Habitual loading results in tendon hypertrophy and increased stiffness of the human patellar tendon

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Couppé C, Kongsgaard M, Aagaard P, Hansen P, Bojsen-Moller J, Kjaer M, Magnusson SP. Habitual loading results in tendon hypertrophy and increased stiffness of the human patellar tendon. J Appl Physiol 105: 805–810, 2008. First published June 12, 2008; doi:10.1152/japplphysiol.90361.2008.—The purpose of this study was to examine patellar tendon (PT) size and mechanical properties in subjects with a side-to-side strength difference of ≥15% due to sport-induced loading. Seven elite fencers and badminton players were included. Cross-sectional area (CSA) of the PT obtained from MRI and ultrasonography-based measurement of tibial and patellar movement together with PT force during isometric contractions were used to estimate mechanical properties of the PT bilaterally. We found that distal tendon and PT, but not mid-tendon, CSA were greater on the lead extremity compared with the nonlead extremity (distal: 139 ± 11 vs. 116 ± 7 mm²; mid-tendon: 85 ± 5 vs. 77 ± 3 mm²; proximal: 106 ± 7 vs. 83 ± 4 mm²; P < 0.05). Distal tendon CSA was greater than proximal and mid-tendon CSA on both the lead and nonlead extremity (P < 0.05). For a given common force, stress was lower on the lead extremity (52.9 ± 4.8 MPa) compared with the nonlead extremity (66.0 ± 8.0 MPa; P < 0.05). PT stiffness was also higher in the lead extremity (4,766 ± 716 N/mm) compared with the nonlead extremity (3,494 ± 446 N/mm) (P < 0.05), whereas the modulus did not differ (lead 2.27 ± 0.27 MPa vs. nonlead 2.16 ± 0.28 GPa) at a common force. These data show that a habitual loading is associated with a significant increase in PT size and mechanical properties.

unilateral; strength; tendon size

HUMAN MOVEMENT COMES ABOUT FROM THE FORCE CREATED BY contracting muscles, which is transmitted to bone via aponer-rosis and tendon. Recent data in human models suggest that tendon tissue is quite metabolically responsive to tensile loading (4, 12, 16). In fact, it has been shown that both a single loading bout as well as long-term habitual loading produce a markedly elevated collagen synthesis response (20, 21, 26). However, to what extent this elevated synthesis yields incorporation of collagen into the load-bearing structure of tendon, and therefore either an increase in tendon size (hypertrophy) or an altered composition and a change in mechanical function, remains ambiguous.

Studies that address the influence of exercise on the mechanical properties of tendon have until recently largely been conducted in animal models. These data show that endurance-like exercise is associated with an increase (1, 35, 39), decrease (39), or unchanged (5, 36) tendon size, and thus they do not provide a coherent picture. In humans, cross-sectional data suggest that endurance training is associated with a larger Achilles tendon cross-sectional area (CSA) (17, 24, 33), which appears to be site specific (17, 24). However, in a recent intervention study it was shown that 9 mo of endurance training in untrained persons left the Achilles tendon CSA unchanged (13). On the other hand, animal data have shown that muscle size is related to the tendon size (8), suggesting that perhaps the magnitude of loading influences tendon size. Several human studies have shown that resistance training over 12–14 wk that produces increases in muscle strength of up to 21% does not result in an accompanying increase in tendon CSA (19, 30, 31), but rather a markedly altered modulus, which implies that there is a change in the composition of the structure rather than the size. However, it was recently shown in humans that resistance training for 12 wk yielded region-specific increases in patellar tendon (PT) CSA, without a change in modulus (18).

Conclusions from studies of cross-sectional design are inevitably hampered by issues of training history, selection bias, and intersubject variations. Additionally, longitudinal training studies may have been of insufficient duration to produce a robust tendon hypertrophy response. Finally, existing training studies (19, 30, 31) have examined tendon size in a region that appears unresponsive to training-associated adaptation. However, some of these limitations may be partially circumscribed by examination of region-specific PT properties in persons who engage in sport where one lower extremity is habitually sub- jected to more loading than the contralateral (“control”) side, such as in fencing or badminton. Therefore, the purpose of the present study was to examine region-specific PT properties in subjects who display a side-to-side strength difference of ≥15% due to persistent sport-induced loading over several years.

MATERIALS AND METHODS

Subjects. Both badminton and fencing involve repeatedly performing rapid forward lunges with a preferred and thus more loaded lead extremity compared with the nonlead extremity, which in this study served as a within-subject control. Saepa et al. (34) and Nystrom et al. (28) found a >14% strength difference between the legs in elite fencers, reflecting a sport-specific loading. The sport-specific loading in badminton and fencing creates a higher impact on the leg and therefore also on the PT compared with other sports without jumping and unilateral rapid lunges (27). A total of 22 athletes volunteered to participate in the study. They were recruited from the Danish National Fencing Center and the International Badminton Academy in Copenhagen, Denmark. Seven elite fencers (n = 4) and badminton (n = 3) players met the criteria of a side-to-side isometric knee extensor

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Maximal voluntary contraction. Maximal voluntary strength was determined by an isometric knee extension. Subjects performed a 10-min warm-up on a stationary bike (5 min at 150 W and 5 min at 200 W) before testing. The subjects were seated in a custom-made rigid chair with both hips and knees flexed to an angle of 90°. A leg cuff was connected to a strain gauge (model KRG-4, Bofors, Bofors, Sweden) through a rigid steel rod perpendicular to the lower leg and was mounted on the leg just above the medial malleolus. The tibia moment arm was measured (from the point of fixation to the lateral epicondyle of the knee) to calculate the knee extensor moment. Force was sampled on a personal computer (PC) at 50 Hz via a 12-bit analog-to-digital converter (model dt 2810A, Data Translation, Marlboro, MA). The subjects performed four to five maximal voluntary isometric knee extension contractions (MVC) separated by 1 min (sampled at 1,000 Hz) (3). The tests were conducted on both legs. A side-to-side difference in strength of ≥15% was defined as follows: (lead extremity − nonlead extremity)/nonlead extremity · 100 ≥ 15%.

Muscle and tendon morphological measurements. The anatomic CSA of the quadriceps femoris muscle was measured 20 cm proximal from the tibia plateau (mid-thigh level) by magnetic resonance imaging (MRI) [Signa Horizon LX 1.5 T, General Electric, longitudinal relaxation time (T1)-weighted spin echo (SE)] using a lower extremity coil. The images were obtained using the following parameters: transverse relaxation time (TR)/echo time (TE) = 500/14 ms, field of view (FOV) 18, matrix 512 × 512, and slice thickness 6 mm (18). The color intensity of each image was adjusted using the National Institutes of Health color scale mode of the software. Tendon CSA and length were measured using the gray-scale image display. The mean value of three measurements of the same image was used for analysis. The reproducibility data showed that the typical error percentage of repeated measures of tendon CSA was 2.5% for repeated measurements at the proximal tendon level, 2.5% for repeated measurements at the mid-tendon tendon level, and 2.0% for repeated measures at the most distal tendon level. The MRI investigator was blinded with regards to the subjects and side.

Assessment of PT mechanical properties. The details of the measurement, including the reliability of the method in our laboratory, has been reported previously (14). The within-day correlation coefficients and typical error percent of repeated measures were 0.95 and 9.9% for stiffness, 0.97 and 5.5% for strain, and 0.94 and 9.4% for modulus. Subjects performed a 5-min warm-up on a stationary bike to secure...
proper preconditioning of the tendon before testing. Thereafter, the subjects were seated in a custom made rigid chair with both hips and knees flexed to an angle of 90°. A leg cuff, which was connected to a strain gauge (model KRG-4, Bofors) through a rigid steel rod perpendicular to the lower leg, was mounted on the leg just above the medial malleolus. An ultrasound probe (7.5 MHz, linear array B-mode, Sonoline Sienna, Siemens, Erlangen, Germany) was fitted into a custom-made rigid cast that was secured to the skin above the PT in the sagittal plane. The ultrasound probe and cast was positioned so that the patella, the PT and the tibia were all visible within the viewing field throughout the ramped contractions (Fig. 3).

The ultrasound S-VHS video images obtained during the ramp trials were sampled at 50 Hz on a PC using frame-by-frame capturing software (model G400-TV, Matrox Marvel, Dorval, Canada). Force was sampled on two separate PCs at 50 Hz via a 12-bit analog-to-digital converter (model dl 2810A, Data Translation). The two computers were interconnected to permit synchronous sampling of all data using a custom-built trigger device (3). The subjects performed four to five slow isometric ramp contractions by applying gradually increasing force on the cuff over a 10-s period while PT displacement and knee extension force were measured simultaneously. Each ramp was separated by a 2-min rest. All measurements were performed on both legs. During the ramp contractions, force was sampled at 50 Hz and filtered at a 1.0-Hz cutoff frequency using a fourth-order zero-log Butterworth filter.

PT force was calculated by dividing the estimated total knee extension moment by the internal moment arm, which was estimated from individually measured femur lengths (37). PT stress was calculated by dividing tendon force by the proximal, mid-, and distal tendon CSA determined from the MRI. PT deformation was defined as the change in distance between the patellar apex and the tibia (14, 23). Tendon strain was calculated as the change in length related to the original length. Each force-deformation curve was fitted to a second- or third-order polynomial fit, which yielded $R^2 > 0.97$. Tendon stiffness ($\Delta$force/$\Delta$deformation) and modulus ($\Delta$stress/$\Delta$strain) were calculated in the final 10% of the force-deformation and stress-strain curves, respectively (22, 23).

Statistical analysis. The two isometric ramp contractions that yielded the greatest force were used for further analysis. To make side-to-side comparisons and thereby account for differences in isometric ramp contractions from side to side, the trials for both sides were subsequently analyzed to the lowest common force for each individual subject. Wilcoxon matched-pairs signed-ranks tests were used to examine whether there was a side-to-side difference in measured variables. Friedman’s analysis of variance, including the Dunn’s multiple comparison test, was used to detect possible tendon region-specific differences along its length. An alpha level of $P < 0.05$ was considered significant. Results are reported as means ± SE.

RESULTS

Quadriceps strength and CSA. In the recreational athletes, there was no side-to-side difference in MVC (dominant 217 ± 14 N·m, nondominant 203 ± 16 N·m) ($P > 0.05$), or quadriceps CSA (dominant 7,159 ± 323 mm², nondominant 6,951 ± 261 mm²) ($P > 0.05$). In the elite athletes, MVC was significantly greater in the lead extremity (239 ± 26 N·m) compared with the nonlead extremity (197 ± 23 N·m) ($P < 0.01$). Similarly quadriceps femoris CSA was significantly greater in the lead extremity (7,907 ± 656 mm²) compared with the nonlead extremity (7,410 ± 561 mm²) ($P < 0.05$).

PT CSA. In the recreational athletes there was no side-to-side differences in PT CSA for the distal (dominant 124 ± 7 mm², nondominant 120 ± 10 mm²), mid- (dominant 75 ± 8 mm², nondominant 74 ± 9 mm²), or proximal (dominant 84 ± 8 mm², nondominant 89 ± 7 mm²) tendon. The CSA of the tendon for the elite athletes are shown in Fig. 2. There was a significant side-to-side difference in CSA at the distal (lead 139 ± 11 mm², nonlead 116 ± 7 mm²) and proximal tendon (lead 106 ± 7 mm², nonlead 83 ± 4 mm²) ($P < 0.05$) but not at the mid-tendon section (lead 85 ± 5 mm², nonlead 77 ± 3 mm²) ($P = 0.218$). The PT CSA was greater at the distal tendon compared with mid- and proximal tendon on both the lead extremity and nonlead extremity ($P < 0.05$).

PT mechanical properties. Mechanical properties determined at maximal force are shown in Table 1. Tendon force and stiffness were higher on the lead extremity compared with the nonlead extremity ($P < 0.05$). In addition, maximal stress was lower on the lead extremity compared with the nonlead extremity at the proximal tendon level ($P < 0.05$). There was no side-to-side difference for deformation, strain, or Young’s modulus based on proximal, mid-, or distal tendon CSA. Stress and modulus were lower at the distal tendon compared with mid- and proximal tendon ($P < 0.01$) on both sides.

Mechanical properties at a common force are shown in Table 2. Tendon stiffness was higher on the lead extremity compared with the nonlead extremity ($P < 0.05$) (Fig. 3). Stress was lower on the lead extremity compared with the nonlead extremity at the proximal (Fig. 4) and distal tendon level ($P < 0.05$). There was no side-to-side difference for deformation, strain, or Young’s modulus based on proximal, mid-, or distal tendon CSA. Tendon stress and modulus were lower at the distal level compared with mid- and proximal tendon on both sides ($P < 0.01$). There was no difference in modulus when an average of the three levels of CSA was used (lead extremity 2.31 ± 0.29 GPa, nonlead extremity 1.99 ± 0.23 GPa).

DISCUSSION

The present study examined PT size and mechanical properties in subjects who had a side-to-side difference in knee extensor strength as a result of habitual sport-specific loading. The main findings were that the lead extremity, which was on average 22% stronger than the nonlead extremity, had a greater distal and proximal PT CSA, which was not evident at the mid-tendon level, indicating a region-specific tendon region-specific properties.
Table 1. Patella tendon mechanical properties based on maximum force

<table>
<thead>
<tr>
<th></th>
<th>Lead Extremity</th>
<th>Nonlead Extremity</th>
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</thead>
<tbody>
<tr>
<td>Force, N</td>
<td>6,886±833*</td>
<td>5,832±631</td>
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<tr>
<td>Deformation, mm</td>
<td>2.8±0.3*</td>
<td>3.1±0.4</td>
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<tr>
<td>Stiffness, N/mm</td>
<td>6.011±906*</td>
<td>4,436±570</td>
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<tr>
<td>Stress, MPa</td>
<td></td>
<td></td>
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<tr>
<td>Proximal tendon</td>
<td>62.1±5.1*</td>
<td>73.0±8.4</td>
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<tr>
<td>Mid-tendon</td>
<td>77.0±6.4</td>
<td>77.1±8.7</td>
</tr>
<tr>
<td>Distal tendon</td>
<td>47.9±4.8†</td>
<td>50.8±3.9†</td>
</tr>
<tr>
<td>Strain, %</td>
<td>5.5±0.5</td>
<td>6.1±0.6</td>
</tr>
<tr>
<td>Modulus, GPa</td>
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<td></td>
</tr>
<tr>
<td>Proximal tendon</td>
<td>2.88±0.35</td>
<td>2.76±0.33</td>
</tr>
<tr>
<td>Mid-tendon</td>
<td>3.65±0.53</td>
<td>2.92±0.34</td>
</tr>
<tr>
<td>Distal tendon</td>
<td>2.22±0.35†</td>
<td>1.98±0.28†</td>
</tr>
</tbody>
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*Values are means ± SE. †Significantly different from nonlead extremity, P < 0.05. ‡Significantly different from mid- and proximal tendon, P < 0.01.

Table 2. Patella tendon mechanical properties based on common force

<table>
<thead>
<tr>
<th></th>
<th>Lead Extremity</th>
<th>Nonlead Extremity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deformation, mm</td>
<td>2.5±0.3</td>
<td>3.0±0.4</td>
</tr>
<tr>
<td>Stiffness, N/mm</td>
<td>4,766±716*</td>
<td>3,494±446</td>
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<tr>
<td>Stress, MPa</td>
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</tr>
<tr>
<td>Proximal tendon</td>
<td>52.9±4.8†</td>
<td>66.0±8.0</td>
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<tr>
<td>Mid-tendon</td>
<td>65.6±5.6</td>
<td>71.2±8.2</td>
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<tr>
<td>Distal tendon</td>
<td>40.9±4.4‡</td>
<td>46.6±4.4‡</td>
</tr>
<tr>
<td>Strain, %</td>
<td>5.0±0.5</td>
<td>5.9±0.6</td>
</tr>
<tr>
<td>Modulus, GPa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal tendon</td>
<td>2.27±0.27</td>
<td>2.16±0.28</td>
</tr>
<tr>
<td>Mid-tendon</td>
<td>2.87±0.39</td>
<td>2.26±0.25</td>
</tr>
<tr>
<td>Distal tendon</td>
<td>1.79±0.25‡</td>
<td>1.54±0.19‡</td>
</tr>
</tbody>
</table>

*Values are means ± SE. †Significantly different from nonlead extremity, P < 0.05. ‡Significantly different from nonlead extremity, P < 0.01. ‡Significantly different from mid- and proximal tendon, P < 0.01.
fencers who had participated in their respective sport for several years. These sports involve a sport-specific loading whereby the athletes frequently perform rapid forward lunges with the preferred lead extremity, which places a considerable eccentric load on the knee extensors. In an elite badminton match, >70 such forward lunges may be performed on the lead extremity (C. Couppe, unpublished data). The sport-specific loading was substantiated by the sizeable side-to-side difference in strength (22%) and quadriceps CSA (7%), which was accompanied by a markedly greater tendon CSA (20–28%) of the lead extremity. The magnitude of the side-specific PT CSA (20–28%), and the lack thereof in recreational athletes, strengthens the notion that mechanical loading is associated with tendon hypertrophy as observed by Kongsgaard et al. (18). The magnitude of the CSA in the present study was similar to previous cross-sectional observations, suggesting that perhaps months to years of loading is required for tendon to hypertrophy, because only a smaller magnitude of tendon hypertrophy was observed after 12 wk of strength training in the Kongsgaard et al. study.

The data of the present study show that the PT on the lead extremity had a greater stiffness (36%) compared with the nonlead extremity (see Tables 1 and 2), whereas there was no significant difference in modulus. The load-assOCIATED increased in stiffness, and lack thereof in modulus, is in accordance with that recently found in young men following resistance training (18). However, others have demonstrated a marked increased in stiffness and modulus after strength training in elderly individuals (30, 31). Although these diverging findings are difficult to reconcile, they may partly be related to age and the method of determining mechanical properties (14). The present findings and those of Kongsgaard et al. (18) suggest that the change in mechanical properties in young men is largely a function of increased in size, rather than a material change, although this needs to be confirmed.

The present data show that the lead extremity had a greater PT CSA in the distal (20%) and proximal region (28%) but not in the midsection of the tendon. Furthermore, there were no PT CSA side-to-side differences in recreational athletes. The magnitude of this region-specific human tendon hypertrophy confirms and reinforces previous cross-sectional data (17, 24, 33) and more recent training data (18). Albeit speculative, perhaps compression in these regions contributes to the synthesis of extracellular matrix proteins in tendinous tissue (25, 32). The midsection of the tendon had the narrowest CSA and thus a greater average stress (~25%) for a given load. Yet, in contrast to the proximal and distal tendon, the middle part of the tendon did not significantly increase in CSA as a result of the sport-specific loading. Interestingly, many PT clinical conditions occur at the insertions (9, 10) where the tendon CSA is larger and where it appears most likely to hypertrophy, and therefore it is doubtful whether whole tendon region specific average stress (and “safety factor”) per se is the most important variable with respect to injury and adaptation. In contrast, the mid-tendon, which is rarely injured, did not appear to display a pronounced hypertrophy response, and it is therefore likely well designed for the imposed loads.

The knee extensor strength and tendon force of the nonlead extremity in the elite athletes in the present study are comparable to that of the recreational athletes examined herein and that reported by others (7, 18, 19). The PT deformation and strain in the present study (~3.1 mm, 5–6%) are also similar to previous reports (18, 38), but markedly different from that reported by others (~4.3 mm, ~9%) (7), which is likely related to dissimilarities in measurement methodology (14). In the present study, the average stress of the PT was 53–73 MPa. However, similar to previous reports (7, 29), the data show that the calculation of tendon stress will largely depend on where along the length of the tendon CSA is obtained. Nevertheless, the considerable variation in PT stress (30–91 MPa) reported in earlier studies (2, 14, 18, 29, 38) in the presence of reason-ably comparable tendon forces (5,600–7,000 N) is most likely a function of both measurement methodology (ultrasonography and MRI) and analysis method when MRI is used. The modulus values reported herein are comparable to previous animal data on isolated tendon (6, 11, 15), but they are noticeably higher than previously reported human in vivo data (2, 18, 38).

This discrepancy can most likely also be explained by the combination of differences in measuring deformation and CSA. It is noteworthy that the modulus at the proximal insertions is strikingly similar between the lead and nonlead extremity (Tables 1 and 2), which suggests that the sport-specific loading has not altered the material properties of the tendon, although this needs to be confirmed with other investigative techniques.

There are inherent limitations associated with the present study. The sample size was limited, which was in part a function of the study design and its inclusion criteria. Furthermore, the ultrasonography-based measurement technique does not permit assessment of region-specific deformation. This means that, although average stress can be calculated for specific location along the tendon, based on CSA, which varies considerably, modulus can only be estimated assuming homogenous deformation and strain along the tendon, which remains unknown in humans, in vivo. Estimating regional modulus for the tendon yielded similar values for the proximal and distal tendon, although the values for mid-tendon approached significance (P = 0.11), and they may have attained significance with a larger sample. Furthermore, albeit not possible with this particular group of athletes, a study design, including tendon biopsies, may have provided some more insight into the composition of the tendons.

In summary, the present study examined region-specific PT size and mechanical properties in subjects who display a side-to-side strength difference of 0.11), and they may have attained significance with a larger sample. Furthermore, albeit not possible with this particular group of athletes, a study design, including tendon biopsies, may have provided some more insight into the composition of the tendons.

In summary, the present study examined region-specific PT size and mechanical properties in subjects who display a side-to-side strength difference of ≥15% due to persistent sport-induced loading over several years. These subjects were examined in an attempt to partly circumscribe issues such as 1) training history, selection bias, and intersubject variations in cross-sectionally designed studies; 2) the relatively short duration of earlier training studies; and 3) the lack of assessment of region specificity in existing training studies. The data showed a regional variation in CSA along the PT, which markedly influenced average tendon stress. The habitually more loaded PT of the stronger extremity had a greater CSA compared with the contralateral side. The lead extremity also displayed greater stiffness than the contralateral side, whereas the modulus did not differ significantly. In sum, these data show that a habitual loading is associated with a robust change of the PT size and mechanical properties.
REFERENCES


