European light skin may have evolved as an adaptation to the Neolithic sedentary lifestyle

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Abstract

Light skin facilitates the penetration of ultraviolet light (UV) radiation through the skin, increasing the synthesis of vitamin D that in turn stimulates bone formation. It has been suggested that light skin appeared in the ancestors of modern Europeans as an adaptation to the conditions of low UV radiation in high latitudes; however, paleogenetic studies have recently shown it did not evolve when Upper Palaeolithic human groups first peopled this continent, around 45,000 years ago, but much later, after the development of agriculture, 10,000 years ago. Neolithic Europeans may have struggled with a decrease of bone formation rate and a reduction of the bone mineral density (BMD) associated with the new sedentary lifestyle. Here I suggest that light skin evolved to increase the vitamin D synthesis (a stimulator of the BMD), balancing out the negative effects on the BMD during the Neolithic. According to the idea, I found that SNPs related to BMD may have changed after the European Agricultural Revolution, and possibly in correlation with skin pigmentation associated SNPs.

1. Introduction

Solar ultraviolet light (UV) radiation can affect organisms in different ways. In humans, UV radiation is critical for developing healthy skeletal and immune systems; it is involved in the syntheses of vitamin D that is needed for the absorption in the intestine of the calcium and phosphorus, which are critical for bone formation (Nair, R. & Maseeh, A. 2012). However, UV radiation can also have harmful effects. For example, it can produce mutations on the DNA with possible deleterious effects on the organisms (such as skin cancer (de Grujil, F.R. 1999; Wu, S. et al. 2014)), or it can destroy folate molecules (also known as vitamin B9), leading to an impaired development of the nervous system in the foetus (Jablonski, N.G. & Chaplin, G. 2017).

Melanin is a natural component responsible for the color of the fur, hair and skin in mammals. This pigment is highly efficient at absorbing the UV radiation that comes from the sun (Singaravelan, N. et al. 2008). Due to the axial tilt of the Earth, the levels of UV radiations are not uniform across continents. As a result, human populations throughout the world have adapted to the different UV radiations by means of regulating the levels and composition of melanin in their skin cells (Jablonski, N.G. & Chaplin, G. 2010).

Dark skin (high concentration of melanin in skin cells) is considered to be the ancestral feature in our species (Lao, O. et al. 2007; Jablonski, N.G. & Chaplin, G. 2017). As the genus *Homo* evolved in the African continent where the UV levels are high, increasing the concentration of melanin in skin cells helped to filter out most of the solar UV radiation. In contrast, in higher latitudes, like those of Europe and Asia, the radiation levels are reduced compared to the Equator. Consequently, it is widely accepted that Europeans evolved low concentrations of melanin in their skin cells as an adaptation that allows to increase the penetration of UV through the skin (Norton, H.L. et al 2007; Jablonski, N.G. & Chaplin, G. 2010; Basu Mallick, C. et al 2013).

For decades, it was believed that light skin evolved in the ancestors of modern Europeans soon after they left Africa, when the first modern human groups reached the high latitudes of Europe, around 45,000 years ago (Fewlass, H. et al. 2020). However, genomic analyses on ancient European human samples showed that alleles responsible for light skin in Europeans appeared and raised to fixation only after the development of agriculture in the Neolithic period that started around 10,000 years ago (Olalde, I. et al. 2014; Mathieson, I. et al. 2015; Ju, D. & Mathieson, I. 2021). This raises two new questions: i) how could pre-Neolithic Europeans that were living at high latitudes, maintain a healthy skeletal system given their dark skin pigmentation? and ii) what changes related to agriculture triggered the selection for light skin?

In this Opinion piece I propose an hypothesis that could answer both questions and analysed the polygenic evolution of the bone mineral density (BMD) and light skin in ancient European samples. Nonetheless, given the low number of pre-neolithic samples, it is essential to be cautious with the results, so additionally, I suggest how this hypothesis can be tested in future studies.

2. European light skin pigmentation evolved during the Neolithic

It has been widely accepted that the dark skin coloration evolved in our earliest human-like ancestors once they lost their fur, to protect against the damaging effects of African excess of UV radiation. Neanderthals and Denisovans seemed to have variable skin and hair pigmentation, as predicted from their genes (Lalueza-Fox, C. et al. 2007; Dannemann, M. & Kelso, J. 2017). However, the ancestors of the *Homo sapiens* living in Africa likely maintained a high synthesis of melanin in the skin cells.

Around 45,000 year ago, a group of *Homo sapiens* migrated from Africa into Eurasia, admixing with Neanderthals and subsequently colonising the whole globe. The hunter-gatherer lifestyle was maintained for tens of thousands of years in Europe until the development of the first agriculture practises around 10,000 year ago in the Near East and their subsequent expansion into Europe.

Functional and genetic studies have revealed that depigmentation of present-day Europeans is mainly associated with alleles in the SLC24A5 and SLC45A2 genes that almost reach fixation in European populations (with frequencies up to 99 and 97%, respectively), but also more than 100 loci has also been associated to light skin pigmentation (Ju, D. & Mathieson , I. 2021). In recent years, paleogenetic studies have shown that Mesolithic foragers carried the ancestral alleles in those genes, whereas the derived alleles started to increase in frequency during the Neolithic (Olalde, I. et al. 2014; Mathieson, I. et al. 2015; Ju, D. & Mathieson , I. 2021).

3. Evolution of the light skin pigmentation in relation to bone mineral density

Bone mineral density (BMD) is the amount of minerals in bone tissues, especially phosphorus and calcium in the form of hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$]. Hydroxyapatite binds to type I collagen, which is secreted by the osteoblasts- resulting in the mineralization of bone tissue (Vieth, R. 2020). The proportion of these minerals in bone tissue depends on both genetic disposition (i.e. people with African origins tend to have higher BMD levels, whereas Eurasians tend to have low levels of BMD (Medina-Gómez, C. et al. 2015)), and environmental factors (i.e.

athletes or people who exercise regularly tend to have higher levels of BMD than sedentary individuals (Kelley, G.A. Et al. 2000; Bellver, M. et al. 2019), as exercise stimulates the maturation of osteoblasts).

It is expected that the presence of dark skin pigmentation of the pre-Neolithic Eurasians and the reduced levels of UV radiation could have compromised the synthesis of vitamin D, by impeding the absorption of calcium in the intestine and consequently, compromising the adequate levels of bone mineral density. However, it has been suggested that Europeans have adapted to these conditions by reducing their innate BMD (Vieth, R. 2020), as anthropological studies have determined that Neolithic individuals had lower BMD than Mesolithic foragers. As the daily levels of physical activities was likely higher in hunter-gatherers than in Neolithic individuals, it could have helped to maintain a high bone formation rate in the formers (Ryan, T.M. & Shaw, C.N. 2015; Chirchir, H. et al. 2015). With the sedentary lifestyle of the Neolithic societies, this stimulus was likely lost, explaining the low BMD levels of the first farmers.

Under this scenario, it is possible that light skin evolved to palliate the deleterious effects in bone formation of the Neolithic sedentary lifestyle. Light skin allows to increase the vitamin D synthesis, which is involved in calcium absorption and can stimulate bone formation rate vía the Vitamin D receptor. Thus, under the new sedentary conditions of the Neolithic, light skin individuals would be able to counteract the low BMD levels with an increment of Vitamin D.

In an extensive BMD-GWAS using 436,824 individuals from the UK Biobank Morris, J.A.A. et al 2019, identified 518 associated loci that explain up to 20% of the observed variance in the BMD. As a proof of concept, I used this set of BMD related SNPs and applied it to 265 ancient European genomes. All individuals were obtained from https://reich.hms.harvard.edu/allen-ancient-dna-resource-aadr-downloadable-genotypes-present-day-and-ancient-dna-data and only individuals with information for at least 500,000 genomic sites were kept for the analyses. These ancient individuals have been genotyped with an array of more than 1.2 million SNPs, which include 241 of the BMD related SNPs. I selected individuals with information for at least 200 of the BMD related SNPs. This resulted in a dataset of 265 ancient European genomes encompassing the Palaeolithic, Mesolithic and Neolithic periods.

I obtained a genomic score based on the weight of the risk alleles related to BMD for each individual and compared this genomic score with the age of each sample. The results seem to suggest a significant difference in the BMD across time (Figure 1) (p.value= 0.012), especially during the Neolithic period.

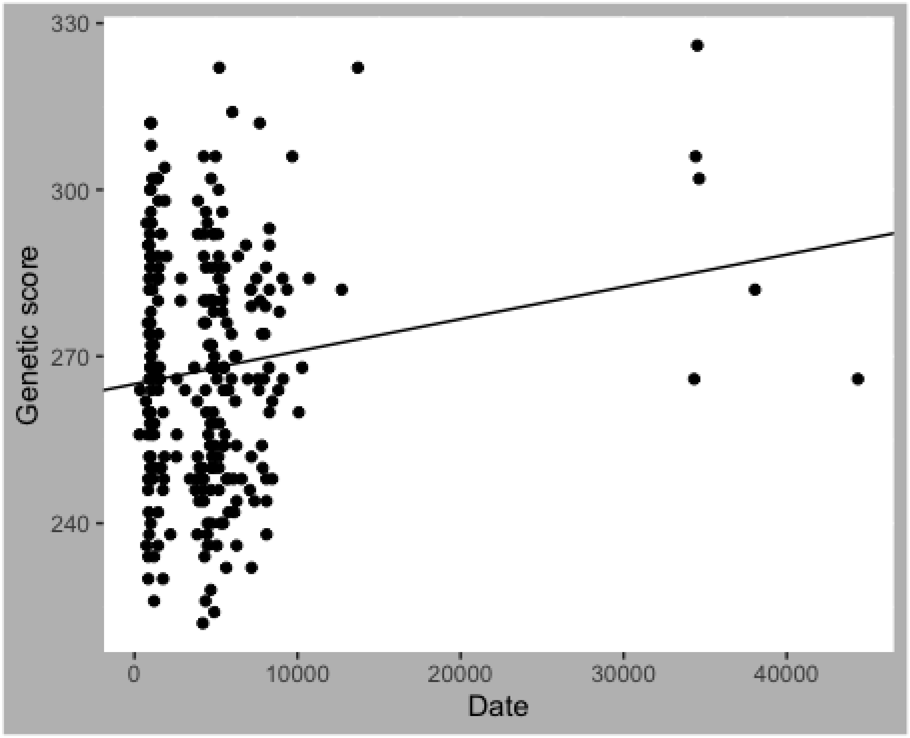

Figure 1. Relationship between the BMD genetic score through time in 265 Eurasians ancient samples (p.value= 0.012). Time starts with the oldest sample recovered, Ust'Ishim, from around 44,266 years ago (y.a). Each dot represents an individual.

Recently, Dan, J. & Mathieson, I. 2021, used a dataset of 170 SNPs related to skin pigmentation, also obtained from the UK Biobank database, and confirmed the evolution of light skin pigmentation in Europeans started after the development of the agricultural practices, and continued during the Neolithic. I applied this set of SNPs to the ancient dataset. I kept those 134 individuals with at least 150 of the skin pigmentation related SNPs. I saw a significant correlation among mean of light skin related alleles through time (Figure 2) (p.value = 2.84e-05), consistent with the idea of the selection for light skin during the Neolithic (Olalde, I. et al. 2014; Mathieson, I. et al. 2015; Ju, D. & Mathieson, I. 2021).

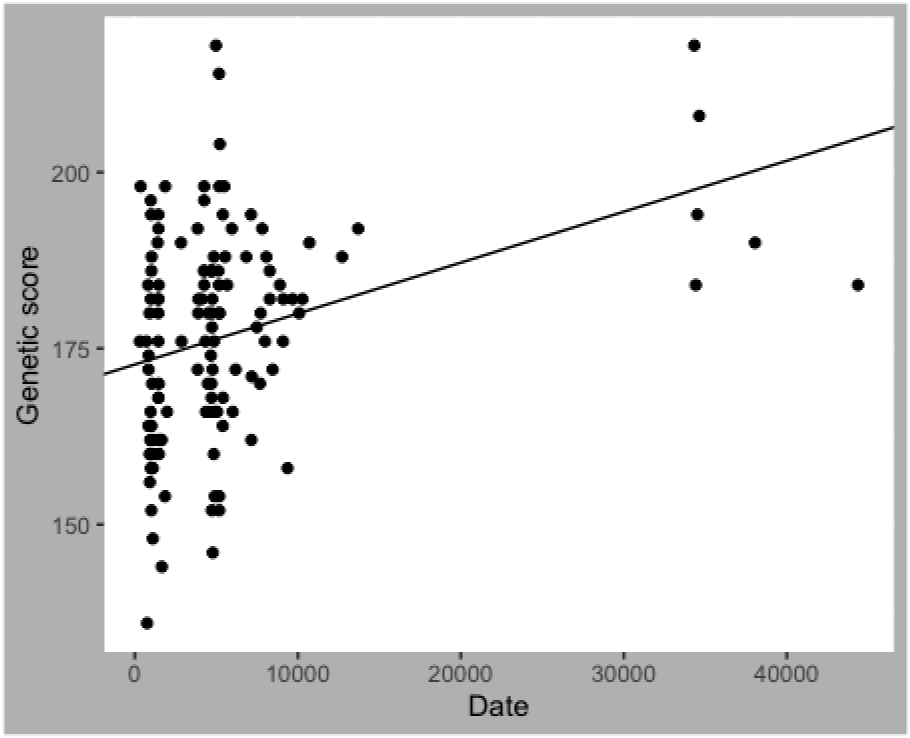

Figure 2. Relationship between the SKIN pigmentation genetic score through time in 134 Eurasians ancient samples (p.value= 2.84e-05). Time starts with the oldest sample recovered, Ust'Ishim, from around 44,266 years ago (y.a). Each dot represents an individual.

Additionally, I compared the means for the BMD and light skin related alleles of 134 ancient individuals for which both measurements were possible. I found a moderate statistical correlation among both parameters (P.value = 0.014), suggesting a possible co-evolution among these two traits.

These results suggest changes in the BMD genetic architecture in Europeans after the Agricultural Revolution, possibly in relation with the light skin pigmentation. However, given that just a few pre-neolithic individuals have been sequenced to the need coverage for this kind of analyses, all these results have to be taken very carefully.

5. Conclusions and future research

To date, BMD differences between foragers and farmers have been determined directly by comparing the skeletons of individuals of these different lifestyles. However, the development of the ancient DNA field opens a new range of other analyses. Here, I have seen changes in BMD related SNPs after the Agricultural Revolution, that may be associated with light skin evolution during the Neolithic. As, only few mesolithic and palaeolithic individuals are available and I suggest that future ancient DNA studies may focus on obtaining new pre neolithic genomes. Another possible approach to improve our understanding of these potential selective processes, would be by genotyping and measuring the BMD directly in the same ancient individuals, so the trait can be both inferred by direct measurements and indirectly by its genotype.

Importantly, the evolution of light skin is not a unique feature of Europeans. Genetic studies have shown that light skin has evolved in parallel in Asiatic populations (Norton, H.L. et al 2007; Basu Mallick, C. et al 2013). The high latitudes of the Asia continent and the convergent development of the farming practises in East Asia thousands of years ago, open the possibility that depigmentation evolved in East Asians for the same reason that I suggest for Europeans. Further human paleogenetic studies covering different periods and lifestyles in Asian populations could determine if light skin evolved in this continent after or during the development of the farming practises as it has happened in Europe. Accordingly, it has recently been suggested that the evolution of light skin in East Asia started around 10,834 years ago (Adhikari, K. et al. 2019), and curiosingly, similar estimates have been suggested for the domestication of the rice in this area, between 13,500 and 8,200 years ago (Molina, J. et al. 2011).

Finally, some domestic animals, such as dogs and pigs, show low BMD levels as compared to their wild relatives (Aerssens, J. et al. 1998). Indeed, depigmentation with respect to their wild relatives has also been observed in nearly all domesticates. A pleiotropic effect of genes related to the neural crest, initially selected for tameness, has been suggested to cause the general depigmentation patterns (Wilkins, A. S. et al. 2014). However, taking into account the less-mobile lifestyle of domesticated animals in comparison with their wild relatives, it is plausible that their depigmentation mechanism could mirror that observed in humans. For instance, light skin pig breeds tend to be originated in northern Europe, whereas some southern varieties, like the Iberian pig, show darker skin coloration (Ramirez, O. et al. 2014). Future paleogenetic studies should slo investigate potential associations between light skin pigmentation and bone development in different domesticates, as compared to their contemporaneous wild relatives, as well as in ancient Europeans. I think that the recent and innovative field of paleo epigenomics (Gokhman, D. et al. 2017; Gokhman, D. et al. 2019; Mathov, Y. et al. 2020) offers a potential methodology to test these ideas by comparing differentially methylated regions related to bone development or bone mineral density in ancient neolithics and pre-neolithic Europeans.

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Competing interests

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