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What makes a champion? Explaining variation in human athletic performance☆

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Abstract

Variation in human athletic performance is determined by a complex interaction of socio-cultural, psychological, and proximate physiological factors. Human physiological trait variance has both an environmental and genetic basis, although the classic gene–environment dichotomy is clearly too simplistic to understand the full range of variation for most proximate determinants of athletic performance, e.g., body composition. In other words, gene and environment interact, not just over the short term, but also over the lifetime of an individual with permanent effects on the adult phenotype. To further complicate matters, gene and environment may also be correlated. That is, genetically gifted individuals may be identified as children and begin training pulmonary, cardiovascular, and muscle systems at an early critical age. This review covers evidence in support of a genetic basis to human athletic performance, with some emphasis on the recent explosion of candidate gene studies. In addition, the review covers environmental influences on athletic performance with an emphasis on irreversible environmental effects, i.e., developmental effects that may accrue during critical periods of development either before conception (epigenetic effects), during fetal life (fetal programming), or during childhood and adolescence. Throughout, we emphasize the importance of gene–environment interaction (G × E) as a means of understanding variation in human physiological performance and we promote studies that integrate genomics with developmental biology.

Keywords: Gene and environment effects on sports peformance; Gene–environment interaction; Complex traits; Polymorphism; Developmental effects; Fetal programming; Genomics

1. Introduction

Having recently won the Tour de France for a record seventh consecutive year, Lance Armstrong is without a doubt the greatest cyclist of his generation. His performance may come close to a theoretical ceiling of human metabolic potential (for Tour

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de France riders see Hammond and Diamond, 1997), and indeed many athletes in various disciplines may be pushing up against the limits of what is possible. How do such exceptional athletes arise? In an even broader sense, how do we explain the full range of human athletic ability, from forgettable to incredible? For elite athletes, a reasonable hypothesis is that they possess a fortuitous combination of genes that are either necessary or sufficient to produce their athletic phenotype. However, an equally important consideration is lifelong experience, from early intrauterine exposures to the advanced training techniques employed by professionals. In other words, to understand human variation in performance it is necessary to consider both gene *and* environment (main effects), but also gene–environment interactions ($G \times E$, where the effect of one factor depends on the level of the other factor), and gene–environment correlations. The latter, gene–environment correlation, is not necessarily a trivial issue when it is considered that children tend to gravitate- or are urged towards -athletic disciplines in which they show an early aptitude. Exactly how the totality of such processes account for inter-individual variation in athletic performance is largely unknown. In particular, the process of $G \times E$ acting over a lifetime may be the key to understanding much of human complex trait variability. In this regard, we review evidence in support of a genetic basis for human athletic performance, but we also review the emerging literature that shows lasting effects of environmental experience, particularly early in-utero experience, on the adult athletic performance phenotype. Neither topic is reviewed exhaustively, but rather the overarching purpose of the paper is to draw attention to a new direction in exercise physiology (variation in human performance) which demands an integrative research approach, i.e., simultaneous consideration of gene and environment effects.

2. Genetics and human physical performance

"Champions, they are naturally selected. They begin at their own level, and Lance was at that level, for sure." -Dr. Michele Ferrari, commenting on the first time he conducted physiological tests on a young Lance Armstrong (Coyle, 2005).

The genetic basis of human athletic performance has been reviewed previously and readers are referred to a number of excellent papers and volumes that treat this topic in detail (Bouchard and Malina, 1983; Bouchard et al., 1997; Patel and Greydanus, 2002; Myburgh, 2003; Rupert, 2003; Heck et al., 2004; Macarthur and North, 2005). Three introductory points are worth making. First, the cumulative evidence, going back more than one century, is all but overwhelming in support of the general idea that genes are responsible for some of the variation in human athletic performance. The sub-sections below detailing this evidence are organized by methodological approach including quantitative genetics and segregation analysis, linkage analysis, and candidate gene studies. The second point is that despite the obvious role of genetics in human physical performance, there is little unequivocal evidence in support of a specific genetic variant with a major gene effect on a relevant performance phenotype, at least across the normal range of human trait distributions. This may be because complex traits are fundamentally polygenic (many genes with small effects), or because researchers have failed to take into consideration the full range of environmental effects, or both. Third, there has been a recent explosion of interest in the genetic basis of human athletic performance paralleling the development of new and accessible genotyping and DNA sequencing technologies. This growth of interest is well documented in the yearly human gene map for performance and health-related fitness phenotypes which was first published in 2001 and which is now in its fifth iteration (Rankinen et al., 2001b, 2002b, 2004; Perusse et al., 2003; Wolfarth et al., 2005). The number of yearly publications identifying genes, genetic markers, or chromosomal regions in the context of human athletic performance has increased dramatically since the early 1990s, as shown in Fig. 1.

2.1. Quantitative genetics and segregation analysis

The analysis of quantitative traits in family based studies provided the first direct evidence of a genetic basis for human athletic ability. The theoretical and mathematical foundations of this discipline were established at the beginning of the 20th century by plant and animal breeders with two major goals: (1) to infer the amount and nature of genetic variation *within* a