

Power athletes

Gene driven power athletes? Genetic variation in muscular strength and power

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Strength phenotypes are under strong genetic control, but much research is still required

Muscular strength and power are important components of fitness essential for the execution of a variety of daily and sporting activities. Static or isometric strength, explosive strength or power, and dynamic (sometimes called functional) strength are generally considered in epidemiological studies.

Analyses of the genetic determinants of strength provide information concerning the contribution of both genes and environmental factors. Interaction effects between genes and environment (the dependence of weight training response on genes) and the identification of genes or coding variants in relation to strength characteristics are also of interest.

METHODOLOGICAL CONSIDERATIONS

Power and strength show normal variation in the general population, as is typical for quantitative, multifactorial phenotypes that are influenced by both multiple genes (polygenic) and environmental factors. The search for the genetic basis of muscular strength and power is based on two approaches: the unmeasured genotype approach (top down) and the measured genotype approach (bottom up).

When the measured genotype is not available, inferences concerning genetic influences on a phenotype are based on statistical analyses of the distributions of strength measures in related individuals and families based on the theoretical framework of biometrical genetics. Twin and family studies are the two major strategies used to identify genetic and environmental contributions to muscular strength. The heritability coefficient derived thereof is specific for the studied population and can be estimated using ANOVA or genetic modelling techniques.

Two major complementary strategies are available in humans to identify genes using the measured genotype approach. The first method is localisation and identification by quantitative

trait loci linkage analysis of chromosomal regions harbouring loci that make up the genetic component of muscle strength phenotypes. The second approach is allelic association studies in which a case control design is used to verify if, for example, strength athletes (cases) differ in genotype or allelic frequencies from non-athletes (controls). A specific (polymorphic) marker allele, mostly within a candidate gene, is investigated (ANOVA) with regard to the level of mean strength performance in groups of different genotypes for this polymorphism. When a positive association is found, the strength increasing allele under study may be the true functional variant or may be in tight linkage (in linkage disequilibrium) with the true functional allele. Frequently, multiple polymorphisms within one or more genes, or even across the genome, are studied. Instead of testing for association with each polymorphism separately, one can analyse haplotypes (compiled sets of adjacent SNPs that are inherited together) and test whether a specific haplotype is associated with increased/decreased strength. Linkage and association studies complement one other or can be seen as two ends of a continuum. Linkage studies need the cooperation of genetically related individuals who, because of a limited number of meioses, have large segments of chromosomes in common. Association studies link individuals separated by a large set of meioses and do not require genetic relationships between subjects.

GENETICS OF STRENGTH Family and twin studies

Beunen *et al*¹ recently reviewed genetic and environmental influences on different strength characteristics. Heritability estimates, based on sibling correlations for grip strength, and pull and push vary from 0.44 to 0.58. Correction for body mass reduced the estimates, but correction for the reliability of the measurements increased the heritabilities. Results

from 15 twin studies, sometimes with small sample sizes or often covering a large age range, provide heritabilities ranging from 0.14 to 0.83. Data on explosive strength or power, often measured with standing broad jump or vertical jump, are less extensive but indicate significant genetic contributions to jumping performance. Functional strength or muscular endurance is mostly evaluated by tests such as bent arm hang, chin ups, sit ups, or leg lifts. In general, heritability estimates from sibling or family studies are lower than those from twin studies. Static strength and power tend to have higher heritabilities than muscular endurance. Gender differences are not always clear, but genes seem to play a more prominent role in male than in female strength determination.

Data on time specific genetic and environmental regulation of strength performance variability are limited. During adolescence, tracking in static strength is largely determined by stable genes and stable unique environments during pre-adolescence. The genetic contribution to tracking in static strength is larger in boys than in girls.² Heritability estimates for grip strength in men and women in the second half of life (45 years and older) vary between 0.14 and 0.52.^{3,4} It seems reasonable to conclude that with the aging process and decline in muscle function, the genetic component of isometric strength is lower in older adults than it is during the growth process. No clear gender difference can be detected in any of the studies thus far reported.

Genetic factors in trainability of strength

Physical activity and specific, high resistance strength training are environmental factors that contribute or add to the observed differences in muscular strength and power between individuals both when young and in adulthood. The genotype*training interaction determines whether the observed heterogeneity in trainability is related to the genotype. In a 10 week high resistance strength training study of arm flexors in 25 MZ and 16 DZ male twins (22.4 ± 3.7 years), responses in static and dynamic arm flexor strength and arm cross-sectional area were analysed using bivariate genetic models. Evidence for a genotype-environment interaction was found for the increase in one repetition maximum (1RM), static strength, and concentric flexion at 120°/s.⁵

Gene powered? Gene hunting for muscular strength

A yearly update is provided by the journal *Medicine and Science in Sports and Exercise* on the "Human gene map for performance and health related fitness phenotypes". In

the 2004 update,⁶ 14 association studies were included (12 in normal subjects and two in patients), of which seven were published in 2004. Allelic variations in several candidate genes showed significant associations with static or dynamic strength phenotypes. These allelic variations were observed in growth differentiation factor 8 or myostatin (GDF8 K153R), insulin-like growth factor 2 (IGF2 ApaI), ciliary neurotrophic factor (CNTF null), vitamin D receptor (VDR BsmI and FokI), type I collagen alpha1 (COL1A1 Sp1), angiotensin converting enzyme (ACE – insertion/deletion), glucocorticoid receptor (NRC3C1 ER22/23ER), and ciliary neurotrophic factor receptor (CNTFR C174). More recently, a stop codon polymorphism in the ACTN3 gene has been associated with power related sports⁷ and responses to strength training,⁸ as individuals carrying the XX genotype lack alpha-actinin-3 protein in the Z-disk of type II muscle fibres.

Linkage analysis was performed with polymorphic markers in genes of the myostatin pathway in the Leuven Genes for Muscular Strength Study, with (suggestive) linkage demonstrated for knee flexor and extensor strength with several markers in the myostatin pathway (D2S118, D6S1051, D11S4138,⁹ D13S1303, D12S1042, D12S85, and D12S78¹⁰) but not with myostatin itself.

CONCLUDING REMARKS

Although strength phenotypes are under moderately strong to strong genetic control, there is still a long way to go before conclusive results

concerning genetic polymorphisms associated or linked with these phenotypes can be presented. Each contributing gene will explain only a small portion of the observed interindividual differences. Most of the association studies have not yet been replicated in independent samples, only one group of researchers has performed linkage studies, and no genome-wide linkage or association analyses have yet been published. Additionally, when looking beyond the genomic sequence variations, alternative splicing induces “one gene-many proteins” relationships, and RNA interferences are now studied as interfering agents that can mimic loss of function phenotypes. Furthermore, the study of (heritable) epigenetic factors involved in strength related gene expression will probably increase exponentially in the future.

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