CASE REPORT

Citius and longius (faster and longer) with no α -actinin-3 in skeletal muscles?

Alejandro Lucia, Jesús Oliván, Félix Gómez-Gallego, Catalina Santiago, Marta Montil, Carl Foster

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The muscle protein α -actinin-3 (ACTN3) is normally thought to be expressed in type II muscle fibres and to be necessary for high-power, high-velocity muscle contractions, such as those typically seen in speed/power athletes. The authors report the case of a Spanish elite long jumper (two times Olympian, personal best of 8.26 m) whose genotype for the ACTN3 gene is 577XX (ACTN3 deficient). These data suggest that there might be notable exceptions to the concept that ACTN3 is the “gene for speed”.

The expression of α -actinin-3 (ACTN3) is almost exclusively restricted to type II (fast twitch) muscle fibres.¹ In these fibres, ACTN3 constitutes the predominant component of the Z disc, where it acts as a lattice structure that anchors actinin-containing thin filaments and stabilises the muscle contractile apparatus.¹ Compared to the I subtype, ACTN3 may confer type II fibres with a higher capacity for the absorption/transmission of force at the Z line during rapid contractions.² It also interacts with proteins involved in numerous signalling and metabolic pathways² and may promote the formation of type II fibres or alter glucose metabolism in response to training.^{2–4} Further, ACTN3 may be evolutionarily optimised to minimise the tissue damage caused by eccentric muscle contractions in type II fibres.³

Despite the evolutionary conservation of ACTN3, a significant proportion of healthy individuals (for example, ~18% of Caucasians of European ancestry) are totally deficient in this protein as they are homozygous for a premature stop codon polymorphism (577X) in the ACTN3 gene.⁵ Although this genetic variation is associated with no known disease phenotype and may confer a beneficial effect on endurance performance,^{3,6} it is believed to preclude top-level athletic performance in power and sprint activities, as opposed to the 577R polymorphism, which may favour sprint/power performance.⁴ ACTN3 is the first structural skeletal-muscle gene for which a genotype-sports performance phenotype association has been demonstrated. No female elite sprint (judo, velodrome cycling, speed skating) athlete from Australia³ and no top-level (world class) track and field sprinter from Finland has been reported to be ACTN3 deficient (XX genotype).⁷ Although 8% of Australian elite male power athletes were athletes of the XX genotype (suggesting that androgen hormones might compensate for ACTN3 deficiency), all Olympic-class power athletes were heterozygotes or homozygotes for the functional R allele, associated with the presence of ACTN3 in skeletal muscle.³

CASE REPORT

We report the case of a 37-year-old white male (Spaniard of European ancestry) who was an Olympic-class long jumper during the 1990s despite carrying the ACTN3 XX genotype. He provided written informed consent and the study was approved by the ethics committee (Universidad Europea de Madrid, Spain).

Genomic DNA was extracted from subject's peripheral blood obtained according to standard phenol/chloroform procedures followed by alcohol precipitation. Details of genotype determination have been previously reported² and are the same as those described in a recent study from our laboratory.⁶

At age 16, he won the gold medal in the World Championships in the under-17-year-old age category, with a personal best of 8.00 m (a better performance than former Olympic champion Carl Lewis at the same age). Subsequently, he achieved 8.00+ m performances six times. His lifetime personal best was 8.26 m (92.3% of world record) and he won six indoor/outdoor Spanish championships. He competed in two Olympic games (1992 and 1996) and in several European and World championships. He was also a good sprinter, as he broke some Spanish records (60–200 m) in younger age categories.

DISCUSSION

We report a case of extreme performance phenotype in a sprint/power athlete despite being a carrier of a genotype thought to be very unfavourable for this type of event. To the best of our knowledge, this is the first report of ACTN3 deficiency in an truly Olympic-class power/sprint athlete. Especially remarkable, despite this unexpected genotype, was his performance (world champion) at age 16, with very little training (<1 year). At this young age, he had done relatively little specific training for developing his jumping technique and thus factors independent of training and technique/biomechanics (for example, genetic factors) would have played a large role in his performance.

ACTN3 is largely responsible for generating forceful muscle contractions at high velocity.⁴ At least theoretically, ACTN3 deficiency should impair long jump performance given the characteristics of this event. Although long jump performance is determined by multiple variables, the two main limiting factors for attaining greater jump distances have been thought to be ACTN3-dependent—that is, the ability to generate a high running speed and a single high-speed, high-power eccentric-concentric contraction during the jump itself.⁸

In world-class decathletes, performance in explosive power specialities such as the 100 m sprint or the long jump is negatively correlated with performance in the more endurance-oriented 1500 m race.⁹ These data would support the hypothesis of a “trade-off” between sprint and endurance phenotypic traits, such that an individual is inherently predisposed toward performance in one or the other.¹⁰ In humans, this appears to have been achieved, at least partly, through the maintenance of genetic variation by balancing natural selection.³ Such phenomenon would explain genetic differences among individuals (for example, Olympic-class sprinters vs Olympic-class endurance athletes), which has been thought to be those demonstrated for the ACTN3 locus. The present data suggest that there might be notable exceptions to the original concept that implicates ACTN3 as the “gene for speed”.⁴ Although there is a high likelihood that ACTN3 is important to high-intensity

What is already known on this topic

- *ACTN3* is the first structural skeletal-muscle gene for which a genotype-sports performance phenotype association has been demonstrated.
- *ACTN3* might be the "gene for speed" as the common XX genotype (associated with total lack of α -actinin-3 in skeletal muscles) seems to preclude top level (Olympic class) sprint/power performance.

What this study adds

- We report a case of extreme performance phenotype in an Olympic sprint/power athlete (>8 m performance in long jump) despite being a carrier of a genotype (XX) thought to be very unfavourable for this type of event.
- Although more research is needed, the present data suggest that there might be notable exceptions to the concept of *ACTN3* being the "gene for speed".

skeletal muscle function, other factors, potentially including the nature of the myosin heavy chain, the ability to coordinate and sequence complex muscle actions (for example, combination of sprint, take-off and landing abilities in the long jump) and muscle properties (muscle mass, the ratio of muscle fibre to tendon cross sectional area, relative length of fibres and tendons, etc), may be of substantially greater importance than the intrinsic characteristics of muscle protein—even at the highest levels of human muscular performance.

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Authors' affiliations

A Lucia, J Oliván, F Gómez-Gallego, C Santiago, M Montil, Department of Physiology, Universidad Europea de Madrid, Madrid, Spain

C Foster, Department of Exercise and Sport Science, University of Wisconsin-La Crosse, La Crosse, Wisconsin, USA

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Correspondence to: Professor A Lucia, Department of Physiology, Universidad Europea de Madrid, Villaviciosa de Odón, Madrid 28670, Spain; alejandro.lucia@uem.es

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