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EDITORIAL COMMENT

Genetic predisposition for essential hypertension, based on studies of genetic polymorphisms in modern global human populations: The perspective of evolutionary biology

Perspetivas de biologia evolutiva da predisposição genética para hipertensão arterial essencial, estudada com base em polimorfismos genéticos nas atuais populações humanas globais

Manuel Bicho

Laboratório de Genética e Instituto de Saúde Ambiental (ISAMB) da Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal

The article by Sousa et al. in this issue of the *Journal*[1] raises several interesting questions related to the association of the C825T polymorphism of the *GNB3* gene, which codes for the beta 3 subunit of G proteins (responsible for the transduction of messages resulting from activation of G protein-coupled receptors), with hypertension and cardiovascular risk.

The first question concerns differences in susceptibility to essential hypertension in modern human populations that result from the natural selection of genes over the last 30 000 years associated with environmental factors during the global expansion of humanity after ancestral populations left Africa, as described in an important article by Young et al.[2] The factors acting at that time were temperature and humidity, inversely related to latitude in Africa, which activated compensatory adaptive hypertensive mechanisms secondary to decreased volume-dependent blood pressure associated with severe loss of sodium chloride by sweating. Young et al.[2] identified several polymorphic variants of five genes encoding proteins involved in these compensatory mechanisms of volume change and vascular reactivity secondary to salt loss. The genetic variant most strongly associated with current global variation in susceptibility to hypertension is the C825T polymorphism of the *GNB3* gene. The frequency distribution of genetic variants associated with adaptive mechanisms, especially the one analyzed by Sousa et al., is independent of the continent where they occur, as shown by the similarity of their distribution in Native Americans of the equatorial zones to that of modern African populations. We performed a study[3] of the Hp1 polymorphic variant (only found in humans) of haptoglobin, an acute phase protein that for more than 30 years has been associated with higher blood pressure sensitivity to sodium.

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E-mail address: manuelbicho@fm.ul.pt

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In this work we found very similar allelic frequencies of the *HP* gene in Honduras (Central America) and in Mozambique (Africa). These countries are at similar latitudes, although in the case of Native American populations the adaptations occurred over the course of less than 20 000 years. This is the result of movements in Eurasia, in the opposite direction (north to south) to the initial movement subsequent to the departure from Africa of the original populations in which these gene variants were initially fixed.

With regard to the same Hp allele, we published a paper in the *Journal* in 2000,[4] the results of which showed a different nocturnal blood pressure response in salt-sensitive hypertensive individuals, compared to normotensive and non-sensitive individuals, after a change of diet from low to high sodium. The Hp1-1 allele was found in 100% of both normotensive and hypertensive salt-sensitive subjects. In this study we also showed that in urban settings in modern African populations, these individuals have increased cardiovascular risk, even compared to those in the current African diaspora, which confirms the epidemiological transition of these populations with respect to the original ones 50 years ago.

As further evidence of the effect of these ancestral gene variants, the work by Sousa et al. shows that the risk for obesity conferred by the 825T allele of the *GNB3* gene in Madeira, also demonstrated in other populations, is associated with a higher risk of essential hypertension.[5] The frequency of this morbid allele is higher in hypertensive patients than in controls in the population of the Madeira archipelago, in contrast to those found in a larger population (the PHYSA study) on the mainland.[6,7] Regardless of the differences in sampling methods between these two studies, the explanation for the association of this variant with hypertension on this Portuguese island, which is not observed on the mainland, probably lies in the fact that the Madeira population is a genetic isolate in which the effect of stratification of these genes is likely to be maximized, despite its common ethnic origins with mainland populations.[8]

Conflicts of interest

The author has no conflicts of interest to declare.

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