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A response to letter to the editor: A genetic-based algorithm for personalized resistance training

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COMMENT

Following the recent publication of our paper, "A genetic-based algorithm for personalized resistance training" [1], we read with interest the recent Letter from Karanikolou et al. [2] discussing the proposed limitations within our study.

First, to clarify a point; the Authors of the Letter say: "Based on this derived power/endurance score, subjects were assigned to either an endurance or power genotype training group involving low-intensity or high-intensity resistance training, respectively". This is incorrect, the subjects were assigned the power or endurance training protocol randomly in a double blind study, so that neither athletes nor trainers knew the outcome of the 'power/endurance' (P/E) algorithm until they were revealed after all the training and tests were complete.

It is apparent that there is some confusion in the Letter as to what the aim of this study was. It was a training intervention study; the intervention in this case being the use of a specific algorithm. This was not a genetic association (observational) study and we tested only one hypothesis; that is, genetically matched athletes (i.e. high-intensity trained with power genotype or low-intensity trained with endurance genotype) show greater improvements in performance tests in response to high- or low-intensity resistance training compared to genetically mismatched athletes (i.e. high-intensity trained with endurance genotype or low-intensity trained with power genotype). The genetic associations for five specific genetic markers listed in our paper were for information only and they were not the main results, since we used a panel of 15 gene polymorphisms previously reported to be individually associated with physical performance and muscle-specific traits in more than two studies. Given the fact that each contributing gene can explain only a small portion of the observed inter-individual differences in training-induced effects, we used a polygenic (P/E) score to reveal an effect on training responses.

There are key differences between our intervention study and gene-association studies:

Intervention studies

- The primary goal of intervention studies is to test the efficacy of specific actions (training, treatments or preventive measures) by assigning individual subjects to one of two or more action options.
- Generally involves less than 100 participants due to the complexity of methodology (longitudinal, multiple testing, possible dropping out, high cost);
- Each participant is known, with personal interaction and current and accurate biophysical data;
- Each participant followed the training as designed;
- The measurements are very precise and accurate;
- It is double blind and prospective.

Gene-association studies

The primary goal of gene-association (observational) studies (e.g., case-control studies and cohort studies), is to test hypotheses about the genetic determinants of the trait (disease, athletic performance etc.);

- Generally involves more than 200 participants (and, ideally, more than 5000);
- Not blind at all;
- Retrospective study.

The 67 subjects that comprised our paper are similar to that of other training intervention studies. As an example, Helgerud et al. [3] recruited 40 moderately trained subjects in their important study examining the effectiveness of aerobic training interventions. One of the initial studies on the effectiveness of high-intensity intermittent training, by Tabata et al. [4], used 14 subjects and then another 9 participants [5]. These are all highly cited papers and have been used to guide training worldwide ever since. Even studies using genetics to explain differences in muscle phenotype following strength training have utilised subject numbers similar to ours, such as the 51 subjects in Erksine et al. [6]. The Authors of the Letter state that the sample sizes of our studies were not sufficient, but this appears to be based on gene-association, as opposed to intervention, studies. Based on this, we are satisfied that the number of subjects within our studies is adequate, although we accept that higher subject numbers are always desirable.

There also appears to be confusion regarding what the DNAFit Peak Performance Algorithm can be used for. Throughout their letter, the authors mention that genes cannot be used to predict elite sporting performance, which is not suggested at all by us within our paper. We fully agree with Webborn et al. [7] that current genetic tests cannot be used to predict sporting performance and predict talent identification. We also agree that there is a lack of scientific evidence as to the predictive value of genetic tests, direct-to-consumer or otherwise, for the prescription of exercise training programmes, which is precisely why our paper is required. When coming from a place of low evidence, the only way to increase that evidence is to conduct research and replicate the findings, which was our goal in this particular study. Similarly, we agree that further studies with replication are required, and we are currently conducting such research using a genome-wide association study (GWAS) approach.

The Letter authors also claim that a number of the gene polymorphisms used in our paper have not been sufficiently replicated. They point to *TRHR* rs16892496 as an example, which was associated with lean body mass in a GWAS comprised of three independent populations, including 7,415 subjects, by Liu et al. [8]. In more detail it comprised 3 separate studies (not simple „replication attempts"): discovery and replication, and two further replication cohorts including both Caucasians and Chinese [8]. In a more recent study, Miyamoto-Mikami et al. [9] have shown that the rs7832552 in *TRHR* (which is in complete linkage disequilibrium with rs16892496) was associated with sprint/power athlete status. A second SNP, rs1205 in *CRP*, was also questioned. Obisesan et al. [10] reported that this SNP affected baseline C-reactive protein (CRP) levels. Furthermore, Lin et al. [11] have shown that rs1205 had influence on raising CRP levels and reducing handgrip strength. Both Kullo et al. [12] and Kuo et al. [13] reported that CRP levels were inversely associated with VO_2max. As such, we feel comfortable that these SNPs have the required evidence required for their inclusion within the algorithm studied.

As the research in the field of sports and exercise genetics continues, coaches and athletes alike will become increasingly interested. The opportunity for improving exercise training outcomes for non-athletes is also important, especially given the high levels of sedentary behaviour, obesity, and cardio-metabolic issues seen in a high number of populations today. It is our belief that researchers should try to make the results of the body of research usable to the real world. Given the progression of genetic research from twin studies to association studies and GWAS, we believe that intervention studies are required in order to translate research findings into a practical application, and the time for that research is upon us. Whilst we accept that our study does have limitations, we also feel that it is an important step on that journey.

Conflict of interests: the authors declared no conflict of interests regarding the publication of this manuscript.

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