual, along with the presence of archaic DNA in modern populations, is proof that hybrids were actually viable. Therefore, Neandertals, Denisovans, and *H. sapiens* both interbred and produced fertile offspring. According to the biological species concept, this makes them all members of one species.

Interestingly, recent studies suggest that it is not just Neandertals and Denisovans. *H. sapiens* may have also interbred with other groups of hominins in Africa. Clearly, "the greatest opportunity for introgression was in Africa, where AMH and various archaic forms coexisted for much longer than they did outside of Africa" (Hammer, Woerner, Mendez, Watkins, and Wall, 2011). Study "results point to relatively recent genetic exchange with an unknown archaic hominin that diverged from the ancestors of modern humans in the Lower-Middle Pleistocene" (Hammer et al., 2011). Though the exact group of hominins responsible for this introgression is unknown, there are several good candidates. (Hammer et al., 2011). Once these mystery hominins are identified, they too should be added to the species *H. sapiens* on the grounds that they too interbred and created viable offspring with *H. sapiens*.

The expansion of the species Homo sapiens to include other groups of extinct hominins raises interesting questions regarding what it really means to be human. It is unclear as to which, if any, cultural characteristics these archaic hominins shared with *H. sapiens*. Furthermore, there are many questions left to be answered about their language and cognitive abilities. If it is found that archaic hominins lacked these considerations, what is the remaining thread that ties us all together as humans? Though the addition of archaic hominins to our species complicates this question, it may also be the key to finding the answer. Whatever the fundamental characteristic of "humanness" may be, its presence in other groups of archaic hominins may have been recognized by ancient *H. sapiens*, and may have motivated them to interbreed with these other groups of hominins, other humans, to create "hybrid" life.

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