RESEARCH CONTRIBUTIONS

Effect of Contraction History on Torque Deficits by Stretches of Active Rat Skeletal Muscles

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Abstract/Résumé

Effects of contraction history on torque deficits by stretches of active skeletal muscles were examined. After three contractions using maximal and submaximal activation (80 and 20 Hz) at an ankle position of 40° (i.e., long muscle length) and with maximal activation at 120° (i.e., short muscle length), the isometric and stretch torques (15 stretches) of rat plantar flexor muscles (bout 1) were measured. Controls were unconditioned. Stretches (i.e., ankle rotation from 90° to 40°, velocity: 50° · s⁻¹) were imposed on maximal isometric contractions at 90° (i.e., preloaded stretches). All groups performed a second bout following 2 hours of rest after bout 1. After maximal contractions at long muscle length, preload torque at 90° and stretch torque at 40° for stretch 1 of bout 1 were 25% and 18% lower than the other groups. However, for all groups, bout 1 ended and bout 2 began and ended with similar isometric and stretch torques. Stretches early in bout 2, with preloads similar to stretches in bout 1, had greater stretch torques resulting in larger torque deficits. Torque deficits, possibly caused by damage to muscle structures and excitation-contraction uncoupling, were not prevented by a history of isometric contractions. Different contraction histories can result in similar isometric torques but different stretch torques.

Cette étude analyse l'effet des contractions précédentes sur la diminution de force causée par l'étirement des muscles squelettiques actifs. Après trois contractions obtenues par stimu-

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lation électrique maximale et sous-maximale (80 Hz et 20 Hz) des fléchisseurs plantaires chez le rat dont la cheville est à un angle de 40° (muscle allongé), les forces isométriques et celles dues à l'étirement (séance 1: 15 étirements) sont établies après une activation maximale du muscle raccourci (angle de 120°). Un groupe témoin est aussi étudié. Les étirements (rotation de la cheville de 90° à 40°, vélocité: 50° · s⁻¹) sont pratiqués sur des muscles en contraction isométrique maximale, la cheville étant à un angle de 90° (étirement précontraint). Tous les groupes participent à une deuxième séance après 2 h de repos. À la suite des contractions maximales des muscles allongés, la force précontrainte à un angle de 90° et la force due à l'étirement à un angle de 40° (étirement 1, séance 1) sont de 25 % et de 18 % inférieures aux valeurs des autres groupes. Chez tous les groupes, cependant, la séance 1 se termine et la séance 2 commence et se termine sans que les forces (isométriques et dues à l'étirement) ne varient. Les étirements précoces à la séance 2, avec les mêmes contraintes qu'à la séance 1, génèrent plus de force, ce qui entraîne des diminutions de force plus importantes. Les diminutions de force, probablement dues à des lésions aux structures musculaires et à une défaillance électro-mécanique, ne peuvent être empêchées par des contractions isométriques précédentes. Les contractions précédentes peuvent modifier la force due à l'étirement mais pas nécessairement la force isométrique.

Introduction

During dynamic movements, skeletal muscles produce torque while becoming longer. Torque during stretches of active skeletal muscles is greater than the isometric torque at the same muscle length. When untrained skeletal muscles are exposed to repeated stretches while electrically activated, their ability to produce torque during isometric contractions declines; stretch-induced force deficits have developed (Hesselink et al., 1996; Willems and Stauber, 2000a). Similarly, stretch-induced force deficits can be created with voluntary activation of human skeletal muscles which are stretched (e.g., Brown et al., 1997); such force deficits have been taken as indirect evidence of stretch-induced muscle injury (e.g., McCully and Faulkner, 1985) and are primarily related to the amount of force or torque produced during the stretch (McCully and Faulkner, 1986; Warren et al., 1993).

Fatiguing concentric contractions before stretches of active skeletal muscle (i.e., concentric conditioning) influenced the stretch-induced force deficits during recovery (Nosaka and Clarkson, 1997) suggesting that contraction history influenced stretch-induced muscle injury. The effect of a history with isometric contractions on torque deficits by stretches of active skeletal muscles in an intact animal has not been tested. Since isometric contractions of rat plantar flexor muscles produced similar force values throughout a large range of ankle motion (Willems and Stauber, 1999), effects of muscle length with similar isometric torque on the torque deficits by stretches of active skeletal muscles can be studied.

Stretch-induced torque deficits immediately after stretches at high frequencies of electrical nerve stimulation can be due to both fatigue and injury (Hesselink et al., 1996). Adequate rest allows recovery from high-frequency stimulation and should reveal the torque deficit due to injury. In this study, stretch-induced torque deficits of rat plantar flexor muscles after isometric conditioning and after 2 hr recovery from a bout of repeated stretches were examined. We hypothesized that forceful isometric conditioning at long muscle lengths would reduce stretch-induced torque deficits compared with isometric conditioning at short muscle lengths.

Materials and Methods

GENERAL TREATMENT

Female Sprague Dawley rats (3-4 mo, $N = 16$, body mass: 250 ± 1 g [mean $\pm$ SEM]) were used. Animal use complied with Animal Welfare Act P.L. 91-579 and DHHS Guidelines governing the care and use of laboratory animals. All procedures were approved by and followed the guidelines of the West Virginia University Animal Care and Use Committee (WVU-ACUC #9809-02).

Experiments were performed on plantar flexor muscles (i.e., gastrocnemius, plantaris and soleus muscles) in anaesthetized rats (pentobarbital: 75 mg · kg^{-1} i.p.) activated with electrical stimulation of the tibial nerve. Details on dissection procedure for nerve cuff placement, animal positioning, dynamometer and force recording were described elsewhere (Cutlip et al., 1997; Willems and Stauber, 1999). Briefly, common peroneal and sural nerves were cut. A bipolar cuff electrode, made of silastic tubing (Dow Corning, Midland, MI, USA) and steel wires (Cooner wire AS632, Chatsworth, CA, USA), was put around the tibial nerve. The steel wires were connected to an electrical stimulator (Grass SD9 stimulator, Grass Medical Instruments, Quincy, MA, USA). The knee was held in flexion (90°) in a knee holder. Figure 1 shows the position of the rat's foot on aluminum plate and knee holder. The aluminum plate was connected to a dynamometer. During contractions, the foot was kept firmly positioned on the aluminum plate using two cross-bars. The dynamometer is composed of a DC permanent magnet servomotor (Model 1410C) and an Unidex 1 single axis motion controller (Aerotech Inc, Pittsburgh, PA, USA). Below the aluminum plate is a Z-11 / 5 kg load cell (HBM Inc,
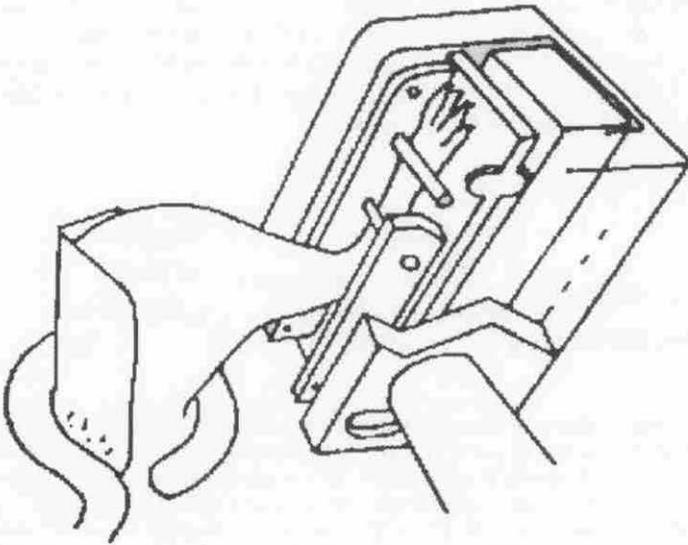

Figure 1. Position of the rat's foot in load cell fixture and knee holder (from Cutlip et al., 1997, reprinted with permission from *Med. Biol. Eng. Comput.* 35: 541).

Marlboro, MA, USA). The axis of rotation of the rat's ankle and dynamometer were visually aligned. Ankle angle was defined as the angle between the tibia and the plantar surface of the foot. Stimulus parameters for high torque (> 90% of maximal torque) muscle activation [200 μs pulse duration, 80 Hz, 4.7 ± 0.1 V (mean ± SEM)] were determined at an ankle position of 120°. A stimulation frequency of 80 Hz provides high torque and results in smaller loss in force during the plateau phase of the isometric contraction (i.e. less fatigue) than the maximal stimulation frequency of 120 Hz (unpublished observations).

EXPERIMENTAL TREATMENT

The overall experimental protocol for isometric conditioning and the two bouts of repeated stretches with a 2-hour rest period between bouts is presented in Figure 2.

   Isometric conditioning. Three protocols of isometric conditioning were used: (a) three contractions with 80 Hz at 120° (i.e. short muscle length; MAX-ISO-SHORT), (b) three contractions with 80 Hz at 40° (i.e. long muscle length; MAX-ISO-LONG), or (c) three contractions with 20 Hz at 40° (SUB-ISO-LONG). Contractions at long muscle lengths were performed with stimulation frequencies of 20 and 80 Hz, respectively, to manipulate the isometric torque output at long muscle lengths during isometric conditioning. Contractions at short muscle lengths with 20 Hz were not performed because isometric contractions only at long muscle lengths caused force deficits (Willems et al., 1999). Controls were not exposed to isometric conditioning (CONTROL). Isometric torques with 80 Hz at long and short muscle lengths were about 90% of the isometric torque produced at optimal ankle angle (Figure 3, recalculated from data in Figure 1 of Willems and Stauber, 1999). Four animals were used in each group. Examples of the torque-time traces of the conditioning isometric contractions (stimulation time 1.9 s, rest periods 3 min) are presented in Figure 4. Rest periods between contractions of 3 minutes minimized muscle fatigue because, at an ankle position of 65°, isometric contractions of 1.9 s with rest periods of 3 min resulted in torque declines of only 0.5% per contraction (Willems and Stauber, 2000a).
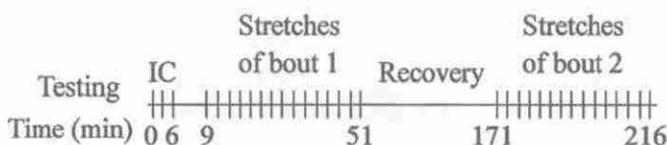

Figure 2. Time sequence of contractions during isometric conditioning (IC), repeated stretches of bout 1 and 2, and recovery (i.e., rest) between the bouts. Vertical lines represent contractions of rat plantar flexor muscles. IC consisted of three isometric contractions at 0, 3, and 6 min either at long muscle lengths with a stimulation frequency of 20 Hz and 80 Hz or at short muscle lengths with a stimulation frequency of 20 Hz, followed by bout 1 with 15 stretches from 9 to 51 min with one stretch every 3 min. After recovery of 2 hours, bout 2 was initiated with 15 stretches from 171 to 216 min with one stretch every 3 min (see methods for details of contractions and stretches).
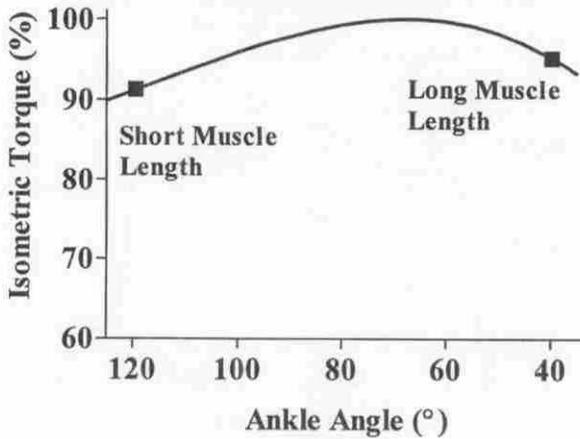
Figure 3. Normalized isometric torque of the rat plantar flexor muscles as a function of ankle position (recalculated from Figure 1 in Willems and Stauber, 1999). Squares indicate the ankle positions considered long (40°) and short muscle length (120°), respectively.
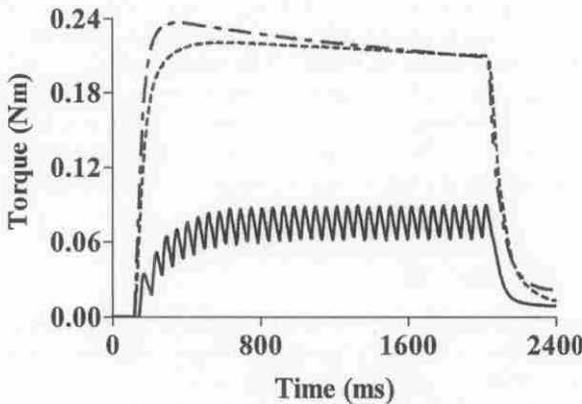

Figure 4. Isometric conditioning. Typical examples of the torque during an isometric contraction (80 Hz) at an ankle position of 40° (short dash) and 120° (long dash) and an isometric contraction (20 Hz) at 40° (solid line).

Repeated stretches and recovery. Two bouts of repeated stretches (15 in each bout) were performed (stimulation frequency 80 Hz). Stretches were initiated after the onset of stimulation (600 ms) by movement of the foot from an ankle position of 90° (isometric preload) to an ankle position of 40° (range of motion 50°) at an angular velocity of $50° \cdot s^{-1}$ (see Figure 5 for examples of torque traces). The passive return of the foot to the starting position was performed after the end
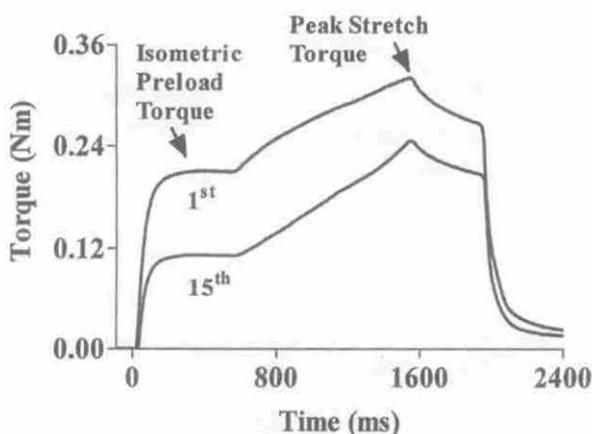
Figure 5. Preload stretches. Typical examples of the torque during the 1st and 15th repetition in bout 1. Arrows indicate the isometric preload torque and peak stretch torque.

of stimulation. Total stimulation time of one repetition (i.e., isometric preload, stretch, and hold-phase following the stretch) was 1.9 s with rest periods of 3 min. Bout 1 was performed following isometric conditioning as described above (see also Figure 2). Bout 2 was performed following a recovery of 2 hours from bout 1.

For two animals, isometric torque was determined every 10 min for 2 hours (between bouts 1 and 2) with isometric contractions of 600 ms with a stimulation frequency of 80 Hz at 90° to illustrate the time course for recovery after bout 1. At the end of the experiments, the rats were euthanized by an intracardial injection of pentobarbital.

DATA COLLECTION AND ANALYSIS

Force was measured under the sole of the foot of the rat and converted to torque values for the plantar flexors by multiplying force values times the distance between the ankle axis of rotation and the border of the proximal component of the thenar pad of the foot (10 mm) (Willems and Stauber, 2000a). For contractions with 80 Hz, the isometric torque was calculated by subtracting the average torque 100 ms before stimulation from the average total torque between 500 and 600 ms after onset of stimulation (i.e., on the tetanic plateau). These calculated values with a stimulation frequency of 80 Hz were > 99% of the highest torque values between 500 and 600 ms after onset of stimulation (data not shown). For contractions with 20 Hz, the isometric torque was calculated by subtracting the average torque 100 ms before stimulation from the highest torque between 500 and 600 ms after onset of stimulation. For each animal, the isometric torques preceding the first five stretches from bout 2 were compared to five stretches of bout 1 with similar isometric torque preceding the first stretch in each series of five stretches. For example,

the first five stretches of bout 2 were compared with five stretches of bout 1 (e.g., stretches 7 to 11) because stretch 1 of bout 2 and stretch 7 of bout 1 had similar isometric torques preceding the stretch. This comparison allows an analysis of a muscle preparation that is able to provide similar isometric torque before a stretch but with a different contraction history. For all muscle preparations, the isometric torques and peak stretch torques for the five stretches in each series from bout 1 and bout 2, based on the similarity of the isometric torque preceding the first stretch in each series of five, were averaged.

Effects of isometric conditioning and recovery on the isometric preload torque were tested using one way analysis of variance (ANOVA). Two way ANOVA with repeated measures was used to test isometric preload torques and peak stretch torques for the first five stretches from bout 2 and five stretches in bout 1 with similar isometric preload levels in the first repetition of each series of five. *Post-hoc* testing for differences was done using Bonferroni t-test. In each group, the isometric torque of the 15th stretch of bout 1 and the 1st stretch of bout 2 (i.e., following recovery of 2 hr) were tested using a Student t-test for paired comparisons. Significance was accepted at $P < .05$. Data are presented as means $\pm$ SEM.

Results

ISOMETRIC CONDITIONING

Isometric torques with 80 Hz at ankle positions of 40° (0.238 ± 0.014 Nm, MAX-ISO-LONG) and 120° (0.224 ± 0.016 Nm, MAX-ISO-SHORT) were similar, as expected from a previous study (Willems and Stauber, 1999), whereas isometric torques at 20 Hz at 40° (0.084 ± 0.006 N, SUB-ISO-LONG) were 35% of the 80 Hz torques at 40°. In the series of three conditioning isometric contractions, changes in isometric torque between the first isometric contraction and the third isometric contraction were –4% (at 40°), –1% (at 120°), and +7% (at 40°) for MAX-ISO-LONG, MAX-ISO-SHORT, and SUB-ISO-LONG, respectively.

BOUT 1

Following isometric conditioning, the first stretch in the group MAX-ISO-LONG was initiated at a 25% lower isometric preload torque and 18% lower peak stretch torque compared to the other groups (power of the ANOVA was 0.59 and 0.75) (Tables 1, 2). No absolute differences in isometric torque and peak stretch torque between MAX-ISO-LONG and the other groups were recorded at the end of the first bout of 15 stretches (Tables 1, 2).

BOUT 2

The recovery of isometric torque and peak stretch torque after a 2 hr period of rest was 13-17% and 12-16%, respectively, compared with the isometric torque and peak stretch torque of the 15th contraction in bout 1 ($P < .05$, Tables 1, 2). Isometric and peak stretch torques for the first and last stretch following the 2 hr rest were similar in all groups (Tables 1, 2) ($P < .05$).

Table 1 Isometric Preload Torque Preceding the 1st and 15th Stretch in Bout 1 and 2 for Control and Experimental Rats

	Bout 1		Bout 2	
	Torque 1st, Nm	Torque 15th, Nm	Torque 1st, Nm	Torque 15th, Nm
CONTROL	0.262 ± 0.015	0.159 ± 0.011	0.180 ± 0.012[#]	0.134 ± 0.005
MAX-ISO-LONG	0.204 ± 0.003*	0.155 ± 0.006	0.179 ± 0.006[#]	0.139 ± 0.006
MAX-ISO-SHORT	0.274 ± 0.020	0.158 ± 0.002	0.184 ± 0.008[#]	0.133 ± 0.010
SUB-ISO-LONG	0.270 ± 0.020	0.141 ± 0.003	0.164 ± 0.003[#]	0.121 ± 0.004

Values are means ± SEM; $N = 4$ per group. CONTROL = no isometric conditioning. MAX-ISO-LONG = 80 Hz isometric contractions at an ankle position of 40°. MAX-ISO-SHORT = 80 Hz isometric contractions at an ankle position of 120°. SUB-ISO-LONG = 20 Hz isometric contractions at an ankle position of 40°. * Significant difference compared with rats in other groups in isometric preload torque preceding the 1st stretch in bout 1, $P < .05$. [#]In each group, significant difference in the isometric preload torque preceding the 15th stretch in bout 1, $P < .05$.

Table 2 Peak Stretch Torque for the 1st and 15th Stretch in Bout 1 and 2 for Control and Experimental Rats

	Bout 1		Bout 2	
	Torque 1st, Nm	Torque 15th, Nm	Torque 1st, Nm	Torque 15th, Nm
CONTROL	0.341 ± 0.012	0.238 ± 0.005	0.266 ± 0.005[#]	0.197 ± 0.013
MAX-ISO-LONG	0.287 ± 0.007*	0.225 ± 0.006	0.256 ± 0.005[#]	0.204 ± 0.012
MAX-ISO-SHORT	0.345 ± 0.016	0.242 ± 0.013	0.281 ± 0.023[#]	0.208 ± 0.021
SUB-ISO-LONG	0.359 ± 0.017	0.246 ± 0.009	0.277 ± 0.012[#]	0.230 ± 0.008

Values are means ± SEM; $N = 4$ per group. For abbreviations see the footnote of Table 1. *Significant difference compared with rats in other groups in isometric preload torque preceding the 1st stretch in bout 1, $P < .05$. [#]In each group, significant difference in the isometric preload torque preceding the 15th stretch in bout 1, $P < .05$.
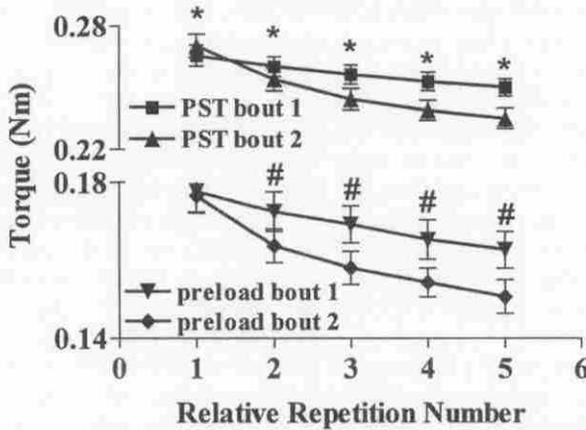
Figure 6. Comparison of isometric preload torque and peak stretch torque following five stretches selected from bout 1 and bout 2 with similar preload torques for the first in the series of five. Relationship between relative repetition number and isometric preload torque and peak stretch torque. Data are presented as means ± SEM. PST = peak stretch torque. *Significant difference for the PST between comparable repetitions in bout 1 and bout 2, $P < .05$. #Significant difference for the preload torque between comparable repetitions in bout 1 and bout 2, $P < .05$.

COMPARISON OF BOUT 1 AND BOUT 2

We tested the effect of stretches on skeletal muscles with a different history of active stretches but with similar isometric torque deficits. Isometric preload torques for the first five repetitions in bout 2 were compared with five repetitions of bout 1 which began with similar isometric preload values (Figure 6). For all groups, the torque decrement was greater in the five repetitions in bout 2 due to a greater peak stretch torque for repetition one in bout 2. After the first repetition in bout 2, the torque decline as a function of repetition number paralleled the repetitions in bout 1 but with lower peak stretch torques.

Discussion

The main finding of the present study was that isometric conditioning did not result in smaller torque deficits after repeated stretches of active skeletal muscles. Surprisingly, before the repeated stretches were even initiated, isometric conditioning with a stimulation frequency of 80 Hz at long muscle lengths resulted in torque deficits when tested at short muscle lengths. The reason for these torque deficits cannot be found in the use of high stimulation frequencies (e.g., 80 Hz), which use can result in failure of the neuromuscular junction and subsequent loss of force (Krnjevic and Miledi, 1958), because isometric conditioning with 80 Hz

at short lengths did not result in torque deficits. The torque deficits after isometric conditioning at long lengths could have been caused by each or a combination of the following four factors. First, isometric contractions at long lengths could mimic effects of eccentric contractions (Wood et al., 1993) and produce a down- and rightward shift of the length-force relationship (Jones et al., 1997). Such shift could result in losses of force that are muscle length dependent with larger losses in force at short than at long muscle lengths. Second, forceful contractions at long muscle lengths are known to result in more fatigue (i.e., larger force losses) at short muscle lengths than at long muscle lengths (Fitch and McComas, 1985, Sacco et al., 1994). It is possible that in our preparation, rest periods of 180 s between 80 Hz contractions of 1.9 s at long muscle lengths were not sufficient for complete recovery of torque at short muscle lengths but sufficient for complete recovery of torque at long muscle lengths. Third, isometric contractions at long lengths showed marked swelling of sarcoplasmic reticulum and were associated with force deficits at short lengths (Willems et al., 1999). Fourth, it is possible that effects of thixotropy (i.e., history-dependent changes in muscle stiffness and passive tension) have contributed to the torque deficits (for a review see Proske et al., 1993). After muscle contraction at a long length, muscle fibers at a short muscle length could fall slack and result in reduced force production. Although thixotropic effects were not present 180 s after 2 s contractions in isolated muscle preparations (Lakie and Robson, 1988), a time-related presence of thixotropic effects in intact muscle-joint systems after near maximum electrical stimulation has not been investigated.

Although isometric conditioning (80 Hz) at long muscle lengths resulted in lower isometric torque and peak stretch torque for the 1st contraction of bout 1, all groups had similar isometric torques and peak stretch torques at the end of bout 1. Several mechanisms could contribute to the torque deficit during a series of muscle stretches: (a) damage to muscle structures involved in force generation and/or transmission such as damage to sarcomeres (Talbot and Morgan, 1996) and connective tissue (Brown et al., 1997); (b) failure of excitation-contraction coupling that was shown to cause 57–75% of the loss of force from 0 to 5 days after the stretches (Ingalls et al., 1998). Both mechanisms are probably operational in our experiments and contribute to the torque deficits. During a bout of muscle stretches, which differ in initial torque (i.e., weak vs strong muscles), the relationship between contraction number and torque deficits was different but reached the same endpoint suggesting a limit to the amount of torque that can be lost by a series of muscle stretches.

Using stretches of active skeletal muscle with high-frequency activation and short rest periods between contractions (i.e., large work-to-rest ratio), the force deficits during and immediately after the test are likely due to both fatigue and injury (Hesselink et al., 1996). However, recovery from fatigue using high-frequency stimulation and repetitive isometric contractions should be complete within 30 min (De Ruiter et al., 1995). In our study, the work-to-rest ratio was small (contraction time 1.9 s, rest period 180 s) to minimize the effects of fatigue during and between the bouts. Indeed, the recovery of isometric torque was tested during the 2 hr of rest and found to be small (Figure 7). In addition, the time course for recovery did not have obvious rapid and slow phases as did our setup after fatigue with high-intensity contractions without stretches (Willems and Stauber, 2000b).
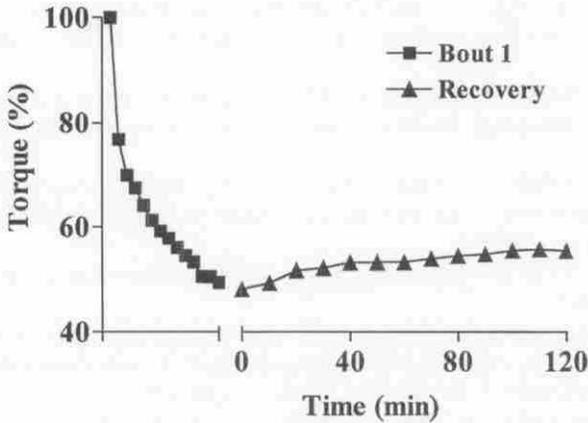
Figure 7. Isometric preload torque expressed as a percentage of the torque during the first repetition of repeated stretches of bout 1 and recovery versus time.

Thus, two hours of rest should have allowed complete recovery from physiological processes involved in high-frequency fatigue; the remaining weakness probably was due to injury.

Additional loss of torque by a second bout of repeated stretches to "injured" muscles was tested. The first contraction in bout 2 created a greater torque deficit compared with contractions of bout 1 with similar isometric preload levels but with larger peak stretch torques. Apparently, skeletal muscles with different contraction histories can have similar isometric torque production but different peak stretch torques. Recovery following 2 hr of rest between bouts was sufficient for some torque restoration whereas, in three minutes of rest between contractions in each bout, little recovery of torque occurred. In our experiments, there appears to be two types of recovery from stretch-induced injury illustrated by the time courses of torque decline. One type occurs in minutes, and the second one occurs over hours. The recovery that occurs in minutes between contractions probably represents some physiological fatigue due to muscle activation such as breakdown of phosphocreatine and increased lactate levels (Haan and Koudijs, 1994). The recovery that occurs over a period of hours (i.e., between bout 1 and bout 2) could represent a repositioning of sarcomeres, a resealing of broken membranes, an alteration in E-C coupling, or a recoil of stretched elastic components of the muscle.

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