INTRODUCTION

Resistance exercise training is widely used to enhance general fitness and athletic potential/capacity across many sporting disciplines including power, strength and endurance events [1, 2]. When properly performed and combined with adequate nutrition, resistance training leads to increases in strength, power, speed, muscle size, local muscular endurance, coordination, and flexibility and reductions in body fat and blood pressure [3].

Effective resistance exercise prescription involves manipulation of several variables specific to the targeted goals, such as intensity or load per repetition (i.e. percentage of one repetition maximum (1 RM)), volume (total number of sets and repetitions), training frequency, muscle action (concentric vs. eccentric), rest intervals between sets, repetition velocity and others [3, 4]. Furthermore, resistance training can be categorized into two common types: low-intensity (~30% of 1 RM and high repetitions) and high-intensity (~70% of 1 RM and low repetitions) resistance training. Low-intensity resistance training (also known as classic strength training) leads to in-
creases in absolute strength [3] and the hypertrophy of all types of muscle fibres [10, 11].

There is a large variability in both muscle size and strength gains in response to resistance training between individuals [4]. In a large study of 585 subjects, Hubal et al. [12] have shown that men and women exhibited wide ranges of strength gain (1 RM: 0 to +250%) and skeletal muscle hypertrophy (cross-sectional area: -2 to +59%) in response to 12 weeks of resistance training, indicating individual training responses may vary widely dependent on factors such as genetic heritage. Accordingly, the level of adaptation experienced by each individual will be dependent on the interaction between specific training performed and genotype. Indeed, there is a general consensus that resistance training programs should be individualized, but little information exists to accurately discern how best to personalize training program design to maximize outcomes [3, 4, 12, 13].

Muscle fiber composition is a heritable (~45%) trait [14], with large variability between individuals. For example, slow-twitch (Type I) content of vastus lateralis ranges from 5-90%. This variability, in turn, may determine individual’s potential to perform different types of resistance training. Accordingly, data show that Type I muscle

TABLE 1. List of genetic variants analysed by DNAFit Peak Performance Algorithm™

| Gene          | Full name                                                                 | Functions and associated phenotypes                                                                 | Polymorphism                        | Endurance or power related allele | References |
|---------------|---------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|-------------------------------------|----------------------------------|------------|
| ACE           | Angiotensin I converting enzyme                                            | Regulates circulatory homeostasis through the synthesis of vasoconstrictor angiotensin II and the degradation of vasodilator kinins. | Alu IVD (rs6464994)                 | Endurance: I Power: C            | [20, 21]   |
| ACTN3         | α-actinin-3                                                               | Stabilizes the muscle contractile apparatus in fast-twitch muscle fibres.                           | Arg577Ter (rs1815739 C/T)           | Endurance: 577Ter (T) Power: Arg577 (C) | [20, 22] |
| ADRB2         | β-2 adrenoreceptor                                                        | Plays a pivotal role in the regulation of the cardiac, pulmonary, vascular, endocrine and central nervous system. | Gly16Arg (rs1042713 G/A)            | Endurance: 16Arg (A)             | [23, 24]   |
| AGT           | Angiotensinogen                                                           | Angiotensinogen is an essential component of the renin-angiotensin system that regulates vascular resistance and sodium homeostasis, and thus determining blood pressure. | Met235Thr (rs699 T/C)               | Power: 235Thr (C)                | [26, 27]   |
| BDKRB2        | Bradykinin receptor B2                                                    | Involved in the endothelium-dependent vasodilation                                                 | rs1799722 C/T                       | Endurance: T                     | [24]       |
| COL5A1        | Collagen, type V, α1                                                      | Encodes the pro-α1 chain of type V collagen, the rate-limiting component of the of type V collagen trimer assembly. | rs12722 C/T (BaiUI)                 | Endurance: T                     | [28, 29]   |
| CRP           | C-reactive protein, pentraxin-related                                     | Involved in several host defense related functions based on its ability to recognize damaged cells and to initiate their elimination in the blood. | rs1205 A/G                          | Endurance: A                    | [30, 31]   |
| GASHBP1 (NRF2) | GA binding protein transcription factor, β subunit 1 (nuclear respiratory factor 2) | Encodes a transcriptional regulator of genes involved in activation of cytochrome oxidase expression and nuclear control of mitochondrial function. | rs7181866 A/G                      | Endurance: G                    | [32, 33]   |
| IL6           | Interleukin-6                                                             | IL-6 is a pleiotropic cytokine expressed in immune and muscle cells. Involved in a wide variety of biological functions, including regulation of differentiation, proliferation and survival of target cells. | -174 C/G (rs1800795)               | Power: G                        | [34, 35]   |
| PPARA         | Peroxisome proliferator-activated receptor                               | Regulates liver, heart and skeletal muscle lipid metabolism, glucose homeostasis, mitochondrial biogenesis, cardiac hypertrophy. | rs4253778 G/C                       | Endurance: G Power: C           | [36, 37]   |
| PPARA1        | Peroxisome proliferator-activated receptor γ coactivator 1 α             | Regulates fatty acid oxidation, glucose utilization, mitochondrial biogenesis, thermogenesis, angiogenesis, formation of muscle fibers. | Gly482Ser (rs8192678 G/A)          | Endurance: Gly482 (G) Power: C   | [38, 39]   |
| TRHR          | Thyrotropin-releasing hormone receptor                                    | Stimulates the release of thyroxine, which is important in developing skeletal muscle.             | rs16882496 A/G                      | Power (muscle mass): C           | [40]       |
| VDR           | Vitamin D receptor                                                       | Involved in sustaining normocalcemia by inhibiting the production of parathyroid hormone and has effects on bone and skeletal muscle biology. | Bsm1 A/G (rs1544410)               | Power: A                        | [41, 42]   |
| VEGFA         | Vascular endothelial growth factor A growth factor active in angiogenesis, vasculogenesis and endothelial cell growth. |                                                                                                      | rs2010963 G/C                       | Endurance: C                    | [43, 44]   |
fibres have high resistance to fatigue and are thus suited for low-intensity resistance or aerobic (endurance) training. IIA fibres are better suited for medium-term anaerobic exercise, and type IIX fibres are adapted for high-intensity (power and strength) exercise [8, 13, 15]. It should be noted that although muscle fibre composition is an informative biomarker, muscle biopsies are highly invasive. Subsequently, the potential value of non-invasive exercise prescription tools, such as genetic profiling, seems worthy of investigation.

Association studies have linked dozens of genetic variants to training responses and sport-related traits, such as strength, skeletal muscle mass, recovery ability and muscle fibre composition [16-19]. However, no intervention studies prescribing training on the basis of a genetic profile of athletes have been carried out. Here we evaluate an algorithm that facilitates training prescription by using a panel of 15 gene polymorphisms associated with physical performance and muscle-specific traits to predict an athlete’s potential for development of power and/or endurance qualities (Table 1). These polymorphisms are located within the genes involved in the regulation of muscle fibre type composition and muscle size, cytoskeletal function, muscle damage protection, metabolism, circulatory homeostasis, mitochondrial biogenesis, thermogenesis and angiogenesis.

The aim of the present work therefore was to test, in two independent studies, the hypothesis that genetically matched athletes (i.e. high-intensity trained with power genotype or low-intensity trained with endurance genotype) show greater improvements in explosive power (countermovement jump) and aerobic fitness (aerobic 3-min cycle test) in response to high- or low-intensity resistance training compared to mismatched athletes (i.e. high-intensity trained with endurance genotype or low-intensity trained with power genotype).

MATERIALS AND METHODS

Study participants. In Study 1, 55 Caucasian male University athletes, all aged 18-20 years, volunteered for the study, and 28 of them (height 180.7 ± 1.5 cm, weight 77.0 ± 2.1 kg) successfully completed it (27 athletes had not completed all aspects of the study due to either injury or illness). Each participant was a member of first or second team, actively competing in British Universities and Colleges Sports (BUCS) leagues. The athletes competed in squash (n = 1), swimming (n = 7), running (n = 1), ski/snowboard (n = 4), soccer (n = 1), lacrosse (n = 2), badminton (n = 1), motorsport (n = 1), cycling (n = 4), cricket (n = 2), volleyball (n = 1), fencing (n = 1) and rugby union (n = 2).

In study 2, 68 male soccer players, all aged 16-19 years, volunteered to participate in the study, and 39 of them (height 176.1 ± 1.0 cm, weight 68.9 ± 1.5 kg) successfully completed it (29 participants were withdrawn from the study due to non-adherence of set training volumes over the 8 weeks, or injury). Each subject was a member of college soccer academy who actively competed in BUCS leagues.

Physiological measurements

All participants undertook a pre- and post-test measure of explosive power and aerobic fitness (endurance performance); namely, a countermovement jump (CMJ) and Aerobic 3-min Cycle test (Aero3), using an Optojump (Microgate, Italia) and Wattbike Pro (Wattbike, Not-

Ethical approval

The two-stage study was approved by the University of Central Lancashire Ethics Committee according to the Declaration of Helsinki. Each participant gave written informed consent after procedures were fully explained. Each participant was free to withdraw from the studies at anytime.

Study design

Study design utilised a time series trial as explained by Batterham and Hopkins [45]. Participants of both studies were randomly allocated to an eight-week high- or low-intensity resistance-training program, after undergoing performance tests for both explosive power and endurance. Participants transitioned from their normal training plan to the designed 8-week intervention followed by an eight-week wash-out period. The study was double blinded, in that all were unaware of their ‘genetic potential status’, as determined by the DNAFit Peak Performance Algorithm™. This also included the lead investigator who coached the participants during the 8 weeks of resistance training.

Prior to involvement in the study, all participants had undertaken weekly strength and conditioning programs, supervised by an accredited strength and conditioning coach, for a minimum of six months and maximum of two and half years. These sessions took place in a free weights facility where technique and adherence was closely monitored at all times. Participants engaged in a minimum of one, and maximum of two (preferentially), sessions per week. No other form of resistance training was undertaken during this time, and participants were actively partaking in other sport-specific training sessions and competitive games in parallel to the intervention. The investigator selected the same exercises for both groups: deadlift, pulldowns, front squat to 90 degrees, dumbbell flat press, step ups to medium high box and vertical jump single effort.

Each group self-selected training loads for each session, were monitored for progressive increases in perceived exertion, using a modified Borg scale, and loads were recorded to ensure progression. The only differences between the training programs were volume modifications. The high-intensity resistance training program consisted of ten sets of two reps over the eight-week study. This gave a total volume of one hundred and twenty reps per session. The low-intensity resistance training program consisted of three sets of ten reps for first two weeks, three sets of fifteen reps for the next three weeks and three sets of twenty for the last three weeks. This gave a total volume of one hundred and eighty reps in the first two weeks, two hundred and seventy in the next three weeks and three hundred and sixty reps in the last three weeks.

Association studies have linked dozens of genetic variants to training responses and sport-related traits, such as strength, skeletal muscle mass, recovery ability and muscle fibre composition [16-19]. However, no intervention studies prescribing training on the basis of a genetic profile of athletes have been carried out. Here we evaluate an algorithm that facilitates training prescription by using a panel of 15 gene polymorphisms associated with physical performance and muscle-specific traits to predict an athlete’s potential for development of power and/or endurance qualities (Table 1). These polymorphisms are located within the genes involved in the regulation of muscle fibre type composition and muscle size, cytoskeletal function, muscle damage protection, metabolism, circulatory homeostasis, mitochondrial biogenesis, thermogenesis and angiogenesis.

The aim of the present work therefore was to test, in two independent studies, the hypothesis that genetically matched athletes (i.e. high-intensity trained with power genotype or low-intensity trained with endurance genotype) show greater improvements in explosive power (countermovement jump) and aerobic fitness (aerobic 3-min cycle test) in response to high- or low-intensity resistance training compared to mismatched athletes (i.e. high-intensity trained with endurance genotype or low-intensity trained with power genotype).
tingham, UK), respectively. Participants performed a standardized warm up before every testing session with the CMJ preceding the Aero3. Subjects were requested to arrive for testing in a rested and hydrated state and to refrain from caffeine intake for at least 12 hours before testing. Testing took place on the same time and weekday on each occasion, to ensure a consistent placement within the subject’s usual schedule.

Genotyping

Upon enrollment into study each participant volunteered a saliva sample, which was collected through sterile and self-administered buccal swabs. Samples were sent to iDna Genetics laboratory (Norwich, UK) within thirty-six hours, where analysis of the genes detailed in Table 1 was undertaken. DNA was extracted and purified using the Isohelix Buccalyse DNA extraction kit BEK-50 (Kent, UK). DNA samples were amplified by real-time PCR on an ABI7900 real-time thermocycler (Applied Biosystem, Waltham, USA).

Calculation of power/endurance ratio

Following the analysis, the DNAFit Peak Performance Algorithm™ was used to determine percentage power/endurance score (P/E) ratio, similar to the research conducted by Egorova et al. [46]. Initially, each allele was given a point (0, 1, 2, 3 or 4) depending on the effect of the polymorphism on performance (power/muscle hypertrophy or endurance with respect to response to training). The strength of the rating was based on the evidence from cumulative literature results averaged over time. The total points for the P/E were expressed as a percentage of P/E and then combined to give the balance percentage. A percentage-ranking list was then compiled using this score. Every other participant on the list then undertook high- or low-intensity resistance training. To clarify, someone who is 75% power but does low-intensity resistance training would be doing mismatched genotype training, while a participant rated as 75% endurance that completed low-intensity resistance training would be doing matched genotype training. A threshold for 50% was used as the splitting value in this process.

Statistical analysis

Statistical analysis was conducted in SPSS, Version 20 (Chicago, IL). The required sample size for this study was validated using the Mann-Whitney test. The chi-square test was used to test genotype distributions for deviation from Hardy-Weinberg equilibrium. The non-parametric 2-sample paired test was performed matching “before” and “after” measurements from each individual tested. A 2-sided Mann-Whitney test for 2 independent samples was used to compare gains in CMJ and Aero3 between groups. Differences in phenotypes between different genotype groups were analysed using ANOVA or unpaired t test. Spearman’s (non-parametric) correlations were used to assess the relationships between the genotype score and performance tests. The squared correlation coefficient $R^2$ was used as a measure of explained variance. Bonferroni’s correction for multiple testing was performed by multiplying the P value with the number of tests where appropriate. All data are presented as mean (standard deviation; SD). Statistical significance was set at a P value < 0.05.

RESULTS

Efficiency of different training modalities. All performance parameters increased significantly (<0.001) in response to low- and high-intensity resistance training when the results of two studies were combined. No significant differences in explosive power (CMJ: 5.4 (5.0) vs. 4.6 (6.1)%, $P = 0.547$) and aerobic fitness (Aero3: 4.3 (3.8) vs. 4.3 (3.7)%, $P = 0.711$) gains were observed between low- and high-intensity resistance training groups, indicating that i) both training modalities can be used to improve these performance parameters and ii) results of responses to both training types can be combined for the analysis where appropriate.

Association analysis between genotypes and phenotypes

With some exceptions for the GABPB1 and VDR gene polymorphisms in Study 2 (due to the low sample sizes in terms of population genetics), genotype distributions of 15 gene polymorphisms amongst all athletes of both studies were in Hardy-Weinberg equilibrium (Table 2).

To assess the association between each polymorphism and performance parameters we used the combined data of two studies. After Bonferroni’s correction for multiple testing the results were considered significant with $P < 0.0033$ (i.e. 0.05/15). In accordance with the literature data (Table 1), we found that athletes with the ACE DD ($P > 0.1$ for CMJ, $P > 0.1$ for Aero3), ACTN3 Arg/Arg ($P = 0.065$ for CMJ, $P = 0.0038$ for Aero3), CRP rs1205 GG ($P > 0.1$ for CMJ, $P = 0.0833$ for Aero3), PPARGC1A Ser/Ser ($P = 0.065$ for CMJ, $P = 0.0499$ for Aero3) and VDR AA ($P > 0.1$ for CMJ, $P > 0.1$ for Aero3) polymorphisms demonstrated a tendency to have greater gains in one or two performance tests compared with the opposite genotype carriers after high-intensity resistance training, while the latter (except for the PPARGC1A polymorphism) better responded to the low-intensity training (ACE II: $P > 0.1$ for CMJ, $P = 0.0355$ for Aero3; ACTN3 Ter/Ter: $P > 0.1$ for CMJ, $P > 0.1$ for Aero3; CRP rs1205 AA: $P = 0.0224$ for CMJ, $P > 0.1$ for Aero3; VDR GG (P > 0.1 for CMJ, $P = 0.0311$ for Aero3). No significant differences in CMJ and Aero3 gains were observed between different genotype groups with respect to the other polymorphisms (data not shown). However, given that the latter 10 polymorphisms have recently been reported to be associated with endurance, power and muscle-specific traits, and the fact that each contributing gene can explain only a small portion of the observed interindividual differences in training-induced effects, we felt justified in retaining all 15 genetic markers for further analysis.

Effect of different training modalities and genetic profiles on performance parameters

Based on power/endurance genotype score (see Methods), in two studies we identified 39 athletes (58.2%) with endurance genotype
and 28 athletes (41.8%) with power genotype profiles. Changes in CMJ and Aero3 tests of athletes with predominantly endurance or power genotype profiles from both studies after 8 weeks of low- and high-resistance training are presented in Tables 3 and 4. In both studies it was shown that athletes with endurance genotype profile had greater benefits from the low-intensity resistance training, while athletes with power genotype profile better responded to the high-intensity resistance training. As expected, the outcomes were more prominent in the Study 2 with homogeneous cohort (i.e. soccer players). Furthermore, we found that power genotype score (%) of athletes from both studies was positively correlated with CMJ (r = 0.56; P = 0.0005) and Aero3 (r = 0.39; P = 0.0199) increases (%) in response to high-intensity training, while endurance genotype score (%) was positively correlated with CMJ (r = 0.37; P = 0.0399) and Aero3 (r = 0.51; P = 0.0032) increases (%) in response to low-intensity training, indicating that power genotype score explained 14-32% of the variation in physiological parameters of athletes. In accordance with power/endurance genotype score and training modality, 34 athletes performed matched training (high-intensity training with power genotype (n=15) or low-intensity training with endurance genotype (n=19)), while other 33 athletes completed mismatched training (high-intensity training with endurance genotype (n=20) or low-intensity training with power genotype (n=13)). In study 1, the athletes from the matched group have significantly increased their results in CMJ (P=0.0005) and Aero3 (P=0.0004). On the other hand, athletes from the mismatched group have shown non-significant improvements in CMJ (P=0.175) and less prominent results in Aero3 (P=0.0134) (Table 5). In study 2, soccer players from the matched group have also demonstrated significantly greater (P<0.0001) performance changes in both tests compared to mismatched group (Table 5).

**Determinants of variability in response to resistance training**

With respect to the changes in CMJ gains (%), the athletes from both studies (n = 67) were divided into tertiles: high responders (increase in CMJ from 7.4 to 19.4%; n = 23), moderate responders (increase in CMJ from 3.5 to 17.5%; n = 25), and low responders (increase in CMJ from 0 to 3.5%; n = 19). We found that power/endurance genotype score and training modality, 34 athletes performed matched training (high-intensity training with power genotype (n=15) or low-intensity training with endurance genotype (n=19)), while other 33 athletes completed mismatched training (high-intensity training with endurance genotype (n=20) or low-intensity training with power genotype (n=13)). In study 1, the athletes from the matched group have significantly increased their results in CMJ (P=0.0005) and Aero3 (P=0.0004). On the other hand, athletes from the mismatched group have shown non-significant improvements in CMJ (P=0.175) and less prominent results in Aero3 (P=0.0134) (Table 5). In study 2, soccer players from the matched group have also demonstrated significantly greater (P<0.0001) performance changes in both tests compared to mismatched group (Table 5).

**Determinants of variability in response to resistance training**

With respect to the changes in CMJ gains (%), the athletes from both studies (n = 67) were divided into tertiles: high responders (increase in CMJ from 7.4 to 19.4%; n = 23), moderate responders (increase in CMJ from 3.5 to 17.5%; n = 25), and low responders (increase in CMJ from 0 to 3.5%; n = 19). We found that power/endurance genotype score and training modality, 34 athletes performed matched training (high-intensity training with power genotype (n=15) or low-intensity training with endurance genotype (n=19)), while other 33 athletes completed mismatched training (high-intensity training with endurance genotype (n=20) or low-intensity training with power genotype (n=13)). In study 1, the athletes from the matched group have significantly increased their results in CMJ (P=0.0005) and Aero3 (P=0.0004). On the other hand, athletes from the mismatched group have shown non-significant improvements in CMJ (P=0.175) and less prominent results in Aero3 (P=0.0134) (Table 5). In study 2, soccer players from the matched group have also demonstrated significantly greater (P<0.0001) performance changes in both tests compared to mismatched group (Table 5).

**Determinants of variability in response to resistance training**

With respect to the changes in CMJ gains (%), the athletes from both studies (n = 67) were divided into tertiles: high responders (increase in CMJ from 7.4 to 19.4%; n = 23), moderate responders (increase in CMJ from 3.5 to 17.5%; n = 25), and low responders (increase in CMJ from 0 to 3.5%; n = 19). We found that power/endurance genotype score and training modality, 34 athletes performed matched training (high-intensity training with power genotype (n=15) or low-intensity training with endurance genotype (n=19)), while other 33 athletes completed mismatched training (high-intensity training with endurance genotype (n=20) or low-intensity training with power genotype (n=13)). In study 1, the athletes from the matched group have significantly increased their results in CMJ (P=0.0005) and Aero3 (P=0.0004). On the other hand, athletes from the mismatched group have shown non-significant improvements in CMJ (P=0.175) and less prominent results in Aero3 (P=0.0134) (Table 5). In study 2, soccer players from the matched group have also demonstrated significantly greater (P<0.0001) performance changes in both tests compared to mismatched group (Table 5).
in CMJ from 2.7 to 7.2%; n = 22) and non- or low responders (increase in CMJ from -8.4 to 2.5%; n=22). There was a significant linear trend for the proportion of matched-trained athletes among the high responders (82.6%), moderate responders (50.0%) and non- or low responders (18.2%) ($\chi^2=18.7, P < 0.0001$). Similarly, when considering increases of Aero3 (%), we found a significant linear trend for the proportion of matched-trained athletes among the high responders (86.4%), moderate (increase in Aero3 from 2.0 to 5.9%; n = 23) responders (47.8%) and non- or low (increase in Aero3 from -6.1 to 1.9%; n = 22) responders (18.2%) ($\chi^2=20.5, P < 0.0001$). In other words, among non- or low responders to any type of resistance efficiency training.
training, 82% of athletes (both for CMJ and Aero3) were from the mismatched group, while high responders were predominantly matched athletes (83% and 86% for CMJ and Aero3, respectively; \( P < 0.0001 \) for the comparison between non- or low responders and high responders). Accordingly, after 8 weeks of resistance training the odds of achieving more favorable outcomes in CMJ and Aero3 were 21 and 28.5 times, respectively, greater (\( P < 0.0001 \)) for matched than mismatched genotype training (when first and third tertiles were compared).

**DISCUSSION**

To the best of our knowledge, this is the first study to examine the efficacy of using genetic profiling methods to target training of both power and endurance qualities of athletes. The results of our study demonstrated that all performance parameters increased significantly in response to 8-weeks of either low- or high-intensity resistance training without differences between the two training modalities, however, the magnitude of training effects was strongly related to the association between genetic profile and training modality. Our main finding is that matching individual genotype with the appropriate mode of training led to more substantial resistance training benefits, particularly in the first athletes from the matched group demonstrated significantly enhanced results in explosive power and aerobic fitness responses in response to high-intensity resistance training, which is consistent with previous findings [48-51].

The likely mechanism through which the polygenic profile (i.e. profile composed of 15 polymorphisms) of athletes was associated with training responses could be the link between genetic variations and skeletal muscle characteristics, such as muscle fibre composition.

There was also a positive correlation between power genotype score of athletes and performance changes in response to high-intensity training, as well as a positive correlation between endurance genotype score and increases in performance tests in response to low-intensity training; findings suggesting that the commonly observed heterogeneity in resistance training-induced explosive power and aerobic fitness responses may be partly explained by genetic factors and selected training modalities. Another important finding was that among non- or low responders to resistance training, most athletes were from the mismatched group, while high responders were predominantly matched athletes. These results suggest personalized training prescription based on genetic profiling may help some individuals overcome unresponsiveness to resistance training.

Exercise training response is influenced by a multitude of determinants including genetics, environmental factors, measurement errors and others. Studies suggest that muscle strength and explosive power are under moderate to high genetic control with heritabilities ranging between 30 and 84% [17, 47]. Numerous studies reported the association between individual differences in strength/anaerobic power phenotypes in response to resistance/anaerobic power training and gene variations [16, 17]. Accordingly, several gene polymorphisms in our study were found to be individually linked with training responses. For instance, the II genotype of the ACE and XX (Ter/Ter) genotype of the ACTN3 genes (known as endurance markers) were associated (or tended to correlate) with increases in aerobic fitness in response to low-intensity resistance training, while the ACE DD and ACTN3 RR (Arg/Arg) genotypes (known as power/strength markers) carriers demonstrated greater improvement of performance parameters in response to high-intensity resistance training, which is consistent with previous findings [48-51].

**TABLE 5. Comparisons of CMJ and Aero3 increases (%) in response to resistance training between matched and mismatched groups.**

| Study   | Matched athletes | Group | Mismatched athletes | \( P_1 \) | \( P_2 \) |
|---------|------------------|-------|---------------------|---------|---------|
|         | \( n = 14 \)     | \( P_1 \) (paired test) | \( n = 14 \) | \( P_2 \) (paired test) |
| Change in CMJ, % | 7.8 (5.9) | 0.0005* | 2.9 (7.2) | 0.175 | 0.0596 |
| Change in Aero3, % | 4.0 (3.1) | 0.0004* | 2.8 (4.3) | 0.0134* | 0.2456 |
| Change in CMJ, % | 7.1 (4.1) &lt;0.0001* | 2.4 (3.5) | 0.0053* &lt;0.0001* |
| Change in Aero3, % | 7.7 (2.2) &lt;0.0001* | 1.9 (1.8) | 0.0004* &lt;0.0001* |
| Studies 1 and 2 | \( n = 34 \) | \( n = 33 \) | \( n = 34 \) | \( n = 20 \) | \( n = 19 \) |
| Change in CMJ, % | 7.4 (4.9) &lt;0.0001* | 2.6 (5.3) | 0.0152* &lt;0.0001* |
| Change in Aero3, % | 6.2 (3.2) &lt;0.0001* | 2.3 (3.1) &lt;0.0001* | &lt;0.0001* |

Note: \( *P_1 \) and \( *P_2 < 0.05 \) - significant increases in CMJ and Aero3 (paired test); \( *P_3 < 0.05 \) - significant difference between matched and mismatched groups. Matched athletes - high-intensity trained with endurance genotype or low-intensity trained with power genotype; mismatched athletes - high-intensity trained with power genotype or low-intensity trained with endurance genotype.
The authors declared no conflict of interests.

We have shown that genetically matched nonperiodized training was effective during resistance training program, one might speculate that even in this case the manipulation of training variables is necessary for long-term resistance training progression. Fourth, the results of our study may be applicable only for specific training goals, such as improvement of explosive power and aerobic performance with one of two different modalities. Although loads of < 45% of 1 RM (i.e., performed with very high repetitions) may increase strength in untrained individuals [54], whereas trained weightlifters appear responsive only to heavier loading [55]. Further research analyzing genetic determinants of improvement of absolute strength and skeletal muscle hypertrophy is needed. Finally, in our study we have used a validated panel of a limited number (n=15) of gene polymorphisms associated with power/strength, endurance and other muscle-specific traits, which could explain only 14-32% of the variation in physiological parameters of athletes in our study. Undoubtedly there are likely to be many more genetic variants associated with responses to different modalities of resistance training that remain to be identified. Therefore, it is logical to conclude that the picture we see in the future may become clearer as more genetic markers are included in the panel.

Conclusions

In conclusion, our results suggest that using genetic profiling to better match individual genotype with appropriate training modality may be a powerful tool to aid more personalized, and precise, resistance training prescription in the future.

Acknowledgements

The authors would like to acknowledge the University of Manchester’s Sport Department and Athletic Union as well as the Portsmouth College for the allowing their students/athletes the chance to volunteer as participants in the study. Also thanks must go to all the coaches of DNA Sports Performance Ltd and Suraci Consultancy who took part in data collection and training for the participants. DNAFit™ supported this original research by providing all genetic testing. Finally the authors would also like to acknowledge the hard work and effort of the participants in this study, who without their hours and hours of testing and training these results would have remained hidden from the world.

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

References

1. American College of Sports Medicine. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. Med Sci Sports Exerc. 2009;41(3):687-708.
2. Vikmoen O, Ellegaard S, Traen Ø, Hollan I, Hanestadhaugen M, Raastad T, Rønnestad BR. Strength training improves cycling performance, fractional utilization of VO2 max and cycling economy in female cyclists. Scand J Med Sci Sports. 2015 Apr 18. doi: 10.1111/sms.12468.
3. Kraemer WJ, Ratamess NA. Fundamentals of resistance training: progression and exercise prescription. Med Sci Sports Exerc. 2004;36(4):674-688.
4. McGlory C, Phillips SM. Exercise and the Regulation of Skeletal Muscle.
Hypertrophy. Prog Mol Biol Transl Sci. 2015;135:153-173.
5. Campos GE, Luecke TJ, Wendeln HK, Tomà K, Hagerman FC, Murray TF, Ragg KE, Ratamess NA, Kraemer WJ, Staron RS. Muscular adaptations in response to three different resistance-training regimens: specificity of repetition maximum training zones. Eur J Appl Physiol. 2002;88(1-2):50-60.
6. Wilson GJ, Newton RU, Murphy AJ, Humphries BJ. The optimal training load for the development of dynamic athletic performance. Med Sci Sports Exerc. 1993;25(11):1279-1286.
7. McBride JM, Triplet-McBride T, Davie A, Newton RU. The effect of heavy- vs. light-load jump squats on the development of strength, power, and speed. J Strength Cond Res. 2002;16(1):75-82.
8. Netreba AI, Popov DV, Liubueva EV, Bravly IAR, Prostova AB, Lemesheva IU, Vinogradova OL. Physiological effects of using the low intensity strength training without relaxation in single-joint and multi-joint movements. Ross Fiziol Zh Im I M Sechenova. 2007;93(1):27-38.
9. Mitchell CJ, Churchill-Verneña TA, West DW, Bund NA, Breen L, Baker SK, Phillips SM. Resistance exercise load does not determine training-mediated hypertrophic gains in young men. J Appl Physiol (1985). 2012;113(1):71-77.
10. Fry AC. The role of resistance exercise intensity on muscle fibre adaptations. Sports Med. 2004;34(10):663-679.
11. Kosek DJ, Kim JS, Petrella JK, Cross JM, West DW, Burd NA, Breen L, Baker SK, Newton RU. The effect of heavy- vs. low-intensity strength training regimens: specificity of repetition maximum training zones. Eur J Appl Physiol. 2002;88(1-2):50-60.
12. Saratova OL. Physiological effects of high-intensity strength training in elite Caucasian and East Asian swimmers. Med Sci Sports Exerc. 2013;45(5):892-900.
13. Yang C, Chang CC, Huang AM, Lin YH, Hsieh YL, Hsieh SS, Caporossi D, Pigoffo Z, Hilley A, Lee RE, Sargent GF, Guibin J, Rogozkin VA, Ahmetov II, Yang N, North KN, Ploutarhos S, Montgomery HE, Bailey ME, Pigozzi F, Hilley A, Lee R, Galloway SD, Guibin J, Rogozkin VA, Ahmetov II, Yang N, North KN, Ploutarhos S, Montgomery HE, Bailey ME, Pigozzi F, Hilley A, Lee R, Galloway SD, Guibin J, Rogozkin VA, Ahmetov II, Yang N, North KN, Ploutarhos S, Montgomery HE, Bailey ME, Pigozzi F, Hilley A, Lee R, Galloway SD.
14. Williams AG. Genetics of muscle strength limits and power: polygenic profile similarity limits skeletal muscle performance. J Sports Sci. 2011;29(13):1425-34.
15. Ahmetov II, Vinogradova OL, Williams AG. Gene polymorphisms and fiber-type composition of human skeletal muscle. Int J Sport Nutr Exerc Metab. 2012;22(4):292-303.
16. Ma F, Yang Y, Li X, Zhou F, Gao C, Li M, Gao L. Association of the gene for rapid skeletal muscle growth with ACE and ACTN3 genotypes. J Appl Physiol (1985). 2019;81(1):e54685.
17. Wang G, Mikami E, Chiu LL, De Perini A, Deason M, Fuku N, Miyachi M, Kaneoka K, Murakami H, Tanaka M, Hsieh LL, Hsieh SS, Caporossi D, Pigoffo Z, Hilley A, Lee RE, Galloway SD, Guibin J, Rogozkin VA, Ahmetov II, Yang N, North KN, Ploutarhos S, Montgomery HE, Bailey ME, Pigozzi F, Hilley A, Lee R, Galloway SD, Guibin J, Rogozkin VA, Ahmetov II, Yang N, North KN, Ploutarhos S, Montgomery HE, Bailey ME, Pigozzi F, Hilley A, Lee R, Galloway SD, Guibin J, Rogozkin VA, Ahmetov II, Yang N, North KN, Ploutarhos S, Montgomery HE, Bailey ME, Pigozzi F, Hilley A, Lee R, Galloway SD, Guibin J, Rogozkin VA, Ahmetov II, Yang N, North KN, Ploutarhos S, Montgomery HE, Bailey ME, Pigozzi F, Hilley A, Lee R, Galloway SD.
18. Staron RS. Muscular adaptations in response to three different resistance-training regimens: specificity of repetition maximum training zones. Eur J Appl Physiol. 2002;88(1-2):50-60.
in European men. J Appl Physiol (1985). 2005;99(3):344-348.

39. Maciejewska A, Sawczuk M, Cieszczyk P, Mozhayaskaya IA, Ahmetov II. The PPARGC1A gene Gly482Ser in Polish and Russian athletes. J Sports Sci. 2012;30(1):101-113.

40. Liu XG, Tan LJ, Lei SF, Liu YJ, Shen H, Wang L, Yan H, Guo YF, Xiong DH, Chen XD, Pan F, Yang TL, Zhang YP, Guo Y, Tang NL, Zhu XZ, Deng HY, Levy S, Recker RR, Papaian CJ, Deng HW. Genome-wide association and replication studies identified TRHR as an important gene for lean body mass. Am J Hum Genet. 2009;84(3):418-423.

41. Wang P, Ma LH, Wang HY, Zhang W, Tian Q, Cao DN, Zheng GX, Sun YL. Association between polymorphisms of vitamin D receptor gene Apal, BsmI and TaqI and muscular strength in young Chinese women. Int J Sports Med. 2006;27(3):182-186.

42. Windelinckx A, De Mars G, Beunen G, Aerssens J, Delecluse C, Lefevre J, Thomis MA. Polymorphisms in the vitamin D receptor gene are associated with muscle strength in men and women. Osteoporus Int. 2007;18(9):1235-1242.

43. Prior SJ, Hagberg JM, Palton CM, Douglass LW, Brown MD, McLennan JC, Roth SM. DNA sequence variation in the promoter region of the VEGF gene impacts VEGF gene expression and maximal oxygen consumption. Am J Physiol Heart Circ Physiol. 2006;290(5):1848-1855.

44. Ahmetov II, Khakimullina AM, Popov DV, Missina SS, Vinogradova OL, Rogozkin VA. Polymorphism of the vascular endothelial growth factor gene (VEGF) and aerobic performance in athletes. Hum Physiol. 2008;34:477-481.

45. Batterham AM, Hopkins WG. A decision tree for controlled trials. Sportsci. 2005;9:33-39.

46. Egorova ES, Borisova AV, Mustafina LJ, Arkipova AA, Gabbasov RT, Druzhesvskaya AM, Astratekova IV, Ahmetov II. The polygenic profile of Russian football players. J Sports Sci. 2014;32(13):1286-93.

47. Calvo M, Rodas G, Vallejo M, Estruch A, Arcas A, Javierre C, Viscor G, Ventura JL. Heritability of explosive power and anaerobic capacity in humans. Eur J Appl Physiol. 2002;86(3):218-225.

48. Montgomery HE, Marshall R, Hemingway H, Myerson S, Clarkson P, Dollery C, Hayward M, Holliman DE, Jubb M, World M, Thomas EL, Brynes AE, Saeed N, Barnard M, Bell JD, Prasad K, Raysen M, Talmud PJ, Humphries SE. Human gene for physical performance. Nature. 1998;393(6682):221-222.

49. Folland J, Leach B, Little T, Hawker K, Myerson S, Montgomery H, Jones D. Angiotensin-converting enzyme genotype affects the response of human skeletal muscle to functional overload. Exp Physiol. 2000;85:575-579.

50. Pescatello LS, Costek MA, Gordish-Dressman H, Thompson PD, Seip RL, Price TB, Angelopoulos TJ, Clarkson PM, Gordon PM, Moya NM, Visich PS, Zoeller RF, Devaney JY, Hoffman EP. ACE ID genotype and the muscle strength and size response to unilateral resistance training. Med Sci Sports Exerc. 2006;38(6):1074-1081.

51. Pereira A, Costa AM, Izquierdo M, Silva AJ, Bastos E, Marques MC, ACE ID and ACTN3 R/X polymorphisms as potential factors in modulating exercise-related phenotypes in older women in response to a muscle power training stimuli. Age (Dordr). 2013;35(5):1949-1959.

52. Sukhova ZI, Ivanitskaia VV, Makarova LF, Poluektova BF, Izazikov VV. Features of the ultrastructural organization of the muscles of skaters in relation to their sport specialization and muscle fiber composition. Arkh Anat Gistol Embriol. 1985;89(12):87-90.

53. Petrella JK, Kim JS, Mayhew DL, Cross JM, Bamman MM. Potent myofiber hypertrophy during resistance training in humans is associated with satellite cell-mediated myonuclear addition: a cluster analysis. J Appl Physiol (1985). 2008;104(6):1736-42.

54. Stone WJ, Coulter SP. Strength/endurance effects from three resistance training protocols with women. J Strength Cond Res. 1994;8:231-234.

55. Häkkinen K, Komi PV, Alén M, Kauhanen H. EMG, muscle fibre and force production characteristics during a 1 year training period in elite weightlifters. Eur J Appl Physiol Occup Physiol. 1987;56(4):419-27.