# Genetic Adaptation to High Altitude

# Resilience, Endurance and Perseverance: the case of Ethiopia's Amhara people.[[1]](#footnote-1)

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# Introduction

Discussions about the sources of development in general and of the origin and dynamics of human cognitive development, have always been controversial and remain unresolved. The dispute centers on the degree to which our character or behaviors are expressions of inborn traits and the extent to which we are shaped by our experience, sociohistorical and physical, and cultural environment, and socialization. Is learning or civilized behavior (decency, humanity, ethical and moral acquisition) a reflection of intellectual capacity (intelligence)? Or is intelligence in some measure the product of learning? Does intelligence exist? If so, how can we objectify, record, and quantify it? How do environmental manipulations such as cognitive skills training and instructional manipulation moderate the influence of intelligence on learning and of learning on intelligence? Above all, how do we explain the relationship between culture and mind? How does “mind/behavior” originate? Addressing these questions is a challenging task and the academic arena seems to be sharply divided. Further, the issue is a volatile one because of its far-reaching social, economic, political, ideological, psychological, and educational implications. This is indisputably an area that needs further research and serious deliberation.

The issue of sources of development has also given rise to competing perspectives about the contribution of biology and the environment to the process of development. Views differ from stressing the overriding importance of biology and neglecting the influence of environment or vice versa, to views that emphasize the reasonable importance of both. According to Lynn & Vanhanen the first line of argument (i.e., biological determinism) is correct, although the data supporting their argument is scant. A common assertion is that environment is much more important than heredity in determining human behavioral differences (Kamin, 1974; Hunt, 1961; Gould,1996; Harrison & Huntington, 2000).

Human diversity in physical features—phenotype—also arises if populations are geographically separated from each other for long periods of time. Some external features, such as skin color and body size, and shape, are highly subject to the influence of natural selection in response to climate. Areas with greater exposure to the sun, such as the tropics, have provided an advantage to persons with naturally darker skin pigmentation, who were more likely to have survived and to have left greater numbers of descendants in successive generations. In northern latitudes with less sunlight, cereal eaters do not receive sufficient Vitamin D, and fair skin provides a survival advantage because it allows for greater absorption of ultraviolet rays, which aids in the production of Vitamin D (Cavalli-Sforza, 1997)

Scholars such as Richard Lynn argue that race differences in intelligence are real, substantially heritable, and *unalterable*. He attempts to give an account of the ―general principles of the evolution of race differences in intelligence. The crucial selection pressure responsible for the evolution of race differences in intelligence is identified, he argues, as the temperate and cold environments of the northern hemisphere, impose greater cognitive demands for survival and act as selection pressures for greater intelligence (Lynn & Vanhanen, 2006). There is no credible evidence for this statement. We maintain that the balance of evidence favors a predominantly cultural and environmental aetiology underlying *racial* differences in so-called intelligence and that the burden of proof is on researchers such as Lynn who argue for the predominance of genetic racial differences.

However, that does not mean that people who reside in different climatic regions, high vs low altitudes do not differ in social and cognitive performances. For instance, new research shows chickadees living at higher, harsher elevations have better problem-solving abilities than their easy-living counterparts. High-altitude locations are usually much colder than areas closer to sea level. This is due to the low air pressure. Air expands as it rises, and the fewer gas molecules—including nitrogen, oxygen, and carbon dioxide—have fewer chances to bump into each other. The human body struggles in high altitudes (Kozlovsky, Branch, & Pravosudov, 2015). “The idea is that if you live in a harsh environment,” says Kozlovsky, “you would need those kinds of abilities to survive.” Generally, research lends support to the conclusion, regardless of the species, animals inhabiting challenging and harsh environments are expected to benefit from certain phenotypic traits including cognitive abilities. In particular, innovation and habituation are traits thought to benefit animals in challenging environments and increase an individual’s probability of survival via increased foraging success. In humans, the research needs to be expanded as there are some conflicting studies. Data on the physical or physiological differences pertaining to high altitude adaptations are abundant. Our review shows that further studies and more data is required to confirm the cognitive ability and emotional differences in humans. However, the existing data *awaken* us for further inquiries in the field. The specific knowledge is more relevant in Ethiopia as there are already some observations on ethnic groups’ behavior germane to altitude and plateaus. Although some observations are speculative and have yet to be substantiated, it is interesting to delve into the major causes of conflicts, war, brutal actions, unspeakable atrocity crimes (as we recently witnessed in Oromia region), moral, and ethical deficiencies along high/low altitude adaptations and settlements. It is apparent that both nature and nurture influence the acquisition of a high-altitude phenotype in humans and while there is some evidence for genetic adaptation in several highlanders, it is evident that these characteristics are expressed in concert with substantial environment-dependent developmental adjustments.

Researchers solve questions about Ethiopians' high-altitude adaptations. Over many generations, people living in the high-altitude regions of the Andes or on the Tibetan Plateau have adapted to life in low-oxygen conditions. Living with such a distinct and powerful selective pressure has made these populations a textbook example of evolution in action, but exactly how their genes convey a survival advantage remains an open question. Now, a University of Pennsylvania team has made new inroads to answering this question with the first genome-wide study of high-altitude adaptations within the third major population to possess them: **the Amhara people of the Ethiopian Highlands**. The authors highlight “several candidate genes for involvement in high-altitude adaptation in Ethiopia, including CBARA1, VAV3, ARNT2 and THRB. Although most of these genes have not been identified in previous studies of high-altitude Tibetan or Andean population samples, two of these genes (THRB and ARNT2) play a role in the HIF-1 pathway, a pathway implicated in previous work reported in Tibetan and Andean studies. These combined results suggest that adaptation to high altitude arose independently due to convergent evolution in high-altitude Amhara populations in Ethiopia” (Scheinfeldt, et al., 2012 p. 1).

# **Biological and Physiological traits**

There has been rigorous research on the relationship between geographic altitude, metabolism, and physiology, to adaptation and intelligence, for a long time. It is obvious that oxygen level decreases with increasing altitude for its mass. Oxygen is a heavy gas, and it is denser in low-land areas than in high altitudes. For this reason, residents of high land areas have less oxygen supply that faces them with hypoxia compared to low land dwellers. Hence, high-altitude dwellers develop their own survival adaptation in physiological developments. Significant variations have been observed in the respiratory and metabolic systems across samples tested in different altitude residents (Brutsaert, et al., 1999). The size of the lung and depth of the chest increases in higher altitude cases so that the optimal level of oxygen can be compressed in the lung (Greksa, Spielvogel, Paz-Zamora, Caceres, & Paredes-Fernández, 1988).

High altitude (3500m-4000m asl) residents in Tibet, Ecuador, and Ethiopia have been sampled for measurements in different studies and uncovered symmetrical results except for the cases in Bale highland dwellers in Ethiopia. Besides the respiratory and physical organs’ size measures, hemoglobin gauges were considered a crucial variable. Successful adaptations to these highland areas were determined by Oxygen saturation in the blood which directly affects the function and development of the brain; and the development of the brain directly affects the level of intelligence; whereas rises in hemoglobin were considered as responses to adaptation trouble (Windsor & Rodway, 2007).

## *Hemoglobin (Hb) and Oxygen Saturation Tests*

Hypoxia research conducted by Cynthia Beall in 2002 showed a higher hemoglobin rate in highlanders compared to lowlanders, generally. Her research in Ethiopia, specifically with

the Amhara people, discovered that Amhara people have comparatively higher hemoglobin and oxygen saturation compared to other people.

The average hemoglobin concentration of Amhara males was 15.9, 0.1 gdl, with a range from 12.7 to 18.9 gdl (n 128). The average hemoglobin concentration of Amharas females was 15.0, 0.1 with a range from 12.0 to 18.2 (n 108) gdl. The Amharas males’ mean hemoglobin concentration was just 0.3gdl (2%) higher than the U.S. sea level mean of 15.3, 0.02, with a range of 10.4–18.7 gdl calculated from the published NHANES (National Health and Nutrition Examination Survey) III data set (12, 13, ††). The Ethiopian females’ mean hemoglobin concentration was 1.6 gdl (12%) above the U.S. Sea level mean of 13.4, 0.02, with a range of 5.2–16.9 gdl. There was no significant difference between the mean hemoglobin concentrations of adults 21 years of age and the younger Ethiopians. (Beall, Decker, Brittenham, & Strohl, 2002) (Beall C. M., 2006).

The studies further explored that not all highland residents in Ethiopia had similar hemoglobin responses and adaptation traits. Traditionally, an elevated hemoglobin concentration has been considered a hallmark of lifelong adaptation to high-altitude hypoxia, though this notion has been refuted recently because of the establishment of the alternative adaptive responses found in Amhara highlanders living in the Simien Mountains of northern Ethiopia (Getu, 2022). According to the findings of Cynthia Beall *et al.* 2002, Getu 2022, and Hoi *et al* 2016, these populations did not have elevated hemoglobin (no erythrocytosis) but had normal hemoglobin saturation and arterial oxygen level, which alerts researchers to explore the possibility of the presence of an alternative adaptive mechanism. Contrary to this, Oromos living in the Bale Mountains of southern Ethiopia have elevated hemoglobin (Getu, 2022) (Cheong, et al., 2016) (NESCent, 2012).

Getu (2022) explains the presence of increased nitric oxide (NO) and cyclic guanosine monophosphate (cGMP) in native Amhara highlanders suggests the possibility of adaptation via vasodilation, which would improve oxygen supply to metabolic tissues. According to the report, native Amhara highlanders showed no indications of chronic mountain sickness and had a higher pulmonary blood pressure without having higher pulmonary vascular resistance. In addition, the cerebral circulation is sensitive to NO and carbon dioxide (CO2) but not to hypoxia, which would likely promote increased cerebral blood flow and increase oxygen delivery to the brain, making Ethiopian high-altitude natives better suited for survival at high altitudes (Getu, 2022).

On the other hand, findings of comparative research uncovered the elevation of hemoglobin concentration, a common adaptive response to high-altitude hypoxia, occurred among Oromos but it was dampened among Amhara highlanders. The researchers hypothesized that Amhara highlanders offset their smaller hemoglobin response with a vascular response (Beall & Strohl, 2021) (Cheong, et al., 2016). Hence, they tested this by comparing Amhara and Oromo highlanders at 3,700 and 4,000m to their lowland counterparts at 1,200 and 1,700m. To evaluate vascular responses, the researchers assessed urinary levels of nitrate (NO3−) as a readout of production of the vasodilator nitric oxide and its downstream signal transducer cyclic guanosine monophosphate (cGMP), along with diastolic blood pressure as an indicator of vasomotor tone. To evaluate hematological responses, they measured hemoglobin and percent oxygen saturation of hemoglobin. In this test, Amhara highlanders, but not Oromos, had higher NO3− and cGMP compared with their lowland counterparts. NO3− directly correlated with cGMP (Amhara R2 = 0.25, P < 0.0001; Oromo R2 = 0.30, P < 0.0001) (Cheong, et al., 2016). Consistent with higher levels of NO3− and cGMP, diastolic blood pressure was lower in Amhara highlanders. Both highland samples had an apparent left shift in oxyhemoglobin saturation characteristics and maintained total oxyhemoglobin content similar to their lowland counterparts. However, deoxyhemoglobin levels were significantly higher, much more among Oromo than Amharas (ibid).

In Amhara, elevated nitric oxide-cGMP enables vasodilation, lower diastolic blood pressure and, by extension, increases blood flow, which offset their relatively lower hemoglobin response. Unlike Amhara, Oromo highlanders produce a much greater hemoglobin response to maintain sufficient oxygen-carrying capacity at the cost of lower body iron stores (ibid) and a higher level of circulating deoxyhemoglobin. This evidence suggests, as the researchers argue, different balances of hemoglobin (Oromo) and vascular (Amhara) adaptive responses to hypoxia among East African high-altitude settlers and natives. They found out that the oxygen saturation value of high-altitude Amhara is higher than estimated from interpolations based on Oromo low- and high-altitude samples, perhaps related to nitric oxide production. Accordingly, they argue that high-altitude Amhara rely on nitric oxide-based vasodilation to offset their dampened hemoglobin response, and their hemoglobin picks up oxygen more efficiently in the lung. In contrast, high-altitude Oromo mainly rely on hemoglobin response of much greater magnitude, and their hemoglobin gives up oxygen more readily (Cheong, et al., 2016).

Therefore, the researchers conclude that the Amhara balance minimally elevated hemoglobin with vasodilatory response to environmental hypoxia, whereas Oromo rely mainly on elevated hemoglobin response. The researchers remark that “results point to different combinations of adaptive responses in genetically similar East African highlanders” (Cheong, et al., 2016). Nonetheless, there is a substantive attribute that brought the difference between Oromos and Amharas in their samples; and that draws more arguments and assertions per se.

A prominent study on the ‘Genetic architecture of adaptations to high altitude in Ethiopia’ obtained phenotype data in the two distinct, but closely related ethnic groups - the Amhara and the Oromo. The research confirms that ‘Ethiopian Amhara and Oromo differ in adaptive phenotypes’ (Alkorta-Aranburu, et al., 2012). In this study, all sampled individuals were born and raised at the same altitude. These samples allowed comparing phenotypes across altitudes within ethnic groups as well as across ethnic groups; and helped sort out the possible factor(s) of differences. Hence, the researchers further envisaged historical and social movements as the length of time that the study subjects stayed or settled at these altitudes/plateaus, affects the measurement(s) significantly.

High Altitude (HA) samples of both ethnic groups had higher Hb than the LA samples, however the Oromo had twice as much elevation in Hb as the Amhara. The elevation in Hb levels is particularly evident for the measurements in males, raising the possibility that other factors (e.g. menstrual cycle) in females affect the power to detect significant phenotypic differences between groups. With regard to O2 sat, HA Amhara had a 5.6% lower O2 sat compared to LA Amhara while HA Oromo had 10.5% lower O2 sat than their LA counterparts. Therefore, we detected significant phenotypic differences not only between populations from the same ethnic group that live at different altitudes, but also across populations from closely related ethnic groups (Oromo and Amhara) that live at the same altitude. Given the low genetic divergence between these two ethnic groups at the genome-wide level (mean FST = 0.0098), the phenotypic differences between Amhara and Oromo highlanders are unlikely to be due to independent genetic adaptations in these ethnic groups; rather they are likely to reflect genetic adaptations that evolved in the Amhara, due to their longer residence at HA. While historical records indicate that **the Oromo have moved to the highland areas (HA) only in the early 1500s,** the Amhara have inhabited altitudes above 2500 m for at least 5 ky and altitudes around 2300–2400 m for more than 70 ky. Therefore, **sufficient time has elapsed for the Amhara to have evolved genetic adaptations to hypoxia**. (Alkorta-Aranburu, et al., 2012).

# **Brain Size and Cognitive Functioning**

According to neuroimaging studies, magnetic resonance imaging (MRI) was mostly used to explore the effects of long-term hypoxic exposure on brain structure and function. Uninterrupted research on the brain structure of high-altitude residents was undertaken by Li & Wang using MRI-T1 sequence to collect image data, and voxel-based morphometry (VBM) analysis and measurement, to infer the effects of long-term hypoxic exposure on gray matter, white matter, and cerebrospinal fluid in brain tissue. Adaptive changes in brain structure have been found after long-term hypoxic exposure (Li & Wang, 2022). Their research uncovered a significant reduction in the thickness of the bilateral insula, right anterior cingulate gyrus, bilateral prefrontal cortex, left anterior central cortex, and right lingual cortex in long-term migrants sampled at high-altitude areas. The studies suggest that when hypoxic exposure time is longer [as is the case with Amharas], adaptive changes occur in brain tissues, such as local cerebral vascular hyperplasia and increase in cortical thickness in local brain areas, to compensate for inadequate blood oxygen levels, while on the other hand, the prolonged hypoxic exposure time [Oromo cases], the whole brain gray matter showed a tendency of atrophy, showing the characteristics of **non-specific injury** (Li & Wang, 2022).

Li and Wang used diffusion tensor imaging (DTI) in their earlier experiments to analyze the correlation between the changes in gray matter volume, white matter fractional anisotropy (FA), and other parameters in the plateau population with physiological parameters and neuropsychological test results. The study found that the reduction of gray matter volume in the Para hippocampus and middle frontal gyrus of the plateau population was positively correlated with the change in vital capacity, and the change in the gray matter volume of the superior frontal gyrus was correlated with the outcome of the mental rotation task, and the change in the thickness of the postcentral gyrus cortex was correlated with the working memory reaction time (Li & Wang, 2022).  These results suggest that long-term high-altitude hypoxia exposure leads to structural changes in the whole brain, and such changes may be the structural basis of cognitive function changes (Ghani, Signal, Niazi, & Taylor, 2020).

Functional magnetic resonance imaging (fMRI) and event related potentials (ERP) were used to investigate the effects of long-term hypoxia exposure on brain function. Regional homoho (ReHo) analysis of resting state brain function of migrants shows that there is a significant increase of ReHo in the right lower sensorimotor cortex, which is correlated with the response time of memory search task. Voxel-mirrored homotopic connectivity (VMHC) analysis showed that bilateral visual cortex signals were significantly enhanced and correlated with subjects’ hemoglobin concentration, suggesting that long-term hypoxia exposure may affect the synchronization and connectivity of spontaneous brain neural activity. This may be the brain function basis for cognitive function changes (Li & Wang, 2022).

These studies suggest, without proper evolvement, settlement at high-altitude produces substantial impairments in several cognitive performances. Thus, the brain tends to use Event-Related Potentials (ERPs) that are evoked by multiple or diverse stimuli - intentionally giving stimuli special psychological meanings (Helfrich & Knight, 2019). For this reason, groups of such individuals can be more prone to influences of activism as sources of stimuli, herd mentality and driven to mob actions without analyzing the causes, pros, and cons of their own actions. Significant changes have been measured in psychomotor performance, mental skills, reaction time, vigilance, memory, and logical reasoning at altitudes above 3,000 m (9,843 ft) (Bahrke & Shukitt-Hale, 2012) (Bahrke and Shukitt-Hale, 1993).

A research project with the title ‘Effects of 92% oxygen administration on cognitive performance and physiological changes of intellectually and developmentally disabled people’ has concluded that enriched oxygen can positively affect, at least in the short-term, the working memory of those with intellectual and developmental disability (Kim, et al., 2015). A study on Mountain Chickadee shows that ‘*chickadees living at higher, harsher elevations have better problem-solving abilities than their easy-living counterparts*' (Greenspan, 2015). Similarly, one may tentatively infer that the complex relationship between high altitude, health status, resilience, endurance, and the cognitive and spiritual skills of the Amhara people of Ethiopia is more complex than their easy-living fellow counterparts living elsewhere in the country. However, we need further investigations and extensive data, both ethnographic and quantitative, to conclusively confirm the conjecture.

# **Discussion**

It has been explicitly expressed in the research that hemoglobin rises to Oromo samples in response to adapting to high altitudes. The rise of hemoglobin is premeditated to contain optimal oxygen needed in the body. On the other hand, sufficient oxygen saturation in the blood has been observed in the Amhara samples, without any hemoglobin troubles. The extent of oxygen saturation in the blood is the predominant factor for the development and function of the brain. Lower Oxygen saturation in the blood results in slower brain development. The slower its development, the smaller its size, and less capable of analysing complex problems. On the other hand, high (dense) oxygen in the blood facilitates the development of the brain, enhancing its size. People who have higher oxygen saturation have deeper chest and larger lungs as well, according to the reviewed scientific literature.

Hence, it is possible to make a logical inference that the groups who scored significantly lower blood oxygen saturation while still living in high altitudes, have smaller brains that may need to evolve yet, to withstand the high-altitude settlements in the southern and central Ethiopian highlands.

The longitudinal research discovered huge differences between Oromos and Amharas who live in almost similar altitude and lifestyles. The researchers indicated their assumptions in their conclusion section “…different combinations of adaptive responses in genetically similar east African highlanders”. Accordingly, the length of time that subjects lived in the research context was a crucial factor. In the case of Ethiopian highlands, the main reason why Oromos have fewer adaptation responses to altitude hypoxia compared to Amharas was clearly stated. The Oromos in the sample group have yet to settle long enough in the plateaus, to evolve the genetic changes; while Amharas responded positively because they seem to have settled in these areas thousands of years. This might provide insight on who was indigenous and native ethnic group in ancient Ethiopia and which ethnic groups are newcomers or relatively new to the proper Ethiopia.

Aside from the biological and Physiological changes, people who lived in similar altitudes and lifestyles had varied scores in multivariate analysis of cognitive, psychosocial, and cultural aspects. Hence, the variables – other than physiological traits, can have explanatory and realistic effects that emanate from genetic provenance. Metabolism measures such as haemoglobin and oxygen saturation influence the growth and size of the brain. Research shows that compared to other Ethiopian research subjects, and control groups in the USA, the Amhara exhibit immense endurance, resilience, and perseverance in harsh environments and adversity.

The reason the Oromo have fewer adaptation responses to altitude hypoxia in the Ethiopian highlands, compared to the Amhara, is that the Oromo sample group has not settled long enough in the plateaus to evolve genetic changes. In contrast, the Amhara have settled in these areas for thousands of years, resulting in a positive response. This information provides insight into some significant traits of the indigenous and native ethnic groups in ancient Ethiopia and identifies which ethnic groups were latecomers or relatively new to proper Ethiopia.

It is also reported in the studies that there is an unspecific injury in the brain of cases from Bale [Oromos] that responded in hemoglobin rise to their altitude adaptation. ‘What sort of injury happened to their head? And what needs to be done?’ ought to be scrutinized sooner than later as these might have implications for coexistence, harmony, and peace in East Africa.

Although intelligence may well be adaptive, in the sense that it enables humans to solve problems and improve their reproductive success, the assumption that intelligence is an adaptation to deal with evolutionarily novel problems ignores the possibility that intelligence might simply be a serendipitous by-product of the way the human brain evolved. In this sense, intelligence would be more accurately described as an ―adaptable trait (i.e., one that is flexible and responsive to the context in which individuals develop and live) as opposed to an ―adaptive trait (i.e., one elected to fulfill a particular purpose, such as dealing with evolutionarily novel problems). Indeed, there is no reason why problem solving would necessarily evolve as a fixed response to novelty rather than as a trait that would develop in response to its environment, and the very nature of intelligence (particularly the way in which it enables humans to respond to, learn from and extrapolate between novel problems) suggests that it is unlikely to constitute a fixed response. And while Kanazawa assumes that the principal benefit of intelligence is that it is important for solving evolutionarily novel problems, intelligence would have also been subject to selection if it improved humans’ ability to solve evolutionarily familiar problems in ways that improved their reproductive fitness. Only under circumstances where no increase in problem solving was necessary or beneficial, would there be no such selection for intelligence. (Ellison, 2007 p. 196)

The scope of these studies has been limited to high-altitude areas of Bale, Arsi, Welega, Shewa, and other northern parts of the country; and hence inferences are made accordingly. It does not include the multi-ethnic Ethiopian communities living in the low land (low altitude) sections of the country, such as Afar, Somali, and many other peripheral areas.

*Part Two will continue…*

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1. The data collection and analysis were conducted in collaboration with Desalegn Birara, PhD candidate at the University of Gent, Belgium. [↑](#footnote-ref-1)