The BASES Expert Statement on Genetic Research and Testing in Sport and Exercise Science

Produced on behalf of the British Association of Sport and Exercise Sciences by Dr Alun Williams, Prof Andy Miah, Prof Roger Harris, Prof Hugh Montgomery and Dr Henning Wackerhage

Introduction

Differences in the DNA sequence between humans are responsible for much of the variation in sport- and exercise-related traits. For example, the heritability (the proportion of phenotypic variation in a population which is due to inter-individual genetic variation) may be as high as 50% for maximal oxygen uptake ($\dot{V}O_{2max}$) (Bouchard *et al*., 1998) and its trainability (Bouchard *et al*., 1999). However, we know comparatively little about the molecular variations in the DNA sequence that add up to the often 50% or more estimated heritability for major sport- and exercise-related traits such as cardiovascular fitness, strength, maximal-intensity exercise ability and muscle fibre composition (reviewed in Hagberg *et al*., 2011), although the science is progressing. Consequently, an era where genetic testing in sport and exercise contexts becomes commonplace is approaching, and this raises several ethical concerns. This statement summarises an original BASES position stand on this topic (Williams *et al*., 2007).

Background and evidence

Scientific progress

Sport and exercise genetics (also referred to as athleticogenomics or kinesiogenomics) remains in its infancy, with a requirement for greater replication of the hundreds of genotype-phenotype associations reported to date (Hagberg *et al*., 2011). Examples of promising but still contested associations between genetic variants and aspects of exercise performance include an insertion/deletion (I/D) polymorphism in the *ACE* gene associated with the training-responsiveness of oxygen uptake during exercise, a single nucleotide polymorphism (SNP) in the *ACTN3* gene associated with sprint performance and a SNP in the *HIF1A* gene associated with endurance performance.

Those polymorphisms identified to date account, individually, for only a small proportion of the inter-individual variability in phenotype. To explain a larger proportion of the variability requires either the identification of rare variants of large effect or favourable combinations of many common variants. Evidence for rare variants of large effect is currently limited to one or two mutations such as those in the myostatin and erythropoietin receptor genes. However, using 6-10 common variants, elite athletes in certain sports have been shown to differ in polygenic profile from non-athletes and from elite athletes in other sports (e.g., Ahmetov *et al*., 2009) and such differences will become clearer as larger panels of appropriate variants are included. It is estimated that if more than ~15-20 common variants contribute to sporting ability (most scientists suspect it is many more), then more genetic potential exists in the human species than is ever likely to manifest itself in one individual (Williams & Folland, 2008).

Recently, 21 SNPs were identified that appear to capture the heritable component (approximately 50% of total inter-individual variability) of the response of $\dot{V}O_{2max}$ to endurance training (Bouchard *et al.,* 2011). While this observation needs replication, it shows great promise for increasing the ability to predict individual responses to exercise training in advance - something that has been desirable but, until now, impossible. One could envisage GPs (and indeed health care trusts) using genetic tests to predict changes in $\dot{V}O_{2max}$, systolic blood pressure or fasting blood glucose of a patient in response to an exercise programme. Such information could be used to place greater emphasis on exercise for those likely to respond and on drugs for those less likely to respond to exercise training. Similarly, one could envisage care strategies (exercise training and pharmaceuticals) for the maintenance of muscle mass and function during ageing being informed by a prediction of training responsiveness based on genetic information. Sport and exercise scientists should seek to generate sufficient evidence to determine whether a "personalised medicine" or "exercise for all" approach (or some combination of the two) is the most effective strategy to prevent and treat disease.

Ethical concerns

Human genetic research requires ethics committee approval and must comply with the World Medical Association's Declaration of Helsinki. Recommendations of bodies such as the Human Genetics Commission should also be followed. We conclude that the ethical concerns about genetic research itself are relatively small because of the scrutiny imposed by ethics committees and other bodies.

One specific aspect of genetic research in the sport and exercise sciences that is potentially problematic is the investigation of inter-racial differences. Some scientists are fascinated by the remarkable success of East African endurance athletes and of sprinters of West African descent, and this has stimulated research aimed at identifying the reasons for this success. However, using molecular genetic methods in these efforts might inadvertently help others perpetuate racial stereotypes about race, performance and intelligence, and some people reject genetic research where ethnic groups are compared for this reason. Yet some ethnic groups are underrepresented in clinical trials, despite suffering more from some diseases. Thus, there are both advantages and disadvantages for investigating genetic differences between ethnic groups.

Looking beyond research *per se*, towards an era where our understanding of the role of genetics in sport and exercise is greater than now, there are various applications that raise ethical concerns. In sport, for genetic performance tests to be treated differently from more traditional physiological tests requires the identification of fundamental differences between traditional and genetic performance tests. This reflects the "genetics exceptionalism" concept, concerning whether genetic testing or data are special and thus require bespoke regulation. Genetic and traditional performance tests are similar in many ways, but we see two important differences. The first is that unexpected, major disease associations are more likely to be discovered after a genetic test has been conducted than after a traditional performance test. Genetic counselling before a genetic test can help to prepare an individual for the potential implications of such findings. The second difference is that genetic tests (i.e., tests of DNA sequence) can be carried out as soon as genomic DNA can be obtained; in sharp contrast to a traditional performance test, a genetic performance test conducted on an embryo will yield the same information as

Left: Eero Mantyranta, multiple Olympic medal winner, had a rare mutation in his EPOR gene

a genetic test performed on an adult. Consent cannot be obtained from embryos or very young children.

Many forms of sport and exercise are effective at improving health, yet some activities increase the risk of injury, disease or sudden death, and there is a genetic component to those risks. Thus, it is foreseeable that genetic tests will be developed to stratify this risk. For example, genetic tests could be used to make choices about an athletic career by judging injury risk, to determine insurance costs or coverage for sports participation, to help a sports club decide whether or not to employ an athlete, or to assist the individualisation of care for an at-risk or injured athlete. Genetic testing may play an important role in pre-participation screening and reduce the incidence of sudden death in sport. Simultaneously, problems might arise because of difficulties keeping genetic test results confidential, especially those of high-profile athletes. A conflict of interest could occur between clubs and athletes and some healthy athletes might erroneously be prevented from competing because genetic tests of future poor health or injury are unlikely to achieve 100% predictive accuracy.

Conclusions and recommendations

The future of sport and exercise science will become increasingly focused on genetic research and testing as the relevant molecular technologies become faster, cheaper and more widely available (Lander, 2011). Sport and exercise scientists need to ensure that they keep abreast with genomic science to capitalise on recent and anticipated findings in an ethically acceptable manner. It is recommended that:

- Sport and exercise scientists should maintain their awareness of potential unwanted consequences of genetic information and of the potential misuse of genetic data to justify discriminatory views or practices. Sport and exercise scientists should engage knowledgeably in public debates to minimise those risks.
- Genetic testing in the sport and exercise context (with the possible exception of pre-participation risk screening) should only be conducted on mature individuals who fully understand the relevant issues and a system of counselling should be introduced.
- Pre-participation risk screening should not be obligatory and the confidentiality of such testing has to be ensured.
- Sport and exercise scientists should be aware of the risk that a prominent "individualised medicine" public narrative could undermine the more general advice given to large population groups regarding the value of exercise and other lifestyle factors in disease prevention and treatment.
- Genetic testing should be used in the fight against doping in sport where appropriate, to link biological samples to athletes, test claims that a genetic mutation was responsible for a positive doping test or unusual biochemical data, and test for gene doping. ■

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