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Skeletal muscle signature of a champion sprint runner

Scott Trappe, Nicholas Luden, Kiril Minchev, Ulrika Raue, Bozena Jemiolo, and Todd A. Trappe
Human Performance Laboratory, Ball State University, Muncie, Indiana

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Trappe S, Luden N, Minchev K, Raue U, Jemiolo B, Trappe TA. Skeletal muscle signature of a champion sprint runner. *J Appl Physiol* 118: 1460–1466, 2015. First published March 6, 2015; doi:10.1152/japplphysiol.00037.2015.—We had the unique opportunity to study the skeletal muscle characteristics, at the single fiber level, of a world champion sprint runner who is the current indoor world record holder in the 60-m hurdles (7.30 s) and former world record holder in 110-m hurdles (12.91 s). Muscle biopsies were obtained from the vastus lateralis at rest and 4 h after a high-intensity exercise challenge (4 × 7 repetitions of resistance exercise). Single muscle fiber analyses were conducted for fiber type distribution (myosin heavy chain, MHC), fiber size, contractile function (strength, speed, and power) and mRNA expression (before and after the exercise bout). The world-class sprinter's leg muscle had a high abundance (24%) of the pure MHC IIx muscle fibers with a total fast-twitch fiber population of 71%. Power output of the MHC IIx fibers (35.1 ± 1.4 W/l) was 2-fold higher than MHC IIa fibers (17.1 ± 0.5 W/l) and 14-fold greater than MHC I fibers (2.5 ± 0.1 W/l). Additionally, the MHC IIx fibers were highly responsive to intense exercise at the transcriptional level for genes involved with muscle growth and remodeling (*Fn14* and *myostatin*). To our knowledge, the abundance of pure MHC IIx muscle fibers is the highest observed in an elite sprinter. Further, the power output of the MHC IIa and MHC IIx muscle fibers was greater than any human values reported to date. These data provide a myocellular basis for the high level of sprinting success achieved by this individual.

single muscle fiber; fiber type; gene expression; athlete; performance

HUMAN SKELETAL muscle fiber types exist in a continuum with a multitude of protein isoforms, metabolic profiles, and excitation-contraction characteristics (6, 33, 42).[1] Classification of muscle fiber types can be based upon several of these parameters with the myosin heavy chain (MHC) isoform generally accepted as the most informative given the influential role MHC has in contractile speed and power output of the muscle fiber (6, 34). Human skeletal muscle contains three MHC isoforms (I, IIa, IIx) that form three pure MHC fiber types (I, IIa, IIx) and three hybrid fiber types (I/IIa, IIa/IIx, I/IIa/IIx) (35). Muscle fiber composition among healthy individuals is heterogeneous with pure MHC I and IIa muscle fibers as the predominant fiber type, while the pure MHC IIx muscle fiber is generally less than 2% of the muscle fiber population (2, 31, 54). It is well documented that endurance athletes contain a high percentage of slow-twitch (MHC I) muscle fibers (10, 18). Likewise, the power output of the muscle fibers (MHC I and IIa) from endurance athletes is lower than untrained and resistance-trained individuals (18, 44, 53). While it is known that sprint athletes contain a high percentage of fast-twitch (MHC IIa) muscle fibers (3, 9, 17, 24, 32), no information is available on the power output of the MHC IIa muscle fibers from elite sprinters, which may provide more insight into the sprinting ability of these individuals.

We had the unique opportunity to examine the single muscle fiber contractile characteristics (strength, speed, and power) from the leg muscle (vastus lateralis) of a world champion sprint runner. Our primary interest was power normalized for myofiber volume since this provides an integrated performance index incorporating quantitative and qualitative aspects of contractile function. We also investigated muscle fiber type-specific gene expression before and after a high-intensity exercise bout. There are limited human fiber type-specific gene expression data available and our approach provided a way to gauge how the fast muscle fibers from an elite sprinter respond to an intense training bout at the molecular level. Surprisingly, a large portion of the sprinter's muscle contained the rare and powerful MHC IIx muscle fiber. As a result, we were able to gain new insight into the power output from both the MHC IIa and MHC IIx muscle fibers from an elite sprinter and examine how responsive these fiber types were to exercise at the level of the gene. The skeletal muscle data presented here represent a unique muscle phenotype for an elite sprint athlete.

METHODS

The world champion sprinter was recently retired at the time of testing with excellent overall fitness. Prior to volunteering for this research, the project objectives and testing procedures were explained to the subject by a member of the investigative team. The subject was informed of the risks and benefits of the research and gave his written informed consent to participate in the study protocol approved by the Human Subjects Institutional Review Board at Ball State University.

Muscle Biopsy Procedure and Exercise Bout

Following an overnight fast and 48 h cessation of exercise, a resting vastus lateralis muscle biopsy was obtained (5). The subject then warmed up for 10 min on a bicycle ergometer (Monarch 828E, Vansbro, Sweden) followed by four sets of seven maximal supine squats with 2 min rest between each set (1, 49). Following 4 h of rest, a second muscle biopsy was obtained from a different incision ~5 cm proximal to the initial muscle biopsy. The rationale for the 4-h postexercise biopsy time point was based upon our previous postexercise mRNA time course investigations (26, 37). The preexercise muscle sample was divided into longitudinal sections (~20 mg), placed in cold skinning solution (see below), and stored at −20°C for analysis of single muscle fiber physiology and fiber type (myosin heavy chain, MHC) composition. From the pre- and 4-h postexercise muscle biopsies, a longitudinal muscle strip was placed in RNA*later* (Ambion, Austin, TX) and stored at −20°C for gene expression analysis.

Skinning, Relaxing, and Activating Solutions

The skinning solution contained (in mM) 125 K propionate, 2.0 EGTA, 4.0 ATP, 1.0 $MgCl_2$, 20.0 imidazole (pH 7.0), and 50% (vol/vol) glycerol. The compositions of the relaxing and activating solutions were calculated using an interactive computer program

[1] This article is the topic of an Invited Editorial by Will G. Hopkins (19a) and an Invited Editorial by Anne Hecksteden and Daniel Theisen (18a).

Address for reprint requests and other correspondence: S. Trappe, Human Performance Laboratory, Ball State Univ., Muncie, IN 47306 (e-mail: strappe@bsu.edu).

described by Fabiato and Fabiato (13). These solutions were adjusted for temperature, pH, and ionic strength using stability constants in the calculations (16). Each solution contained (in mM) 7.0 EGTA, 20.0 imidazole, 14.5 creatine phosphate, 1.0 free Mg^{2+}, 4.0 free MgATP, KCl, and KOH to produce an ionic strength of 180 mM and a pH of 7.0. The relaxing and activating solutions had a free Ca^{2+} concentration of pCa 9.0 and pCa 4.5, respectively (where pCa = $-\log Ca^{2+}$ concentration).

Single Muscle Fiber Physiology Experiments

On the day of an experiment, a 2.5- to 3.0-mm muscle fiber segment was isolated from a muscle bundle and transferred to an experimental chamber filled with relaxing solution where the ends were securely fastened between a force transducer (model 400A, Cambridge Technology, Lexington, MA) and a direct current torque motor (model 308B, Cambridge Technology) as described by Moss (30). The force transducer and torque motor were calibrated before each experiment. Instrumentation was arranged so a muscle fiber could be rapidly transferred back and forth between experimental chambers filled with relaxing (pCa 9.0) or activating (pCa 4.5) solutions. The apparatus was mounted on a microscope (Olympus BH-2, Japan) to view the fiber (×800) during an experiment. Using an eyepiece micrometer, sarcomere length along the isolated muscle was adjusted to 2.5 μm, and the fiber length (FL) was measured (48). All single muscle fiber experiments were performed at 15°C.

Unamplified force and length signals were sent to a digital oscilloscope (Nicolet 310, Madison, WI), enabling monitoring of muscle fiber performance throughout data collection. Analog force and position signals were amplified (Positron Development, Dual Differential Amplifier, 300-DIF2, Inglewood, CA), converted to digital signals (National Instruments, Austin, TX), and transferred to a computer (Micron Electronics, Nampa, ID) for analysis using customized software. Servomotor arm and isotonic force clamps were controlled using a computer-interfaced force-position controller (Positron Development, Force Controller, 300-FC1).

For each single muscle fiber experiment, a fiber with a compliance (calculated as FL divided by *y*-intercept) > 10% and/or a decrease in peak force (P_o) of > 10% was discarded and not used for analysis. The within-fiber test/retest of a single muscle fiber in our lab for the measurements of size, force-power relationships, P_o, and contractile velocity were <1%. The coefficients of variation for the force transducer and servo-mechanical lever mechanism during the time frame of this investigation was <1%. Following completion of single muscle fiber physiology experiments, each fiber was solubilized in 80 μl of 1% SDS sample buffer and stored at −20°C until assayed for MHC fiber type.

Single muscle fiber physiology analysis. Individual muscle fibers were analyzed for diameter, force-velocity relationships, peak force (P_o), and maximal unloaded shortening velocity (V_o). Experimental procedures were identical to those previously used in our human studies (47, 48).

Single muscle fiber diameter. A video camera (CCD-IRIS, DXC-107A; Sony) connected to the microscope and computer interface allowed for viewing and storage of single muscle fiber digital images. Fiber diameter was determined from an image taken with the fiber briefly suspended in air (<5 s). Fiber width (diameter) was determined at three points along the segment length of the captured image using NIH public domain software (Scion Image, release Beta 4.0.2, for Windows). For the fiber size-dependent variables (i.e., P_o/CSA and normalized power), cross-sectional area (CSA) was determined with the assumption that the fiber forms a cylindrical shape while suspended in air.

Single muscle fiber Po. Force and position transducer outputs were amplified and sent to a microcomputer via a Lab-PC+ 12-bit data acquisition board (National Instruments). Resting force was monitored and then the fiber was maximally activated in pCa 4.5 solution. Peak active force (P_o) was determined in each fiber by computer subtraction of the baseline force from the peak force in the pCa 4.5 solution.

Single muscle fiber V_o. Fiber unloaded shortening velocity (V_o) was measured by the slack-test technique as described by Edman (12). The fiber was fully activated in pCa 4.5 solution and rapidly released to a shorter length, such that force fell to baseline. The fiber shortened, taking up slack, after which force began to redevelop. Then, the fiber was placed in pCa 9.0 solution and returned to original length. Computer analysis determined the duration of unloaded shortening, or time between onset of slack and redevelopment of force. Four different activation and length steps (150, 200, 250, and 300 μm; ≤15% of FL) were used for each fiber, with the slack distance plotted as a function of the duration of unloaded shortening. Fiber V_o (FL/s) was calculated by dividing the slope of the fitted-line by the fiber segment length (data were normalized to a sarcomere length of 2.5 μm).

Single muscle fiber power. Submaximal isotonic load clamps were performed on each fiber for determination of force-velocity parameters and power. Each fiber segment was fully activated in pCa 4.5 solution and subjected to a series of three isotonic load steps. This procedure was performed at various loads so that each fiber underwent a total of 15-18 isotonic contractions.

For the resultant force-velocity relationships, load was expressed as P/P_o (P = force during load clamping, P_o = peak isometric force developed before submaximal load clamps). Force and shortening velocity data points were derived from the isotonic contractions and fit by the hyperbolic Hill equation (19). Only individual experiments in which R^2 was ≥ 0.98 were included for analysis.

Fiber peak power was calculated from the fitted force-velocity parameters (P_o, V_{max}, and α/P_o, where α is a force constant and V_{max} is the *y*-intercept). Absolute power (μN·FL/s) was defined as the product of force (μN) and shortening velocity (FL/s). Normalized power (W/l) was defined as the product of normalized force and shortening velocity.

Fiber Type Analysis

Following the single fiber contractile measurements, the MHC isoform profile was analyzed for each fiber segment using SDS-PAGE. To complement the single fiber physiology MHC isoform profile, additional fiber segments (~5 mm in length) were isolated and also analyzed for MHC isoform content using SDS-PAGE. In this way, a large number of single muscle fiber segments were analyzed to determine fiber type distribution. Each single fiber segment was solubilized in 80 μl of 1% SDS sample buffer and stored at −20°C until assayed. Briefly, samples were run overnight at 4°C on a Hoefer SE 600 gel electrophoresis unit (San Francisco, CA) utilizing a 3.5% (wt/vol) acrylamide stacking gel with a 5% separating gel (55). After electrophoresis, gels were silver stained as described by Giulian et al. (15). MHC isoforms (I, I/IIa, IIa, IIa/IIx, IIx, and I/IIa/IIx) of each single muscle fiber were identified according to migration rate as we have previously described (55).

Gene Expression

Basal state and 4-h postexercise mRNA expression of *Fn14* and *myostatin* were assessed in isolated MHC I, MHC IIa, and MHC IIx fibers via reverse transcription quantitative real-time PCR (qPCR) as we have previously described (21, 57). *Fn14* and *myostatin* were selected based upon their involvement in muscle growth and remodeling and our previous work showing these genes were responsive to a resistance exercise bout that was similar in nature to the current investigation (26, 37, 40).

Muscle fiber separation and MHC isoform identification. As we have previously reported (21, 57), a small muscle bundle from each muscle biopsy sample was placed in a petri dish filled with RNA*later*. Approximately 100 individual muscle fibers (~5 mm length) were separated under a light microscope from the muscle sample. Approx-

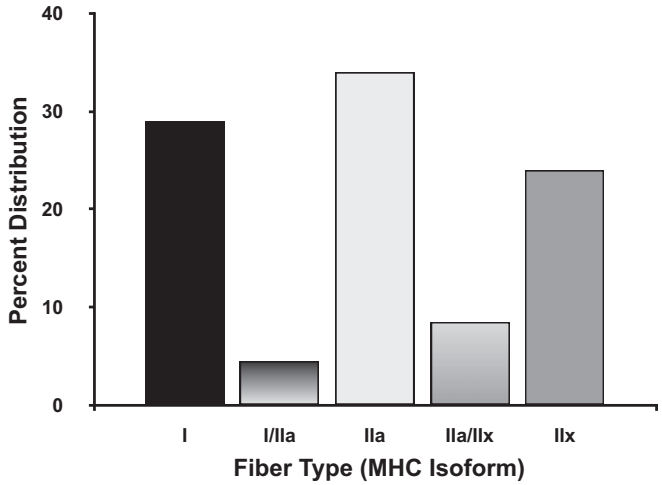

Fig. 1. Myosin heavy chain (MHC) distribution of isolated single muscle fibers (n = 329) from the vastus lateralis of the champion sprinter.

imately one-third of each isolated muscle fiber was clipped and placed in 40 μl of SDS sample buffer for MHC isoform determination by SDS-PAGE as described above. The remaining two-thirds of each muscle fiber was placed in a tube containing 0.5 ml of RNA isolation reagent, TRI reagent, and 2 μl of PolyAcryl Carrier (Molecular Research Center, Cincinnati, OH) and stored at −80°C until RNA extraction after MHC isoform determination.

Total RNA extraction and pooling. Following MHC isoform identification, total RNA from individual muscle fibers (basal state: 20 MHC I, 20 MHC IIa, and 20 MHC IIx fibers; 4 h postexercise: 20 MHC I, 20 MHC IIa, and 8 MHC IIx fibers) was extracted in TRI reagent according to the manufacturer's protocol (Molecular Research Center). The RNA pellet obtained at the end of each extraction of the same MHC isoform were combined and dissolved in 40 μl of DNase- and RNase-free water. Therefore, a pool of RNA from single fibers was generated for each fiber type to create fiber type-specific RNA samples.

Reverse transcription and qPCR. Oligo(dT) primed first-strand complementary DNA (cDNA) was synthesized using SuperScript II RT (Invitrogen, Carlsbad, CA). Quantification of mRNA transcription (in duplicate) was performed in a 72-well Rotor-Gene 3000 Centrifugal Real-Time Cycler (Corbett Research, Mortlake, NSW, Australia). Glyceraldehyde 3-phosphate dehydrogenase (*GAPDH)* was used as a reference gene as previously described by our laboratory (21, 38). All primers used in this study were mRNA specific (on different exons and crossing over an intron) and designed for qPCR analysis (Vector NTI Advance 9 software; Invitrogen) using SYBR Green chemistry. Details about primer characteristics and sequences for *Fn14/TNFRSF12A* (NM_016639.2) and *myostatin/MSTN* (NM_005259), as well as qPCR parameters, have been previously reported (26, 31). A melting curve analysis was generated to validate the presence of only one product. Details about reverse transcription and qPCR reaction parameters have been reported previously (38). Relative gene expression analysis comparing expression of a gene-of-interest in relation to a reference-gene, based on the distinct cycle (Ct) differences, was calculated with the $2^{-\Delta Ct}$ (arbitrary units $\times$ 10^3) model (25), as previously described in detail (57).

A six-point (1.0, 0.5, 0.25, 0.125, 0.062, 0.031) serial dilution curve (cDNA made from 500 ng of total RNA of human skeletal muscle; Ambion) was generated for each qPCR run to evaluate reaction efficiencies. The amplification calculated by the Rotor-Gene software was specific and highly efficient (efficiency = 1.1 ± 0.05; R^2 = 0.996 ± 0.001; slope = 3.16 ± 0.08).

Data Analysis

Single muscle fiber size and performance characteristics from the champion sprinter are presented as means ± SD. Distribution of MHC fiber type profile is expressed as a percentage of the total fiber pool analyzed. Gene expression in arbitrary units (AU) was calculated as discussed above. Gene expression data shown as fold change (see Fig. 3) were calculated as the ratio of the final value (post exercise) to the initial value (preexercise) considering the unique situation with one subject.

RESULTS

Muscle Fiber Type Distribution

A total of 329 fibers were analyzed for MHC composition, and the percent distribution is shown in Fig. 1. MHC IIx fibers represented 24% of the muscle, while MHC IIa and MHC I muscle fibers represented 34% and 29%, respectively. MHC hybrid isoforms comprised 13% of the muscle, with 4.5% as MHC I/IIa and 8.5% as MHC IIa/IIx.

Single Muscle Fiber Physiology

A total of 56 muscle fibers were analyzed for size and contractile performance, and the data are summarized in Table 1. Muscle fiber MHC I and IIa size was similar and ~11% larger than the MHC IIx muscle fibers. Specific force of fibers containing the MHC IIx and IIa isoforms was similar (187–197 kN·m^2) and ~36% greater than the MHC I fibers. Single muscle fiber speed and power followed a hierarchal pattern (IIx > IIa/x > IIa > I) across the fiber type spectrum. Of note was that the MHC IIx fibers were 50% faster and 78% more powerful than the MHC IIa fibers. Normalized power, which incorporates size, strength, and speed into the measurement, is shown in Fig. 2. Normalized power of the MHC IIx fibers was double compared with the MHC IIa fibers and 14-fold greater than the MHC I fibers.

Muscle Fiber Type-Specific Gene Expression

Preexercise and postexercise mRNA levels (arbitrary units, AU) were examined in each fiber type-specific sample. *Fn14* induction was most pronounced in the MHC IIx fibers (MHC IIx pre 0.01, post 6.57 AU) with a 506-fold induction 4 h after

Table 1. *Single muscle fiber characteristics from the vastus lateralis of the world champion sprinter*

Fiber Type	Size (CSA), μm^2	P_o, mN	P_o/CSA, kN·m^2	V_o, FL/s	V_{max}, FL/s	Power, μN·FL/s
MHC I (n = 20)	6,013 ± 1,026	0.84 ± 0.15	141 ± 18	1.20 ± 0.20	0.89 ± 0.13	15 ± 4
MHC IIa (n = 22)	6,249 ± 596	1.17 ± 0.12	187 ± 13	4.04 ± 0.40	3.92 ± 0.46	107 ± 18
MHC IIa/x (n = 4)	4,702 ± 1,274	0.93 ± 0.26	197 ± 16	5.75 ± 0.21	5.55 ± 0.19	165 ± 47
MHC IIx (n = 10)	5,517 ± 890	1.08 ± 0.12	196 ± 12	6.05 ± 0.60	5.82 ± 0.59	191 ± 17

Data are presented as means ± SD. MHC, myosin heavy chain; CSA, cross-sectional area; P_o, peak force; V_o, unloaded shortening velocity (from slack test); V_{max}, shortening velocity (from force-velocity relationship); FL, fiber length.

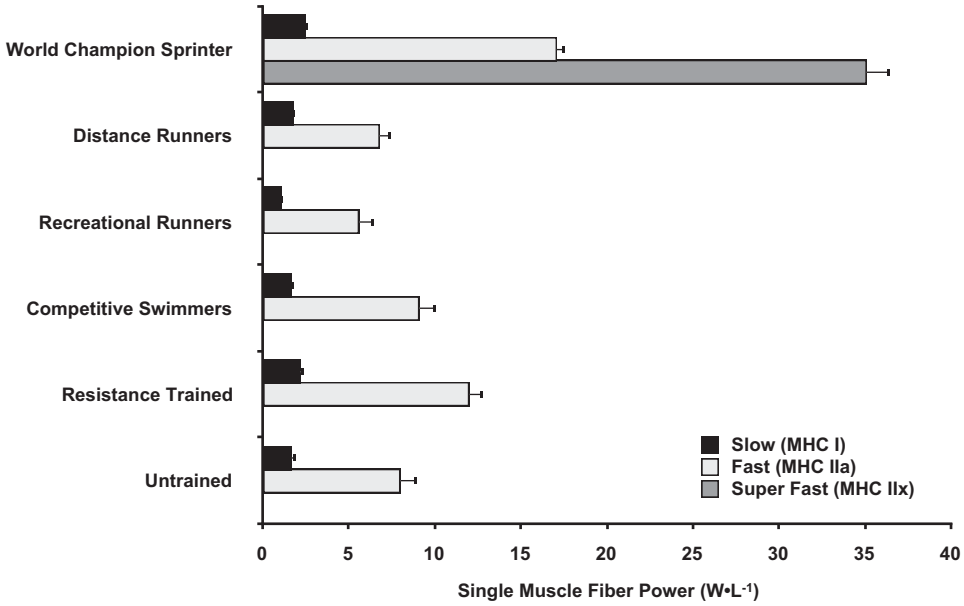

Fig. 2. Single muscle fiber power from the world champion sprint runner compared with other athletic and recreational populations from our laboratory. The distance runners were college athletes (n = 8 men, age 22 ± 1 yr) that were running 95 km/wk (18); the recreational runners were college students (n = 8, 4 women/4 men, age 21 ± 1 yr) that were running ~25 km/wk (18); the competitive swimmers were college athletes (n = 6 men, age 20 ± 1 yr) that were highly conditioned and tapered for their championship meet (46); the resistance trained were college students (n = 9 women, age 21 ± 2 yr) that had completed 12 wk of high-intensity resistance training (39); the untrained (n = 6 men, age 25 ± 1 yr) were healthy inactive individuals (47). For the world champion sprinter, the error bars reflect the variability among the fibers tested from this individual (mean ± SD). The error bars for each population reflect the variability of mean power output between subjects (mean ± SE).

the resistance exercise bout, which was substantially greater than the MHC IIa and MHC I fibers (MHC I pre 0.20, post 5.66; MHC IIa pre 0.04, post 3.04) (Fig. 3*A*). *MSTN* followed an inverse pattern compared with *Fn14* after exercise with the greatest reduction in expression in the MHC IIx muscle fibers (MHC I pre 0.08, post 0.07; MHC IIa pre 0.27, post 0.03; MHC IIx pre 0.54, post 0.02) (Fig. 3*B*).

DISCUSSION

The single muscle fiber profile from the world champion sprint athlete's leg muscle was remarkable compared with reports in the literature. Three unique aspects of this sprinter's muscle were apparent. First, there was a large proportion of pure MHC IIx muscle fibers observed from the sprint champion. Second, the power output of the MHC IIa and MHC IIx muscle fibers was higher than any human values reported to date. Third, genes involved with muscle growth and remodeling were highly responsive to intense exercise and most pronounced in the MHC IIx fibers.

Previous skeletal muscle reports from elite sprinters have shown a high proportion of fast-twitch MHC IIa fibers, but very few (<6%) of the pure MHC IIx muscle fibers (3, 24, 32). From mixed muscle homogenate preparation using SDS-PAGE analysis, sprinters have ~15% of the MHC IIx isoform (3, 24). However, when the SDS-PAGE homogenate data were directly compared with the SDS-PAGE single muscle fiber approach, the majority of the MHC IIx isoform was identified as the MHC IIa/IIx hybrid muscle fiber type (3). Comparable to sprinters, body builders have ~18% of the MHC IIx isoform present, but again this is from a mixed muscle homogenate SDS-PAGE analysis, and thus the pure MHC IIx muscle fiber content is unknown (11). When the MHC IIa/IIx hybrid muscle fibers from the sprint champion are combined with the 24% pure MHC IIx muscle fibers, the total fiber population with MHC IIx isoform present was 32.5%, further highlighting the high content of MHC IIx present in this individual.

The only other athlete model that is comparable to the current findings in the sprint champion comes from the animal kingdom. Kohn and colleagues have shown a strong positive linear relationship between sprinting speed and MHC IIx content among various mammalian species (22). Cheetahs, for example, have ~70% MHC IIx content and can reach speeds up to ~125 km/h (20, 22). The horse and wildebeest both have ~30% MHC IIx content (similar to current study), but can run much faster (~75 km/h) than the sprint champion (~30 km/h) (22). Certainly, biomechanics play an important role when comparing animal and human running speeds along with other structural, metabolic, and genetic traits. Nevertheless, these animal data strongly support the idea that sprinting ability is related to MHC IIx content.

Prior to the current study, reports of humans with a relatively high MHC IIx content were limited to spinal cord injured (SCI) patients and healthy individuals subjected to long-term bed rest (4, 14, 27). Interestingly, SCI patients have ~40% of their muscle as pure MHC IIx muscle fibers with the total MHC IIx content increasing to ~75% when the MHC IIa/IIx hybrid muscle fibers are taken into consideration (4, 27). Following 90 days of strict bed rest, MHC IIx content increased to ~39%, with only 1.5% as pure MHC IIx muscle fibers and the remaining as MHC IIa/IIx (28%) and MHC I/IIa/IIx (9%) hybrid muscle fibers (14). These unique disuse profiles have likely occurred from a slow- to fast-twitch muscle fiber transition, and it appears many years of extreme disuse (at least longer than 90 days) can result in significant expression of the pure MHC IIx fiber type. The contrast among the SCI patients, bed rest, various athlete groups, the animal kingdom, and the current study are interesting and point to genetic, evolutionary, and environmental factors that are likely controlling the expression of the MHC IIx protein across these paradigms.

A hierarchal pattern in single muscle fiber power output (MHC IIx > IIa > I) was observed in the current study, which aligned with previous work (8). A typical power output of a MHC IIa muscle fiber is ~5–12 W/l across various athletic and nonathletic groups from our laboratory (see Fig. 2). These human MHC IIa power output values are in close agreement with other laboratories (27, 51, 53). Limited human MHC IIx

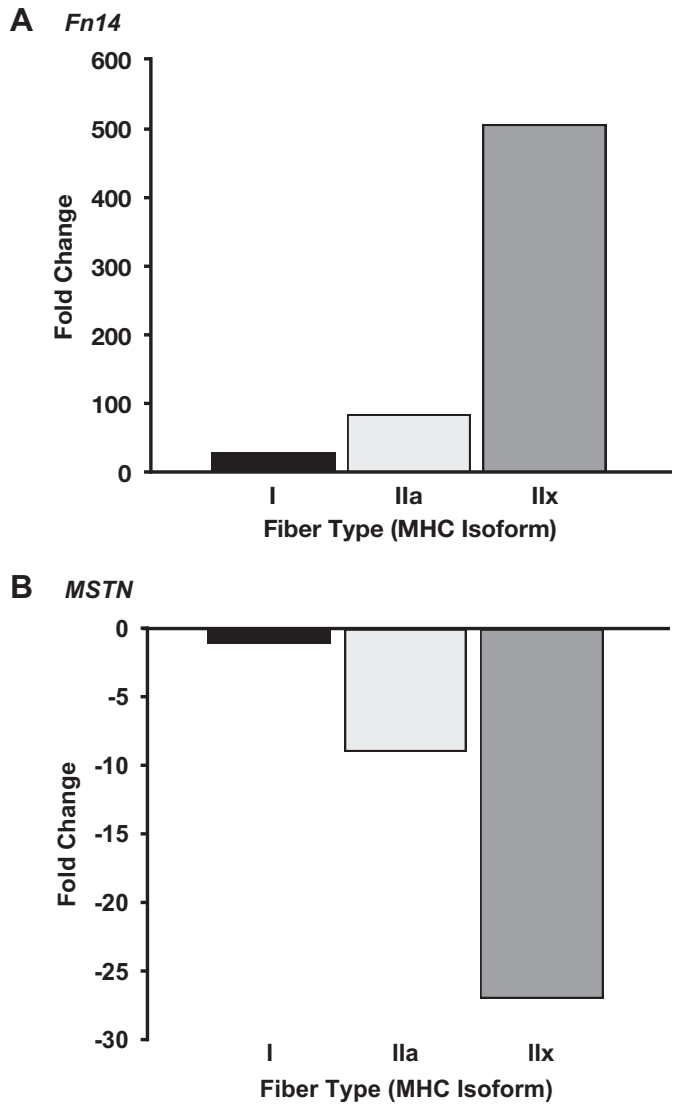

Fig. 3. Fiber type-specific mRNA profile from pooled MHC I, MHC IIa, and MHC IIx muscle fibers in response to a high-intensity resistance exercise bout for *Fn14* (*A*) and *MSTN* (*B*).

fiber power data have been reported in the literature with ~15–17 W/l the range for healthy untrained individuals (27, 51, 53). The sprint champion's MHC IIa and MHC IIx fiber power was approximately double for each respective fiber type compared with these previous reports. Also interesting to note was that the sprint champion's MHC IIa fiber power (17 W/l) was similar to the MHC IIx fiber power of untrained individuals.

The earlier fiber type discussion highlighted a high content of pure MHC IIx fibers in SCI patients and animals that provides additional perspective. The MHC IIx fiber power from the SCI patients was ~11 W/l (27), which is ~30% less than untrained humans (27, 51, 53), suggesting a deviation between fiber type and function with extreme disuse. In contrast, the lion and caracal have a MHC IIx fiber power of ~30 W/l (23), which is comparable to the champion sprinter. All the human data highlighted here were gathered at 15°C while the animal data were collected at 12°C. Temperature is known to influence muscle fiber performance (7) and suggests the animal data may have exceeded that of the champion sprinter had the muscle been evaluated at the same temperature. Collectively, the MHC IIx power profile from humans (healthy, extreme disuse, athletes) exhibits a spectrum of functionality with a two- to threefold greater power output found in the elite sprinter.

The exceptional power output from the champion sprinter appears to be driven by both the force-generating capacity and the contractile speed of the muscle fibers. Force per unit size of the fibers was similar among the fast-twitch muscle fibers (MHC IIa, IIa/IIx, and IIx) from the sprint champion, which was ~50% higher than MHC IIa fibers from untrained individuals and ~100% higher than endurance-trained runners from our laboratory (18, 47). The pattern of increasing contractile velocity for each fiber type mimicked the hierarchal pattern observed with fiber power. This was confirmed from both methodical approaches (V_o and V_{max}) for measuring contractile speed. The contractile speed from the sprinter's MHC I and IIa muscle fibers was slightly faster than untrained individuals (47) and much faster than distance runners (18) tested in our laboratory. From the small sample size of human MHC IIx fiber data in the literature, the sprinter's MHC IIx fibers contracted ~10–40% faster compared with untrained healthy individuals and SCI patients (27, 47, 52). Thus the greater power output of the fast muscle fibers from the sprint champion, and in particular the MHC IIx fiber type, appears to be qualitative (speed) and quantitative (specific force). The reason for these performance differences is currently unknown and requires more research. Several candidates have been suggested that can influence contractile performance, such as myosin light chain composition and/or phosphorylation status, alterations in myosin kinetics, and alterations in cell architecture (6, 29, 36, 41, 50).

Muscle fiber type-specific gene expression investigations in human skeletal muscle are relatively new (21, 40, 57), with these data providing the first insights into gene alterations with exercise in the human MHC IIx fiber type. As noted in Fig. 3, both the *Fn14* and *MSTN* response 4 h following exercise was the most pronounced in the MHC IIx muscle fibers. While *MSTN's* role as a negative regulator of skeletal muscle mass has been well established (28, 43, 45), *Fn14* has recently emerged as an important component for muscle growth and remodeling (31, 37, 40). *Fn14* is a cell surface receptor in numerous tissues, including skeletal muscle, and is part of the TNF-α superfamily signaling through the NF-κB pathway (56). The dynamic mRNA alterations with exercise, particularly the MHC IIx muscle fibers, are indicative of a high degree of muscle plasticity at the molecular level. The fiber type-specific transcriptional regulation with exercise is likely a genetic trait of this individual and may serve as a mechanism to maintain the rare MHC IIx phenotype observed in the sprint champion's muscle.

The combined functional superiority of the fast-twitch muscle fibers along with the high abundance of the rare and powerful MHC IIx phenotype represent a unique muscle signature that provides a myocellular basis for the high level of sprinting success achieved by this individual. This individual's genetic traits in combination with years of specific training are the most likely explanations for the unique skeletal muscle profile. At the time of our evaluation, the sprint champion was in excellent condition near the end of his competitive career.

Thus our profile does not necessarily reflect the state of the skeletal muscle when in peak form. The data reported here broaden the knowledge of human muscle fiber types and their functionality and provide an interesting framework for further inquiry into athletic phenotypes and performance of human skeletal muscle.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: S.T. and T.A.T. conception and design of research; S.T., N.L., K.M., U.R., B.J., and T.A.T. performed experiments; S.T., N.L., K.M., U.R., and B.J. analyzed data; S.T., U.R., and T.A.T. interpreted results of experiments; S.T. prepared figures; S.T. drafted manuscript; S.T., N.L., K.M., U.R., B.J., and T.A.T. edited and revised manuscript; S.T., N.L., K.M., U.R., B.J., and T.A.T. approved final version of manuscript.

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