BIOLOGICAL SIGNIFICANCE OF NEURAL CREST

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SUMMARY : Craniofacial features, pigmentation, stature and body proportions are certain racial characteristics and they are known to be the results of permanent anatomical and physiological changes under the influence of geographically determined differences. But genetic and embryonic mechanisms involved have not been elucidated yet. We thought that neural crest which gives rise mainly to facial tissues, pigment cells and peripheral neurons may be the embryonic origin of racial characteristics. To confirm this hypothesis, we have reviewed recent literature and found that almost all racial characteristics are in close relationship with the neural crest derivatives. We concluded that environmental factors affect exclusively the structures of neural crest origin through the genetic mechanisms and racial characteristics are the result of this interaction.

***Key Words :** Adaptation, Biology, Neural Crest, Race.*

INTRODUCTION

When we were studying the facts with neural crest, an embryonic structure giving rise to head mesenchyme, peripheral neurons and pigment cells (31); we noticed that a relationship might be present between racial characteristics and neural crest derivatives since main racial characteristics are also present in craniofacial region, pigmentation and body build (6). We planned this study to bring out their possible relationships.

RACIAL DIFFERENCES

Animal species which occur in territories with different climates, soils, and other environmental conditions, often exhibit local variations in their appearance, bodily structures, and physiological functions. Such locally distinct populations of a species are known as races. Mankind is a single biological species differentiated into several races. Three major races of the human species are recognized : the Caucasoid, the Mongoloid, and the Negroid (25). Each of these groups is distinguished from the others by the possession of certain characters :

Physical characters (6) are stature, body proportions, skin color, craniofacial morphology and body hair distribution. Functional racial differences are adrenocortical activity which is lower in highly pigmented races (41); basal metabolism which is higher in races living near the Pole (39); calcium-phosphorus metabolism (27, 29, 35, 37); blood pressure which is higher in blacks (2); cranial capacity which is higher in Mongoloid and lower in blacks (10) and lactose intolerance (38).

BIOLOGICAL ADAPTATION

Racial characteristics are suggested to be the results of adaptations to environment over long periods of time (39). The relative isolation of human ancestors and the adaptation of each population to the pressures of the very diverse environments seem to be important in this variation. Such gradual changes in the structure and physiological mechanisms are mainly ascribed to a complicated process briefly indicated as "biological adaptation". Racial differences thus reflect current environmental pressures, genetic drift, and the present adaptation of human varieties to their environment. Each such environment would have its own advantage and disadvantage for the physical types (genetically based) living within in.

The actual mechanism of biological adaptation is unknown, and it is difficult to prove that the various physiological changes could have resulted in permament anatomical and physiological adaptations, but the following considerations make it appear likely :

a) The princpile of optimal design : "For a prescribed set of biological functions of given intensities, such as rate of metabolism, velocity of locomotion, etc., the design of an organism (both internally and externally) is such as to be optimal with respect to economy of material and energy expenditure" (39).

b) Biometeorological rules : Adaptation to the climate in general is governed by three rules (6, 10, 20, 39) : Gloger's Rule : "Pigmentation is greatest in warm and humid areas". Bergmann's Rule : "Animals are smaller in warmer than in cooler climates". Allen's Rule : "The extremities of the body are shorter in cold climates".

c) Craniofacial adaptations : It has long been known that environmental factors such as diet, nutrition, culture and climate influence craniofacial morphology and growth. For example, the shape of the nasal aperture is strongly affected by climate. In hot, moist climates, it is generally broad; in cold dry climates it is narrow. A restricted air intake under cold conditions would seem to be essential to lessen the danger of chilling the lungs (6). On the other hand, the Mongoloid face has been suggested to be the result of the large masseter muscles used in chewing tough food, with consequent enlargement of the bones to which these muscles are attached (12). In another study a short-term variation in craniofacial dimensions was observed in two Finnish samples, one exposed to a hard and the other to a soft diet. Hard diet, which requires more chewing force and time, was observed to promote vertical growth of the ramus and anterior translocation of the maxilla (24). Head posture was also shown to contribute to the determination of craniofacial morphology (40).

d) Surface features : The tightly curled hair seen on certain races is said to provide an "air cushion" cooling the scalp. Lack of hair over the body of negroids is obviously advantageous for effective heat loss through sweating (6). Epicanthic fold, a surface feaure of Mongoloids, might be developed to protect the eyes from freezing by fatty layers padding the lids. But, a number of racially distinctive suface features have no obvious advantage such as thick, everted lips and short, wide ears of the Negroids.

e) Functional adaptations : Low lactose digestion capacity in adulthood was suggested to be the normal condition in humans (as in other mammals), and high frequencies of adult persistence of lactase activity resulted from adaptation in populations relying heavily on lactose-rich dairy products (38). The high-altitude populations of the world also appear well adapted to their environment. Because, while a short term acclimatizational process contributes to native abilities, it appears that either developmental change or genetic adaptation is necessary for people to become fully functional at the higher elevations (10).

The previous considerations make it reasonable to assume that prolonged environmental stimuli may lead to permanent changes, which will vary for different geographical areas. although the deeper biological mechanisms involved are still unknown, we suggest that neural crest derivatives might be the structures upon which environment operates to produce permanent anatomical and physiological changes.

NEURAL CERST

The neural crest is a transient embryonic structure of vertebrates composed of cells that originate along the line of fusion of the neural tube. These cells migrate along defined pathways throughout the embryo to reach final locations where they differentiate into a number of different cell types (19). In the human embryo, the migrations are initiated at approximately gestational day 22. The migration is either laterally under the surface epithelium or down beside the neural tube. Crest cells migrating

beside the neural tube form primarily components of the peripheral nervous system; those migrating under the surface ectoderm in the trunk region form exclusively pigment cells, while in the head and anterior neck region they also form skeletal and connective tissues (14). The derivatives of neural crest are summarized in Table 1 and the large contribution of neural crest cells to the craniofacial skeleton and connective tissues is demonstrated in Figure 1 (14, 31, 42).

	Trunk crest	Cranial crest
Neural derivatives	Spinal ganglia Sympathetic ganglia Pelvic plexus Suppordive cells	Cranial sensory ganglia Parasympathetic ganglia Meninges Supportive cells
Endocrine derivatives	Adrenal medulla	Calcitonin (C) cells ACTH and MSH cells? Carotid body and sinus
Skeletal and connective tissues	None	Head mesenchyme Aortopulmonary septum
Pigment cells	Almost all pigment cells	Small contribution

Table 1 : Summary of neural crest derivatives (Modified after Johnston, 1990).

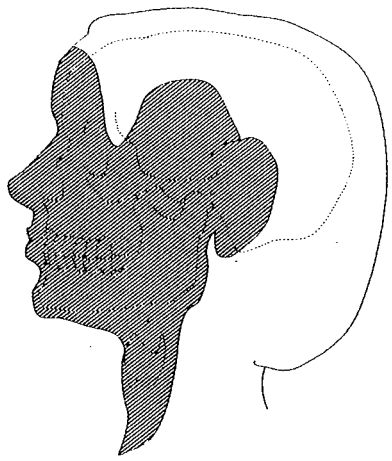

Fig - 1 : Contributions of neural crest cells to the craniofacial skeleton and connective tissues (dart area) (Modified after Johnston 1990).

UNDERLYING MECHANISMS FOR THE DIVERSITY

a) Genetic mechanisms : Genetic plasticity is the ability of a genetic system to produce a viable phenotype in variable environments (10), that means that the expression of phenotypes is controlled by the interaction of genotypes and environments (36). Two people of the same sex differ in their DNA by only 0.1 percent. Even Bill Clinton and Nelson Mandela would be 99.9 percent identical if they were to be compared with their genetic material. Chimps, average six times that much difference among themselves. That's because the longer a group has existed, the greater its diversity. Thus it appears that chimps have been around six times as long as humans. When different geographic and ethnic groups of humans are compared, those of African origin exhibit more gene diversity than those of Caucasian or Asian origin. From this it can be deduced that Homo sapiens originated in Africa about 200,000 years ago and later spread to the rest of the world (22). It appears likely that future research will show a complex interaction which regulates both the genetic information and the genetically plastic development of the adult morphological and functional organism.

b) Craniofacial diversity : Both genetic and environmental factors seem to be important in the determination of craniofacial morphology, but patterns of differential gene action are still unclear (16). At this point, we suggest that craniofacial diversity results from the tissues of neural crest origin. Because, both neural crest derivatives and facial diversity seem to have same components in this region (Fig 1).

c) Effects of ultraviolet radiation : The phenomenon of tanning on exposure to sunlight results from an enhanced tyrosinose activity in the melanocytes that leads to the formation of new melanin.

The pigmentation of the skin protects the underlying tissues against the potentially harmful effects of ultraviolet radiation. Melanocytes which are differentiated from neural crest cells seem to play a critical role in the determination of color and related racial differences. Since, the number of melanocytes is approximately the same in all human races, racial differences in color are attributable to differences in the activity of these cells (10).

d) Effects of temperature : Increased basal metabolic rate in races living near the Pole resulted mainly from an enhanced thyroid acitivity. Epinephrine also seems to be involved in the changes of metabolic rate (9). Since basal metabolic rate is regularly related to body surface area; difference in body shape will also be a passive mode of temperature buffering (22). It seems that stature and body proportion differences between populations are resulted at least in part from different average temperature levels in the world and thyroid hormones and androgens seem to be involved in the determination of body build : In humans, there are two periods of rapid growth, the first in infancy and the second in late puberty just before growth stops. The contributions of hormones to growth are shown diagrammatically in Figure 2. The first period of accelerated growth is partly a continuation of the fetal growth under the effect of thyroid hormones (9). Growth velocity in this period is different between populations (11, 18, 21), but population differences in thyroid activity do not seem to correlate with thyrotropin levels (3, 17, 28, 32, 33). On the other hand, second growth spurt occurs at the time of puberty under the anabolic effect of androgens, but

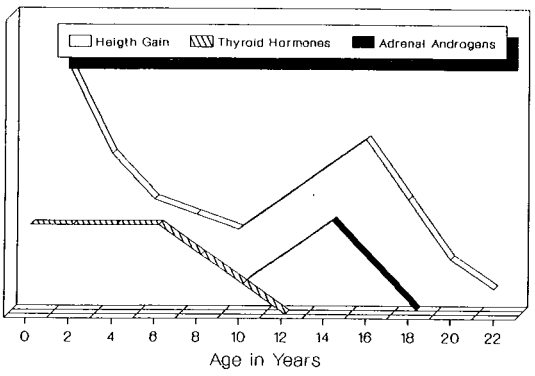

Fig - 2 : Contributions of hormones to growth spurt periods. First and second accelerated growths are due to thyroid hormones and adrenal androgens respectively (Modified after Ganong, 1989).

this increase occurs without any change in the secretion of cortisol or ACTH. Furthermore, the growth hormone is secreted in a steady state until puberty and between population differences do not seem to be present in growth hormone levels. As an example, African pygmies, shortest people in the world have normal plasma growth hormone and somatomedin levels before puberty, but they show no pubertal growth spurt (9).

Although thyroid hormones and androgens seem to be responsible for the stature and body proportion differences; it has not been understood yet where the ontogenetic control comes from. Here we suggest in the light of neural crest derivatives and with the help of literature data that it comes from parafollicular cells for the thyroid hormones; and from adrenal medulla for the androgens. We know that both the parafollicular cells and the adrenal medulla are derived from neural crest. Following considerations will make it appear likely : Changes in thyroid hormone levels following ambient temperature changes seem to be the result of a balance between central and peripheral control mechanisms. In warm-blooded animals, parafollicular cells seem to be peripheral structures controlling the thyroid gland activity (15, 23). The presence of biogenic amines in some parafollicular cells has led to the hypothesis that they communicate with follicular cells by means of chemical signals. The storage of serotonin with calcitonin may ensure that both hormones would be released together, on appropriate stimulation, by exocytosis. One, calcitonin, might be destined to act on a distant target, bone; the other, serotonin, might be destined to act locally on follicular cells (26). The biological significance of the spatial integration of follicular and parafollicular cells, which, in lower vertebrates remain separate, then seems to be a functional coordination of both epithelial cell lines. This fusion must facilitate the adaptation of the follicular cells to environmental changes (especially temperature changes). Therefore, it is reasonable to accept that with their ontogenetic control on follicular cells, parafollicular cells play a certain role in the determination of thyroid activity and consequent body proportion differences between populations. As for the calcitonin of the parafollicular cells, its exact physiologic role is uncertain. We suggest that it may be responsible for the population differences in calcium and phosphorus metabolism, since osteoporosis is particularly a disease of white, postmenopausal women, and white women were found to have the

lowest calcitonin levels when compared to other races (37).

At the time of puberty, the increase in the secretion of adrenal androgens occurs without any change in the secretion of cortisol or ACTH and secretion of the adrenal androgens is not controlled by gonadotropins (9). We have found histologic evidence for a possible physiological interaction between the adrenal medulla and cortical zona reticularis from where androgens are secreted. The boundary between them is usually irregular with columns of cortical cells projecting some distance into the medulla (7) and adrenal medullary cells were reported to stimulate the cortical cells in a paracrine way (4). This relationship may provide the adrenal medulla to control the pubertal growth spurt pattern by way of adrenal androgens.

Thyroid hormones and adrenal androgens seem to have some additional effects which result in racial characteristics. Since thyroid hormones are necessary for hepatic conversion of carotene to vitamin A; the accumulation of carotene in the bloodstream (carotenemia) in peoples with low thyroid activity seems to be responsible for the yellowish tint of the skin. The adrenal androgens androstenedione and dehydroepiandrosterone are known to determine the hair form and body hair distribution (9).

e) Blood pressure : The carotid sinus and aortic arch receptors which are the derivatives of the neural crest are stimulated by distension of the structures in which they are located, and so they discharge at an increased rate when the pressure in these structures rises. In chronic hypertension, this baroreceptor reflex mechanism is "reset" to maintain an elevated rather than a normal blood pressure (9). Population differences in blood pressure may be attributable to different functional levels in these receptors. Aortopulmonary septum another crest derivative may also be involved in the pathogenesis of hypertension.

f) Neural mechanisms : Peripheral nervous system which also forms from neural crest seems to be involved in adaptive changes and consequently in several racial differences (1, 5, 13). For example, the intestine is capable of adapting to a variety of physiological and pathological challenges; and sympathectomy or vagotomy abolish its adaptive mechanisms (8). A racial difference was also reported to be present in symphathetic nervous system-mediated energy expenditure (30). Population differences in lactose intolerance may also be attributable to the functional differences in enteric nervous system which is a part of peripheral nervous system.

CONCLUSION AND FUTURE CONSIDERATIONS

It seems that environmental factors affect exclusively neural crest derivatives some of which in turn control certain secondary structures ontogenetically. Resulted characteristics would then bring out the races. These interactions are summarized in Table 2. There may be additional environmental

Environmental Factors	**Involved crest derivatives**	**Secondary contributions**	**Resulted racial differences**
UV rays	Pigment cells		Pigmentation
Climate Chewing	Head mesenchyme		Craniofacial morpohogy
Climate Nutrition Altitude	Peripheral nervous system		Autonomic and sensory functions
Temperature	Adrenal medulla	Cortical hormones	BMR *, Hair Stature
Temperature	C cells	Thyroid hormones	BMR, Proportions Bone metabolism
?	Baroreceptors Chemoreceptors APS #		Blood pressure?
Heat (Shipman 1991)	Leptomeninges		Cranial volume?

* BMR : Basal metabolic rate
\# APS : Aortopulmonary septum

Table 2 : Possible mechanisms leading to races (Adapted from several sources).

factors affecting the organisms and additional secondary factors leading to racial differences.

In conclusion, biological adaptation seems to be limited to those structures of neural crest origin and biological significance of some neural crest derivatives especially aortopulmonary septum, adrenal medulla, and leptomeninges remains to be established.

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