Effects of knee injection on skeletal muscle metabolism and contractile force in rats


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Summary

Objective: We tested the hypothesis that intrusion of the knee joint capsule alters quadriceps muscle metabolism and function independently from the damage induced to knee cartilage.

Methods: Adult rats were separated into four groups: intraarticular injections of saline (SAL; n = 9); intraarticular injections of papain, a model for osteoarthritis (PIA; n = 7); sham injections (SHAM; n = 8); and controls (CTL; n = 5). 31P magnetic resonance spectroscopy (31P-MRS) was performed after 2 weeks. Spectra were obtained from the left quadriceps: two at baseline, eight during electrical stimulation with simultaneous measurement of contractile force, and 15 during recovery. 31P-MRS data were presented as the ratio of inorganic phosphate (Pi) to phosphocreatine (PCr), concentrations of PCr [PCr], intramuscular pH, and the rates and time constants of PCr breakdown during stimulation and PCr recovery. Intramuscular cytokine concentrations were measured within the quadriceps. Histologic slides of the knees were scored for severity of cartilage damage.

Results: The interventional groups produced values of Pi/PCr ratio, [PCr], contractile force and pH that were significantly different from CTL. These changes in muscle function were accompanied by higher concentrations of interleukin-1 observed with PIA and SAL. We did not observe any effect of cartilage damage on muscle function or metabolism.

Conclusions: Knee joint intrusion alters quadriceps muscle metabolism with accelerated depletion of energy stores and fatigue during stimulation. This study demonstrates that needle intrusion into the knee joint results in muscle dysfunction, independently from the extent of cartilage damage.

Key words: Magnetic resonance spectroscopy, Skeletal muscle, Cartilage, Cytokine.

Introduction

Patient rehabilitation from knee injury, as a result of trauma, degenerative disease, and/or surgery, including minimally invasive procedures such as arthroscopy, is hindered by the onset of quadriceps weakness. Knee trauma has also been shown to increase the risk of osteoarthritis (OA)1,2, which is a leading cause of mobility limitations in late life3. The response of the quadriceps muscle group to joint damage has been attributed to alterations in muscle excitation, suggested to be a consequence of disuse atrophy as a result of pain4,5.

One paradigm for improving muscle function is to alleviate joint related pain. Nonsurgical strategies have been developed for reducing the pain associated with joint damage and more specifically OA6–7, all of which provide some degree of pain relief, allowing for more normal joint motion. Nonetheless, a reduction in pain associated with OA and other joint trauma does not necessarily improve muscle function8. Further investigation of quadriceps dysfunction, as it relates to joint trauma, is necessary to better understand the relationship between muscle function and joint health.

Phosphorus magnetic resonance spectroscopy (31P-MRS) has been used extensively to study the metabolic response of skeletal muscle to exercise9,10 and disease11–14. The attractiveness of this technique is its ability to identify phosphocreatine (PCr), adenosine triphosphate (ATP) and inorganic phosphate (Pi), which are integral to muscle bioenergetics. 31P-MRS measurements investigate the kinetics of the creatine kinase (CK) reaction. This reaction

\[\text{PCr}^2- + \text{MgADP}^2- + \text{H}^+ \rightarrow \text{MgATP}^2- + \text{Cr}\]

catalyzes the transphosphorylation between PCr and adenosine diphosphate (ADP). This is central to the regulation of
muscle bioenergetics through oxidative phosphorylation. Changes in Pi and PCr can be used with the CK reaction kinetic expression to indirectly reflect levels of ADP. Shifts in the frequency of the Pi peak can also be used to noninvasively measure intracellular pH. During exercise, the accumulation of lactic acid, a by-product of glycolysis, reduces the intramuscular pH, which accompanies muscle fatigue. In addition, $^{31}$P-MRS measurements may be acquired near real time, noninvasively, and in vivo. This allows investigators the opportunity to study skeletal muscle as a dynamic system without the use of more invasive techniques, e.g., biopsy punches. While $^{31}$P-MRS provides insight into the metabolism of skeletal muscle, measurements of cytokine concentrations are necessary for determining the presence of muscle inflammation which may occur as a result of patient illness.

Skeletal muscle has been recently reported to express pro-inflammatory cytokines. These cytokines, most notably interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-α, are known to initiate catabolic processes in skeletal muscle, which lead to atrophy. Muscle tissue response varies considerably between cytokines. In general, IL-1 and TNF-α have pro-inflammatory properties that initiate protein breakdown. IL-6, which is stimulated by elevated levels of IL-1 or TNF-α, initially serves as a pro-inflammatory cytokine in critically ill patients, but over time anti-inflammatory properties are manifested. These cytokines include the attenuation of the production of IL-1 and TNF-α and promote the production of other anti-inflammatory factors.

We conducted a study to test whether intraarticular knee injections, accompanied or not with patellar tendon damage, result in alterations in quadriceps muscle force and metabolism. $^{31}$P-MRS was used to monitor metabolic response to exercise, simultaneously with contractile force. In addition, cytokine concentrations within the quadriceps muscle group were measured to determine the presence of inflammation.

**Methods**

**ANIMAL MODELS**

This study was reviewed and approved by the National Institute on Aging Animal Care and Use Committee. Three-to-four-month-old female Fisher 344 rats (Harlan, Indianapolis, IN) were separated into four study groups: papain-induced arthritis (PIA, $n = 7$), saline-injected controls (SAL, $n = 9$), injection shams (SHAM, $n = 8$) and noninvasive controls (CTL, $n = 5$). Cartilage damage was induced in the PIA animals using Huang and colleagues’ protocol. A 4% papain solution was made by dissolving papain (Sigma–Aldrich, St. Louis, MO) into 10 ml of normal saline and filtrated through a bacterial filter. A 0.03 M cysteine solution was used as the activator. Ten microliters of papain and cysteine solutions were mixed for a total volume of 20 μl. The solution was injected into each knee via the patellar tendon using a 28 g needle. SAL and SHAM served as negative controls in this study. SAL animals were injected with 20 μl of sterile saline solution into each knee. SHAM animals underwent needle entry into the knee joint without injection of any fluid. Injections, including shams, were performed on days 1, 4 and 7 of the experiment. CTL animals were observed for 14 days without intervention. $^{31}$P-MRS and contractile force measurements were acquired simultaneously on the 14th day. The original group populations were six for CTL and nine for the intervention groups. CTL consisted of fewer animals, since no invasive procedures were performed. Some of the animals exhibited continued muscle contraction poststimulation. These contractions resulted in a slower rate of PCr and Pi recovery. Data from animals that showed signs of continued muscle contraction poststimulation were discarded. This resulted in the removal of one data set from CTL, one from SHAM and two from PIA.

**CONTRACTILE FORCE MEASUREMENTS**

All animals were anesthetized with 2% isoflurane/O2 by inhalation prior to and throughout $^{31}$P-MRS experimentation. While under anesthesia, the animals were placed supine and secured in a custom cradle. Two platinum electrodes, used for electrically stimulating the left quadriceps, were placed percutaneously into the lateral aspect of the proximal and distal quadriceps muscle group. Contractile force measurements were acquired by positioning the left knee at an angle of 90°, then attaching a ligature from the left ankle to a Grass FT 10 force transducer (Astro-Med, Inc., West Warwick, RI). The transducer was connected to a strain-gauge conditioner. Pulses of supra-maximal electrical stimulation were delivered from a Grass S11 (Quincy, MA) stimulator with a Grass SIU 5 stimulus isolation unit. The muscle was stimulated using two 200 μs biphasic pulses with an interval between the pulses of 200 ms and an interval between the pulse pairs of 2 s. Powerlab data acquisition hardware and software (AD Instruments, Colorado Springs, CO) were used to measure the developed force during electrical stimulation. Contractile force data were presented and analyzed as the force normalized to the initial force.

$^{31}$P-MRS

$^{31}$P-MRS was performed on the left quadriceps muscle group of each animal using a 1.9 T, 31 cm Bruker ABX Biospec. A custom single tuned two-turn elliptical surface coil, measuring 1.2 x 2.0 cm, was positioned over the left quadriceps muscle group and used for spin excitation and signal reception. Following placement of the surface coil, the animals were inserted within the magnet. Body temperature of the animals was maintained by blowing warm air through the magnet bore (Airtherm World Precision Instruments, Sarasota, FL). Field homogeneity was adjusted by shimming on water to proton line widths of 40–60 Hz. Signal excitation was performed using an adiabatic pulse, which generated a uniform flip angle of 90°. Throughout the duration of the experiment, spectra were acquired over a 1-min signal-averaging period, with a repetition time of 1 s. The protocol included a 2-min baseline period, an 8-min electrically stimulated exercise period, and a 15-min recovery period following cessation of stimulation. Resonance amplitudes were obtained from Lorentzian fits of the spectra.

Both qualitative and quantitative measures were employed for this study. Changes in the rate of ATP utilization were expressed as the ratio of Pi/PCr. As a result of the poor signal-to-noise of Pi at baseline and late in the recovery period, signal intensities were used for both PCr and Pi instead of concentrations. Signal intensities of Pi were assumed zero when within noise values, resulting in a Pi/PCr of zero. Due to sufficient signal-to-noise of PCr, cytosolic concentrations of PCr, [PCr] (mmol/L), were calculated. This was performed by normalizing the signal intensity of PCr by the signal intensity of PCr at baseline and
All calculations were performed using Matlab 7.0 (The MathWorks, Inc., Natick, MA).

Kinetic rate constants were acquired assuming a mono-exponential equation:

$$[\text{PCr}] = [\text{PCr}_0] + [\Delta \text{PCr}] \left(1 - \exp\left(-\frac{t}{T_c}\right)\right), \quad (1)$$

$[\text{PCr}_0]$ represents the initial steady-state concentration at time zero of the period, $[\Delta \text{PCr}]$ is the net change in the concentration during the analyzed period, and $T_c$ represents the time constant for the exponential change during the analyzed period. Coefficients were adjusted to provide the best fit of Eq. (1) to $[\text{PCr}]$ data during stimulation and the complete recovery period using a nonlinear least squares regression. The final data point of the previous period was included in the fits. Rates of change of $[\text{PCr}]$ during stimulation and recovery were calculated from the following expression:

$$R = \frac{[\text{PCr}_{\text{end}}]}{T_c}. \quad (2)$$

$R$ is the rate of change of the metabolite concentration and $[\text{PCr}_{\text{end}}]$ is the concentration of the metabolite at the end of the previous period. Finally, intramuscular pH was determined during electrical stimulation from the chemical shift ($\delta$) of the spectral peaks of Pi and PCr:

$$\text{pH} = 6.75 + \log \left(\frac{[\delta - 3.27]}{[5.69 - \delta]}\right). \quad (3)$$

All calculations were performed using Matlab 7.0 (The MathWorks, Inc., Natick, MA).

INTRAMUSCULAR CYTOKINE MEASUREMENTS

Following the $^{31}$P-MRS experiment, the animals were euthanized by isoflurane overdose. Blood samples were taken by cardiac puncture and centrifuged to separate out serum. The quadriceps muscle group was excised, washed and minced in sterile phosphate-buffered saline (PBS) then centrifuged to obtain the supernatant. Concentrations of IL-1, IL-6, and TNF-$\alpha$ were assayed in muscle supernatant using sandwich–enzyme-linked immunosorbent assay (ELISA) kits (BioSource International, Camarillo, CA). The individual cytokine concentrations from the quadriceps of the right and left legs were comparable; hence the average concentration was determined and used in subsequent analyses.

CARTILAGE DAMAGE ASSESSMENT

The knees of all animals were disarticulated, and the lateral and medial sides of the femoral and tibial plateaus were fixed with 10% neutral buffered formalin prior to histologic preparation. The knees were then decalcified using 20% ethylenediamine tetracetic acid (EDTA). The decalcified femur and tibia were embedded in paraffin, and then 5 $\mu$m microsections were prepared and stained with hematoxylin and eosin and with safranin O. The weight bearing regions of cartilage were scored using a scoring system (Table I) modified from Yoshimi et al. and Mankin et al. Each knee joint was assigned a severity grade (0–4) based on the presence or absence of each of the eight features in the tibial and femoral cartilage. Grade 0 joints exhibited no evidence of any of the features depicted in Table I. Grade 1 joints (mild) exhibited an uneven cartilage surface (flaking) and superficial fibrillation that did not extend beyond the intermediate layer. Grade 2 joints exhibited the additional feature of chondrocyte enlargement (increased ratio of the area of nucleus to cytoplasm in chondrocytes) and hyalinization (loss of normal staining). Joints with evidence of deep fibrillation extending beyond the intermediate zone and cartilage pitting were classified as Grade 3. Grade 4 joints exhibited evidence of cartilage loss in the intermediate or deep layers. All scoring was performed blinded by a single observer (Dr Gurkan).

STATISTICAL ANALYSIS

Results are presented as the means ± s.e.m. A two-way repeated-measures analysis of variance (rm-ANOVA) was used to determine group differences and group—time interactions (group $\times$ time) for Pi/PCr, $[\text{PCr}]$, pH, and contractile force normalized to initial force. Group comparisons of the rate and time constants for $[\text{PCr}]$ change during stimulation and recovery, cartilage damage grade and cytokine concentrations were analyzed using a two-way ANOVA. Finally, Pi, $[\text{PCr}]$, and pH were analyzed at each time point using an unpaired $t$ test. Statistical significance was assessed at $P < 0.05$. All statistical tests were performed using SPSS 14.0 statistical software (SPSS Inc., Chicago, IL).

Results

PIA exhibited the greater cartilage damage. OA score for PIA was approximately twice as high as animals that underwent needle insertion without injection of fluid (SHAM) or were injected with saline (SAL). Noninvasive controls (CTL) had a score that was an order-of-magnitude smaller than PIA (Table II). No obvious lameness or gait abnormalities were observed in any of the animals.

The ratio of the signal intensities of Pi and PCr (Pi/PCr) during baseline, electrical stimulation and early recovery is presented in Fig. 1. Initial stimulation of the quadriceps muscle

<table>
<thead>
<tr>
<th>Table I</th>
<th>\textbf{The characteristic pathological changes and joint grading of induced cartilage damage in the rat knee}</th>
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<tbody>
<tr>
<td>\textbf{Grade}</td>
<td>\textbf{0}</td>
</tr>
<tr>
<td>\textbf{Grade 0}</td>
<td>+</td>
</tr>
<tr>
<td>\textbf{Grade 1}</td>
<td>+</td>
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<tr>
<td>\textbf{Grade 2}</td>
<td>+</td>
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<tr>
<td>\textbf{Grade 3}</td>
<td>+</td>
</tr>
<tr>
<td>\textbf{Grade 4}</td>
<td>+</td>
</tr>
</tbody>
</table>

| Partial cartilage loss | + |
| Complete cartilage loss | + |
group resulted in a rapid increase in \( \text{Pi}/\text{PCr} \) for all groups. CTL attained a steady-state values of \( \text{Pi}/\text{PCr} \) (~2) before the interventional groups. SHAM and SAL generated similar results with statistically larger steady-state values of \( \text{Pi}/\text{PCr} \) (3.5 \( \pm \) 4.5) when compared to CTL. These statistical results were determined by both the \( t \) test at specific time points and rm-ANOVA over the entire stimulation period. PIA did not appear to reach steady-state values during stimulation. Instead, PIA showed a steady increase in \( \text{Pi}/\text{PCr} \). This resulted, as determined by rm-ANOVA, in insignificant differences with the other groups during stimulation. Nonetheless, PIA generated initial values of \( \text{Pi}/\text{PCr} \) that were significantly lower than SAL, and for later values significantly higher than CTL. During early recovery, CTL continued to produce statistically lower values of \( \text{Pi}/\text{PCr} \) than the remaining groups at specific time points and over the entire period (rm-ANOVA: \( P < 0.05 \)). One significant difference was observed between SHAM and SAL (rm-ANOVA: \( P < 0.05 \)). Few significant differences were observed between the interventional groups at discrete time points during early and late recovery. In general, CTL and PIA had the highest \( \text{Pi} \) throughout the experiment, whereas SHAM and SAL generated almost identical results with negligible differences observed at most time points.

The rates and time constants for \( \text{PCr} \) breakdown and recovery are reported in Table III. All groups showed similar rates and time constants for \( \text{PCr} \) breakdown during stimulation. The rate of \( \text{PCr} \) recovery, poststimulation, was higher in CTL than the interventional groups (\( P < 0.05 \)). This is partly attributed to the large \( \text{PCr} \) at the end of the stimulation period ([\( \text{PCr}_{\text{end}} \)] observed in CTL (Fig. 2). SHAM generated a significantly longer time constant for \( \text{PCr} \) recovery than CTL. Although, this was the only significant result, SAL and PIA had produced time constants 28% and 23%, respectively, longer than CTL.

Fig. 3 presents the intramuscular \( \text{pH} \) during electrical stimulation. Intramuscular \( \text{pH} \) was found to be significantly higher in CTL than in SAL and PIA (rm-ANOVA: \( P < 0.05 \)). Significant differences in \( \text{pH} \) were observed between CTL and both SAL and PIA for many of the individual time points. Only at the final two time points were CTL \( \text{pH} \) levels significantly higher than those observed in SHAM. No differences were observed between the interventional groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Severity score</th>
</tr>
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<tbody>
<tr>
<td>CTL</td>
<td>0.17 ( \pm ) 0.17</td>
</tr>
<tr>
<td>SHAM</td>
<td>1.25 ( \pm ) 0.31*</td>
</tr>
<tr>
<td>SAL</td>
<td>0.94 ( \pm ) 0.27</td>
</tr>
<tr>
<td>PIA</td>
<td>3.25 ( \pm ) 0.35*,</td>
</tr>
</tbody>
</table>

Table II: Histological scoring of cartilage damage severity in the knee of CTL, SHAM, SAL, and PIA animals. Scores from both right and left knees were pooled. Data are presented as means \( \pm \) S.E.M. * denote significance from CTL, SHAM, and SAL (\( P < 0.05 \)), respectively.
Contractile force normalized to initial force is presented in Fig. 4. All interventional groups showed a higher propensity for fatigue than CTL. Group \times time interactions, as determined by rm-ANOVA, were observed between CTL and the interventional groups ($P < 0.05$). In general, the quadriceps muscles of the interventional groups were capable of generating a relative contractile force comparable to CTL up to the 3rd minute of stimulation. By the end of stimulation, relative contractile forces in the interventional groups were approximately 20% less than CTL. For the interventional groups, only SHAM and SAL produced statistically different trends (rm-ANOVA: $P < 0.05$), with SAL producing the lowest relative force at the end of stimulation.

Intramuscular cytokine concentrations are presented in Table IV. SAL and PIA exhibited significantly higher levels of IL-1 concentrations than CTL and SHAM. All interventional groups produced higher concentrations of IL-6 than CTL ($P < 0.05$). Between the interventional groups, SAL produced more IL-6 than SHAM ($P < 0.05$). TNF-\(\alpha\) concentrations were similar between each of the four groups. Although not presented, serum cytokine concentrations were consistent between all groups.

**Discussion**

We demonstrated using an animal model that intervention of the knee joint exerts profound effects on muscle metabolism and contractile function. The magnitude of the changes induced in muscle metabolism and contractile force was neither associated with extent of cartilage damage, nor did it differ between injection of an activated papain solution, injection of saline, or intervention with an empty needle. However, injection with papain and saline both induced an inflammatory response in the quadriceps muscle that was not observed with needle intervention alone.

\(^{31}\)P-MRS and contractile force data revealed that muscle fatigue was prevalent in the interventional groups when compared to CTL. Metabolic indices of muscle fatigue include increased acidosis and excessive depletion of PCr reserves during exercise \cite{20,31}. All of these indices were more pronounced in the interventional groups than in CTL. In addition, the interventional groups generated contractile force 20% lower than CTL by the end of stimulation. Though fatigue was common in SHAM, SAL and PIA, the rate and time constant for PCr breakdown were

<table>
<thead>
<tr>
<th>Group</th>
<th>Rate of PCr breakdown (mM min(^{-1}))</th>
<th>Time constant for PCr breakdown (min)</th>
<th>Rate of PCr recovery (mM min(^{-1}))</th>
<th>Time constant for PCr recovery (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTL</td>
<td>-22.45 ± 1.43</td>
<td>1.43 ± 0.09</td>
<td>4.77 ± 0.70</td>
<td>2.74 ± 0.19</td>
</tr>
<tr>
<td>SHAM</td>
<td>-21.73 ± 1.60</td>
<td>1.50 ± 0.07</td>
<td>2.09 ± 0.56*</td>
<td>4.27 ± 0.43*</td>
</tr>
<tr>
<td>SAL</td>
<td>-22.09 ± 1.73</td>
<td>1.53 ± 0.14</td>
<td>2.00 ± 0.52*</td>
<td>3.51 ± 0.30</td>
</tr>
<tr>
<td>PIA</td>
<td>-22.98 ± 2.34</td>
<td>1.57 ± 0.13</td>
<td>2.41 ± 0.66*</td>
<td>3.37 ± 0.42</td>
</tr>
</tbody>
</table>
similar to values observed in CTL. In contrast, CTL generated a higher rate of PCr recovery than the interventional groups. This is partly explained by the elevated levels of [PCr_{end}] found in CTL than SHAM, SAL and PIA (28%, 48% and 41%, respectively). Hence, CTL had the shortest time constant for PCr recovery with values 56% ($P < 0.05$), 28% and 23% smaller than those of SHAM, SAL and PIA, respectively. Replenishment of PCr reserves following exercise is dictated solely by oxidative phosphorylation\textsuperscript{16}. Our results suggest that CTL has a higher oxidative capacity than the remaining groups, which may rely more heavily on glycolytic processes.

Differences in metabolism and contractile force between the interventional groups were not as pronounced as to the differences between the interventional groups and the CTL. Nonetheless, PIA animals, which exhibited a significantly higher score for cartilage damage (Table I) than the other groups, displayed subtle variations in metabolism compared to what was observed in SHAM and SAL. The most notable was the gradual increase and decrease,
respectively, in Pi/PCr and [PCr] during stimulation. Similar profiles were not observed in any other group. The slow progress to steady-state of Pi/PCr and [PCr] resulted in very few significant differences between PIA and the other groups. By the 6th minute of stimulation, Pi/PCr and [PCr] of PIA were comparable to CTL values; by the 10th minute they were in the range of SHAM and SAL. PIA was found to have significantly higher values of [PCr] than SAL, as determined by rm-ANOVA. This statistical result was also observed during early recovery, with negligible differences in PIA values of Pi/PCr and [PCr] to CTL and SHAM. Contractile force and the remaining 31P-MRS measurements did not differ between PIA and the other interventional groups. In contrast, SAL generated higher and lower values of Pi/PCr and [PCr], respectively, than any other group. This group also produced the lowest level of contractile force.

### Table IV

<table>
<thead>
<tr>
<th>Group</th>
<th>IL-1 (pg/ml)</th>
<th>IL-6 (pg/ml)</th>
<th>TNF-α (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTL</td>
<td>523 ± 116</td>
<td>87 ± 8</td>
<td>99 ± 12</td>
</tr>
<tr>
<td>SHAM</td>
<td>629 ± 86</td>
<td>201 ± 25*</td>
<td>100 ± 15 (7/8)</td>
</tr>
<tr>
<td>SAL</td>
<td>925 ± 75*†</td>
<td>317 ± 34*†</td>
<td>124 ± 17</td>
</tr>
<tr>
<td>PIA</td>
<td>950 ± 88*†</td>
<td>254 ± 39*†</td>
<td>106 ± 11 (5/7)</td>
</tr>
</tbody>
</table>

The extent of this shift between the interventional groups cannot be ascertained from our experiments. Nonetheless it is clear that quadriceps dysfunction in SAL and PIA, as observed from cytokine concentrations, has progressed beyond what was seen in SHAM. A possible condition that may have contributed to our results is the presence of joint pain associated with tendon tenderness. Tenderness of the patellar tendon may have occurred from the repeated entry of the needle through the patellar tendon. This may have caused joint pain, which would lead to a decrease in physical activity and eventual muscle wasting. Patellar tendinopathy, which is typically characterized by achin pain localized to the bone–tendon interface, has been shown to result in a decrease in muscle size and force in patients with chronic symptoms. Similarities in metabolism and contractile force between the interventional groups, and their differences from CTL, could be explained by muscle atrophy. This would be a consequence of inactivity due to joint pain associated with tenderness of the patellar tendon. Elevated levels of IL-1 in SAL and PIA, when compared to CTL and SHAM, suggest alterations in muscle tissue beyond what was caused by joint pain associated with tendon tenderness.

Distention of the knee joint capsule, as a result of fluid accumulation in the joint following injection or inflammation, may have also contributed to the dysfunction of the quadriceps in SAL and PIA. Quadriceps avoidance gait patterns were reported by Torry et al., in healthy subjects after an intraarticular injection of saline (60 μl) into the knee joint capsule. These modified gait patterns were shown to be the result of knee joint capsular distension by intraarticular knee joint effusion, and not due to pain or any surgical procedure. In addition to the modification in gait, quadriceps weakness was also prevalent in subjects with distended joints. SAL and PIA may have developed modified gait patterns as a result of capsular afferent activity stimulated by joint capsular distension, which may have influenced muscle function.

This study was performed to demonstrate the relationship between quadriceps function and the deterioration of knee joint health. The presence of cartilage damage did not contribute significantly to the muscle dysfunction observed in this study. A possible explanation may be that cartilage damage severity was not significant enough to elicit a response. Due to the type of QIA model used and experiments performed in our study, it is difficult to directly compare our results to those from other clinical or animal studies. In addition, we could not explain why SHAM generated a significantly longer PCr recovery time constant than CTL, whereas SAL and PIA did not. Nonetheless, we have shown that needle intrusion of the joint capsule through the patellar tendon had a profound effect on quadriceps metabolism and contractile force. The additional injection of fluid, either saline or papain activated solution, into the joint space appeared to cause a localized inflammatory response in the quadriceps muscle group. To our knowledge, this is the first demonstration of an intramuscular inflammatory response as a result of an invasive procedure to the joint capsule. While we cannot definitely rank our findings to patellar tenderness or joint distension, our results clearly highlight the strong interrelationship between proper muscle function and joint health.

In conclusion, our data suggest that invasive procedures into the joint capsule have a profound effect on muscle function. Although it would not be appropriate to generalize our findings to humans, it is conceivable that surgical
intervention of the knee could affect quadriceps muscle function in humans. Given the frequent use of arthroscopy in the management of patients with knee injury and OA, the effects of intervention upon the knee joint on quadriceps muscle function should be investigated. Knowledge of muscle response to arthroscopic intervention of the joint space may help in developing therapies specifically designed for both joint and muscle health.

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References


