Reflex and Intrinsic Changes Induced by Fatigue of Human Elbow Extensor Muscles

LI-QUN ZHANG1-4 AND W. ZEV RYMER1,2,4,5
1Sensory Motor Performance Program, Rehabilitation Institute of Chicago; and 2Department of Physical Medicine and Rehabilitation, 3Department of Orthopaedic Surgery, 4Department of Biomedical Engineering, and 5Department of Physiology, Northwestern University, Chicago, Illinois 60611

Received 16 February 2001; accepted in final form 9 May 2001

Zhang, Li-Qun and W. Zev Rymer. Reflex and intrinsic changes induced by fatigue of human elbow extensor muscles. J Neurophysiol 86: 1086–1094, 2001. Fatigue-induced changes in intrinsic and reflex properties of human elbow extensor muscles and the underlying mechanisms for fatigue compensation were investigated. The elbow joint was perturbed using small-amplitude and pseudorandom movement patterns while subjects maintained steady levels of mean joint extension torque. Intrinsic and reflex properties were identified simultaneously using a nonlinear delay differential equation model. Intrinsic joint properties were characterized by measures of joint stiffness, viscous damping, and limb inertia and reflex properties characterized by measures of dynamic and static reflex gains. Fatigue was induced using 15 min of intermittent voluntary isometric (submaximal) exercise, and a rest period of 10 min was taken to allow the fatigued muscles to recover from acute fatigue effects. Identical experimental and data analysis procedures were used before and after fatigue. Our findings were that after fatigue, joint stiffness was significantly reduced at higher torque levels, presumably reflecting the reduced force-generating capacity of fatigued muscles. Conversely, joint viscosity was increased after fatigue potentially because of the reduced cytosolic acidosis accompanying fatigue. Static stretch reflex gain decreased significantly at higher torque levels after fatigue, indicating that the isometric fatiguing exercise might be associated with a preferential change in properties of spindle chain fibers and bag2 fibers. For matched pre- and postfatigue torque levels, dynamic reflexes contributed relatively more torque after fatigue, displaying higher dynamic reflex gains and larger dynamic electromyographic responses elicited by the controlled small-amplitude position perturbations. These changes appear to counteract the fatigue-induced reductions in joint stiffness and static reflex gain. The compensatory responses could be partly due to the effects of increasing the number of active motoneurons innervating the fatiguing muscles. This shift in operating point gave rise to significant compensation for the loss of contractile force. The compensation could also be due to fusimotor adjustment, which could make the dynamic reflex gain much less sensitive to fatigue than intrinsic stiffness. In short, the reduced contribution from intrinsic stiffness to joint torque was compensated by increased contribution from dynamic stretch reflexes after fatigue.

INTRODUCTION

Neuromuscular fatigue impairs the force-generating capacity of muscles. It is experienced both in everyday physical exercise and in pathological states, such as neurological and muscular disease. During fatigue induced by sustained maximal voluntary contraction (MVC), there is known to be progressive reduction in voluntary muscle force, a reduction in muscle fiber conduction velocity, a prolongation in muscle twitch contraction, a decline in electromyographic (EMG) amplitude, and a shift of EMG power spectra toward the lower frequencies (Bigland-Ritchie et al. 1983; De Luca 1984; Enoka and Stuart 1992). To reach the same submaximal level of force after fatigue, muscle EMG amplitude increases, reflecting the increased unitary recruitment and firing rates required to compensate for the contractile failure (Kirsch and Rymer 1992; Merletti et al. 1990). Despite significant progress in research on muscle fatigue, it is not very clear what are the mechanisms underlying neuromuscular fatigue or at which of the possible sites it occurs (Bigland-Ritchie and Woods 1984). Accordingly, our objective here was to assess the interactions between fatigue-induced changes in intrinsic muscle mechanical and electrical properties and the resulting neurological compensatory responses.

Several studies indicate that both the intrinsic and reflex actions may be affected by muscle fatigue and that neural control mechanisms may be adapted to compensate for the loss of contractile force (Bigland-Ritchie and Woods 1984; Enoka and Stuart 1992). For example, evidence has been provided that during fatigue, motoneuron firing rates may be regulated by a peripheral reflex originating in muscle afferent responses to fatigue-induced changes within the muscle (Balestra et al. 1992; Bigland-Ritchie et al. 1986b; Garland and McComas 1990; Garland et al. 1988; Windhorst and Boorman 1995; Woods et al. 1987). However, it is not very clear how different types of afferents contribute to the reflex inhibition during fatigue (Garland and Kaufman 1995). Some considered that intrinsic muscle and motoneuron properties are most important (Enoka et al. 1992; Kernell 1995; Kernell et al. 1987). Others argued that force-feedback mediated through Golgi tendon organs was significant and helped to reduce the sensitivity of the overall neuromuscular system to fatigue (Kirsch and Rymer 1987, 1992).

Accordingly, the objectives of the present study were to evaluate intrinsic and reflex changes induced by muscle fatigue...
and the associated neural compensatory mechanisms. Roles of dynamic and static stretch reflexes during muscle fatigue were also investigated. Experiments were performed by applying controlled perturbations to human elbow extensor muscles in which fatigue was induced using voluntary intermittent submaximal isometric contractions. Both reflex and intrinsic properties were identified simultaneously using a novel nonlinear delay differential equation (NDDE) model. This model provided a useful tool to differentiate intrinsic and reflexive components of neuromuscular action, to quantify the changes induced by fatigue, and to gain insights into the mechanisms underlying contractile failure. Preliminary results of the study have been presented in conference proceedings (Zhang and Rymer 2000).

**Methods**

Five normal subjects (aged 25–40 yr) without prior history of neurological disorders or musculoskeletal injuries participated in this study. The study was approved by the Institutional Review Committee. All subjects gave informed consent before participating in the experiment. A standard perturbation sequence was applied to the elbow joint to manifest intrinsic and reflex properties before and after fatigue. Fatigue-induced intrinsic and reflex changes were quantified using an NDDE model (Zhang and Rymer 1997).

**Experimental setup**

An elbow joint driving device was used to flex and extend the elbow joint in a closely controlled manner (Fig. 1). The device was driven by a brushed DC servomotor (Cleveland Machine Controls F563). A digital controller using a Texas Instruments TMS320 digital signal processor was developed to control the servomotor. The distal forearm, wrist, and proximal hand of the subject were encased in a polymer cast and secured to the motor shaft through an aluminum beam located beneath the forearm. The motor shaft was set perpendicular to the ground and was aligned with the elbow flexion/extension axis. The elbow was perturbed in the horizontal plane with the beam and forearm parallel to the ground, and thus the gravitational force was constant. During the random angular position perturbations, the subject either remained relaxed or voluntarily generated a designated level of background muscle torque. The difference between the target torque and the measured background muscle torque was displayed in real-time on a computer monitor, and the subject was asked to keep the mean of this matching error at zero throughout a trial.

**Perturbation sequences**

To fully characterize intrinsic and reflex properties of the elbow neuromuscular control system, the joint needs to be perturbed appropriately to manifest both types of properties simultaneously. On the one hand, the bandwidth of the perturbation signal needs to be high so that the joint neuromuscular system receives persistent excitation (Söderström and Stoica 1989) and the subjects can maintain a steady “background” or mean muscle torque during the random perturbations. On the other hand, the bandwidth should be low enough to avoid potential vibratory suppression of reflex muscle activation or impairing muscle contractility (Zhang and Rymer 1997). In addition, the perturbation amplitude needed to be both small enough to avoid inducing severe system nonlinearities and yet large enough to obtain high signal-to-noise ratio. Various perturbation sequences and signal processing procedures were tested. A band-limited Gaussian white-noise sequence with a bandwidth of 6 Hz, and an amplitude standard deviation $\sigma = 1.5^\circ$ was chosen because it was appropriate to elicit both intrinsic and reflex actions. The subjects were generally able to maintain steady background muscle torques during a perturbation trial.

**Joint perturbation protocol**

The subject sat upright in a customized seat. Initial elbow flexion was held at 90°, and the forearm was in the neutral position (0° supination). Shoulder abduction and flexion angles were 90 and 15°, respectively. Elbow flexion angle, perturbing torque, and EMG signals from the lateral, medial, and long heads of the triceps, anconeus, and biceps muscles were recorded during each trial. A rest period of 10 min was then permitted to allow the joint neuromuscular system to receive sustained excitation while the subject was able to recover from the acute fatigue effects. After the

![FIG. 1. Experimental setup for elbow joint perturbation. The motor was mounted on the supporting frame with the motor shaft pointing upward and aligned with the elbow flexion axis. As a safety procedure, the safety screws were used as mechanical stops to restrict the motor range of motion during the perturbation. A torque sensor was mounted between the motor shaft and the aluminum beam. The cast was fixed to the aluminum beam through the coupling. Target matching error was displayed on the computer monitor for real-time background muscle torque target matching during the perturbation trials.](http://jn.physiology.org/doi/10.1152/jn.00761.2000)
rest, the torque and EMG signals were recorded again at both quiescent and MVC levels, as was done before fatigue, to evaluate changes induced by fatigue. Then the same perturbations were repeated using the same levels of muscle torque as were used in the prefatigue period. After perturbation trials, the cast and padding were put back on the elbow-driving device and the same perturbation sequence was repeated, to help determine the inertia of the attachments. Inertia was estimated from these trials, and the difference between the total inertia and attachment inertia was attributed to the limb inertia itself.

**Induction of muscle fatigue**

Muscle fatigue was induced through intermittent submaximal voluntary contraction (Bigland-Ritchie et al. 1986c; Dolmage and Cafarelli 1991). A target torque was displayed on a computer monitor, and the subject was asked to generate a specified level of target torque (muscle force). The thresholds in Eq. 1 were taken as zero in this study for simplicity.

For physiological interpretation of the mathematical model, the NDDE model was represented by physical components (Fig. 2). The top part of Fig. 2 represents the intrinsic muscle (joint) properties, where $K(l)$ and $B(l)$ are the joint elastic stiffness and viscosity, respectively. The bottom part represents the reflex feedback properties of the muscles crossing the joint. In addition to the intrinsic muscle and joint properties, the three position reflex parameters, $r_p(l,d_{1}), r_s(l,d_{2}),$ and $K_d(l,d_{1})$, characterize the stretch reflex actions that are caused by the angular perturbation occurred $d_{1}$ seconds ago. Notice that $r_p(l,d_{1})$ and $r_s(l,d_{2})$ correspond to unidirectional velocity of stretching and shortening, respectively.

A *continuous-time* system identification method was developed to help estimate parameters of the NDDE model directly from sampled data while retaining realistic physical or physiological interpretations. Since the limb and attachment inertia was not affected by fatigue and muscle contraction, the inertia was estimated separately using trials during which the subject was relaxed without any voluntary contraction. The inertia component was dominant in such trials and thus the inertia could be determined more accurately. The estimated inertia was taken as a known constant in subsequent determination of other parameters, which simplified the task and made estimation of other parameters more reliable (Zhang and Rymer 1997). Reflex loop delay $d_{1}$ was also determined separately by tapping the triceps tendon using an instrumented hammer with tapping force recorded and measuring

**Stretch reflexes** are modeled nonlinearly with both dynamic and static reflex gains and with the inherent asymmetry for stretch and release identified. $r_p(l), r_s(l),$ and $K_d(l)$ describe the effects of past positive angular velocity, past negative angular velocity, and past position deviation on current torque, respectively. $d_{1}$ corresponds to the delay from flexion angle change (mainly through the muscle spindles activation) to the reflex contribution to the joint torque. Time delays on both the afferent and efferent sides and the neuromechanical delay are merged and represented by the single time delay $d_{1}$, and $\delta_p$ and $\delta_s$ represent the angular velocity thresholds under which the dynamic flexing and extending of the joint cause virtually no reflexive joint torque (muscle force). The thresholds $\delta_p$ and $\delta_s$ in Eq. 1 were zero for simplicity.

**Simultaneous identification of intrinsic and reflex changes induced by muscle fatigue**

A method was developed recently to help characterize the naturally co-existing intrinsic and reflex actions of muscles and joint in an integrated model (Zhang and Rymer 1997). The elbow joint torque recorded during the random perturbations was determined by both the intrinsic and reflex actions of the elbow muscles and joint. A major difference between the intrinsic and reflex contributions is that the reflex responses are significantly delayed by the reflex loop. The following NDDE model was used with the delayed and nondelayed terms describing the joint reflex and intrinsic actions, respectively:

$$I(l)\ddot{\theta}(t) + B(l)\dot{\theta}(t) + r_p(l)R_p(\theta(t) - \theta_0)\delta_p + r_s(l)R_s(\theta(t) - \theta_0)\delta_s + K(l)\Delta \dot{\theta}(t) + K_d(l)\Delta \theta(t) - t_{ud} = \Delta T(t) + e(t) \quad (1)$$

where $\theta(t)$ is the elbow flexion angle (0° corresponds to full extension) and $T(t)$ the joint perturbing torque. $\Delta \dot{\theta}(t)$ is the deviation from the initial 90° elbow flexion during the small-amplitude random perturbation and $\Delta T(t)$ is the corresponding deviation of joint torque. $I(l)$ is the limb inertia about the elbow flexion axis, $B(l)$ the joint viscosity (usually represented by a dashpot generating resistance proportional to the movement velocity), and $K(l)$ the joint elastic stiffness (usually represented by a spring with its resistance proportional to the spring length change) (Zhang et al. 2000a). $\lambda$ is the operating state that includes the mean joint angle, mean background muscle torque, average fusimotor activity, perturbation bandwidth, and amplitude, and degree of fatigue. $e(t)$ is the modeling error.
the reflex torque response at the elbow (Zhang and Rymer 1997; Zhang et al. 1999, 2000b). The delay from the start of the tapping force to the onset of reflex-mediated elbow extension torque was taken as the reflex loop delay $t_{d1}$.

The same NDDE model of Eq. 1 was used to characterize intrinsic and reflex properties under both pre- and postfatigue conditions. Comparison between the closely matched pre- and postfatigue states provided us with a quantitative tool to gain insights into muscle fatigue.

Fatigue-induced changes in muscle EMG signals

The sampled EMG signal was full-wave rectified and low-pass filtered to obtain the linear envelope (LE). The relationship between the mean EMG LE (representing the average muscle activation) and the mean joint background muscles torque across the different perturbation trials with different levels of background muscle torque was compared between the before and after fatigue conditions to evaluate fatigue-induced change in muscle activation. Furthermore, the computer-controlled small-amplitude position perturbation was a major factor contributing to the variation of the EMG LE during the small-amplitude perturbation. Under closely matched pre- and postfatigue condition with the identical small-amplitude perturbation (as the simulation input of the system), change in the variation of the EMG LE (as the system output) reflected the change in the dynamic stretch reflex gain of the neuromuscular system involved. Therefore change in the variation of the EMG LE was compared before and after fatigue to evaluate the change in the dynamic stretch reflex gain.

RESULTS

General features

Subjects maintained steady “background” or mean muscle torque during the perturbations. For comparable levels of contraction pre- and postfatigue, both the mean and variance of the extensor EMG activity during the perturbation increased after fatigue (Fig. 3). The highest target torque in extension (−50% of the flexion MVC) corresponded to a maximal extension target torque ranged from 56 to 74% of the corresponding extension MVC for the subjects tested. After fatigue, the subjects could no longer generate as much torque and the target torque matching was performed within their torque-generating capacity. Fatigue-induced changes in intrinsic and reflex properties were investigated in comparable ranges of joint torque.

Effects of fatigue on muscle strength

Muscle strength was recorded as maximum joint torque at the beginning of the experiments. The second and third columns in Table 1 give the MVC torques in the flexion and extension directions respectively. The flexion MVC was always higher than the extension MVC, indicating the extensor muscles are routinely weaker than the flexors (Kulig et al. 1984; Singh and Karpovich 1968).

The intermittent isometric extension proved to be a rather effective exercise to fatigue the elbow extensor muscles. Figure 4 shows the elbow extension torque and EMG signals of multiple extensor and flexor muscles during the first 80 s of the exercise. The target torque was set at 60% of the extension MVC. When the subjects could no longer generate the desired level of elbow extension torque during the later portion of the exercise session, they were asked to produce their MVC torque at that time. The finding of increased amplitude of EMG signals near the end of the 80 s (as compared with the EMG signals at the beginning of the exercise) indicates that there was increased motor unit activation during fatigueing contraction (Fig. 4). After the intense fatiguing exercise of elbow extension, the MVC levels (listed in the 3rd–5th columns of Table 1) verify that the elbow extensor MVC decreased substantially with the reduction ranging from about 40–66%.

Effects of fatigue on muscle EMG signal spectrum

As the fatigue exercise progresses, for a given torque level, the power spectrum of the EMG signals increased in amplitude and was shifted toward the lower frequency (Fig. 5). This short-term fatigue effect was modified by a rest period after the fatiguing exercise. For matched torque, the postfatigue EMG amplitudes were higher than their prefatigue counterparts due to the increased motor unit recruitment required to achieve the desired torque; however, the postfatigue EMG spectrum did not display the leftward frequency shift as compared with the prefatigue signal. This is presumably because the 10-min rest period after the fatiguing exercise allowed restitution of muscle fiber conduction velocity to normal levels without permitting significant recovery of contractile force.

Effects of fatigue on joint stiffness and static stretch reflex gain

Figure 6A shows the variation in joint stiffness $K$ and in static stretch reflex gain $K_s$ as functions of the background joint torque. Both $K$ and $K_s$ reflect the torque responses caused by changes in elbow flexion angle, and they have the same unit. Their differences lie in that $K$ describes the intrinsic mechanical properties of muscle and $K_s$ the delayed reflex actions. As shown in Fig. 6A, both $K$ and $K_s$ were reduced after fatigue.
However, because of severe muscle fatigue, the subject could no longer maintain elbow extension torques 25 N/m, and thus postfatigue $K$ and $K_d$ curves were estimated over a narrower range of background muscle torque. Nonetheless it is evident that the difference between the pre- and postfatigue stiffness in Fig. 6A increases gradually with the background muscle torque. In other words, the stiffness reduction became larger as the level of muscle contraction increased.

Fatigue-induced reductions in joint stiffness were observed consistently across all subjects. Figure 7A shows the change in joint stiffness as a function of background muscle torque for five subjects. Student’s $t$-tests of paired difference were performed at each specified level of background muscle torque to check whether joint stiffness was reduced significantly after fatigue. Statistical analysis shows that fatigue-induced stiffness reduction was significant for background muscle torques 1 N/m (significance level $P < 0.05$).

### Effects of fatigue on joint viscosity

The severe muscle fatigue induced in this experiment also caused changes in joint viscosity. As shown in Fig. 6B for one subject, joint viscosity increased measurably after fatigue. The difference between the pre- and postfatigue viscosity in Fig. 6B increased gradually with increasing background muscle torque. Figure 7B shows the fatigue-induced change in joint viscosity averaged over all subjects. Student’s $t$-test with paired comparison indicates that postfatigue joint viscosity increases significantly for background muscle torques 12 N/m ($P < 0.05$).

### Effects of fatigue on dynamic stretch reflex gain

The calculated dynamic stretch reflex gains for stretching ($r_p$) and shortening ($r_n$) the contracting elbow extensor muscles are shown in Fig. 6C. The $r_p$ and $r_n$ before and after fatigue are displayed as functions of the background elbow extensor contraction. Figure 7, C and D, gives the changes in $r_p$ and $r_n$ for all five subjects.

### Table 1. MVC and inertia measurement before and after fatigue

<table>
<thead>
<tr>
<th>Subject</th>
<th>Flexion MVC, N/m</th>
<th>Pre-Fatigue Extension MVC, N/m</th>
<th>Post-Fatigue Extension MVC, N/m</th>
<th>Post-/Pre-Fatigue Extension MVC</th>
<th>Total Inertia, kg · m²</th>
<th>Attachment Inertia, kg · m²</th>
<th>Limb Inertia, kg · m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>71.7</td>
<td>51.9</td>
<td>27.3</td>
<td>0.526</td>
<td>0.096</td>
<td>0.029</td>
<td>0.067</td>
</tr>
<tr>
<td>B</td>
<td>62.8</td>
<td>54.4</td>
<td>32.6</td>
<td>0.599</td>
<td>0.101</td>
<td>0.030</td>
<td>0.071</td>
</tr>
<tr>
<td>C</td>
<td>77.3</td>
<td>54.1</td>
<td>20.8</td>
<td>0.385</td>
<td>0.098</td>
<td>0.025</td>
<td>0.073</td>
</tr>
<tr>
<td>D</td>
<td>65.1</td>
<td>58.3</td>
<td>34.0</td>
<td>0.583</td>
<td>0.100</td>
<td>0.032</td>
<td>0.068</td>
</tr>
<tr>
<td>E</td>
<td>72.8</td>
<td>49.4</td>
<td>16.7</td>
<td>0.338</td>
<td>0.107</td>
<td>0.031</td>
<td>0.076</td>
</tr>
<tr>
<td>Mean</td>
<td>69.9 ± 5.9</td>
<td>53.6 ± 3.3</td>
<td>26.3 ± 7.5</td>
<td>0.486 ± 0.118</td>
<td>0.100 ± 0.004</td>
<td>0.029 ± 0.003</td>
<td>0.071 ± 0.004</td>
</tr>
</tbody>
</table>

Values are means ± SD. Where the fifth column gives the ratio of the post-fatigue elbow extension maximal voluntary contraction (MVC) (the 4th column) over the pre-fatigue extension MVC (the 3rd column). The total inertia in the sixth column represents the sum of the attachment (the cast and aluminum beam) inertia and the limb inertia itself.
averaged for multiple subjects, respectively. Paired t-tests show that the dynamic reflex gain for stretching the contracting elbow extensor muscles is significantly higher than the dynamic reflex gain before fatigue for background muscle torque \(10\) N/m \((P, 0.05)\). To reach the same mean level of background muscle torque after fatigue, the subject relied more on the dynamic stretch reflex and augmented the gain significantly. On the other hand, there is no significant fatigue-induced change in dynamic reflex gain for muscle shortening.

The increase in the dynamic reflex gain shown in the preceding text was corroborated by an increase in the variance of the EMG LE elicited by the small-amplitude perturbations. These perturbations were controlled by the servomotor so as to impose identical movements before and after fatigue (Fig. 8). Paired t-tests showed that the standard deviation of the EMG LE was significantly higher after fatigue than that before fatigue for background torque \(>4\) N/m. The postfatigue increase in the variation of the EMG LE was associated with concurrent increase in the mean EMG amplitude (Fig. 8), which was increased significantly for joint torque \(>2\) N/m, indicating stronger effort needed to reach the same level of joint torque after fatigue (Kirsch and Rymer 1992; Merletti et al. 1990). Both the increased variance of the EMG LE and the increased mean EMG LE could be observed over comparable levels of pre- and postfatigue background muscle torque (Fig. 3).

**DISCUSSION**

The NDDE model provides us with a useful method to quantify reflex and intrinsic mechanical changes caused by muscle fatigue with the model parameters estimated through in vivo experiment on human subjects. The perturbation experiment and the fatigue exercise were done using the same device with the arm fixed to the device at the same posture throughout the whole experiment. The closely matched pre- and postfatigue experimental conditions and identical analysis procedure minimized potential errors and allowed us to estimate the model parameter and their pre- and postfatigue differences more reliably. The results showed that long-lasting contractile fatigue caused changes in both reflex and intrinsic properties of the neuromuscular system especially at higher levels of muscle.
contraction when compensation for fatigue was potentially more important. The compensatory mechanism was reflected in the fatigue-induced changes in the relative contributions of the different intrinsic and reflex components.

We found that the intrinsic stiffness ($K$) was reduced after fatigue and that the stiffness reduction became more severe at the higher background muscle torque. Such a reduction in intrinsic stiffness presumably reflected the reduction in stiffness of the contractile elements and indicates that after fatigue, sarcomere crossbridges could not produce as much net force as they did before fatigue for the same amount of external stretch of muscle fibers (Edman and Lou 1990, 1992). It should be noted that the pre- and postfatigue stiffness comparisons were done at matched mean levels of joint torque. This indicates that even with stronger levels of activation (that are required to reach the same level of torque), the fatigued muscles produced lower stiffness than its prefatigue control.

It is conceivable that the increase in joint viscosity ($B$) after fatigue may be related to the reduction in muscle fiber relaxation rate associated with acidosis accompanying muscle fatigue (Edman and Mattiuzzi 1981; Westerblad and Allen 1993; Westerblad et al. 1993). It has been reported that myofibrillar ATPase activity is reduced in acidosis, which would likely reduce the detachment rate of crossbridges and thus result in prolonged relaxation (Allen et al. 1995; Cooke et al. 1988; Parkhouse 1992). For movements of matched speed, the fatigue-induced reduction in the crossbridges detachment rate and muscle fiber relaxation rate could result in higher resistance after fatigue. In other words, the velocity-dependent viscous resistance force increased after fatigue because of reduced detachment rate and thus increased viscosity.

It is also conceivable that the strenuous fatiguing exercise used in this study could also have altered intrafusal properties. For example, in a study on fatigue-induced neuromuscular changes, Bongiovanni and Hagbarth showed a reduction in la afferent inflow from the spindles that they attributed to intrafusal fiber fatigue (Bongiovanni and Hagbarth 1990; Hagbarth and Macefield 1995). It is known that different intrafusal fibers may have different degrees of resistance to muscle fatigue. For example, in a study on glycogen depletion in intrafusal muscle fibers and related responses at the primary endings, Decorte et al. induced glycogen depletion by long-period stimulation of static $\gamma$ axons in cat. In two experiments with normal circulation, glycogen depletion was observed in a large number of chain and bag$_2$ (static bag) fibers but only in 1 of 19 bag$_1$ (dynamic bag) fibers examined (Decorte et al. 1984). Although it is not certain that extrafusal fatigue is accompanied by intrafusal fatigue (since the intrafusal fiber is not strictly load bearing), it does appear that there may be a change in fiber transduction in fatigue, potentially attributable to altered mechanical properties in the transduction region or potentially because of thermal or metabolic changes. Altered behavior of intrafusal chain and static bag fibers would likely promote the postfatigue reduction in the static stretch reflex gain observed in this study.

When a high-level background muscle torque is to be generated, the dynamic reflex pathway potentially contributes relatively more to counteract fatigue-induced reductions in joint stiffness and static reflex gain. As reflected in the postfatigue experiments, the neuromuscular system increased dynamic stretch reflex gain at the same level of joint torque after fatigue. Since the pre- and postfatigue joint perturbations were identical, the increased postfatigue EMG LE variation elicited by the controlled small-amplitude perturbation provides evidence of increased dynamic reflex gain (Fig. 8).

The underlying mechanisms for the increased dynamic stretch reflex gain could be due to fusimotor adjustment and/or to the recruitment of new motor units required to reach the higher levels of joint torque (Hagbarth and Macefield 1995; Ljubisavljevic et al. 1992a,b). A representative relationship between the variance of the EMG LE and the mean EMG LE is shown in Fig. 9. Paired $t$-test showed that there was small but significant reduction in the slope of the relationship between the variance of the EMG LE and the mean EMG LE after fatigue with $P = 0.024$ (there was no significant difference in the corresponding intercept). This indicates that at matched levels of activation (assuming that such matches could be represented by matched mean EMG LE), the dynamic reflex gain was modestly reduced after fatigue at the higher activation levels. More importantly, at matched background muscle torques, the variation of the EMG LE and the dynamic reflex gain was significantly higher (Fig. 8). This indicates the dynamic reflex gain was enhanced after fatigue through the recruitment of new motor units (to reach higher levels of torque).

Fusimotor adjustment could also play a role and help compensate for fatigue-induced reduction in dynamic reflex gain at matched levels of activation, which could make the dynamic reflex gain much less sensitive to fatigue than intrinsic stiffness. In a related study, the sites of failure during fatigue was investigated by applying controlled stimuli to the neuromuscular system (by tapping the triceps tendon using an instrumented reflex hammer) and evaluating reflex-mediated responses at the levels of muscle activation (for activation failure) and joint torque (for contractile failure) (Zhang and Rymer 2001; Zhang et al. 2000b). Identical tests were done before fatigue, after moderate fatigue, and after severe fatigue. It was found that moderate fatigue caused only contractile failure as indicated by reduction in elbow extension torque but...
not in EMG response to the controlled stimuli, while severe
fatigue was associated with activation as well as contractile
failures as indicated by reductions in both EMG and joint
torque responses to the controlled tendon tapping (Zhang and
Rymer 2001). The severe fatigue induced in the present study
was potentially associated with considerable reduction in EMG
responses to a controlled small-amplitude perturbation. The
finding that only small reduction in EMG response (and in
dynamic reflex gain) was observed in severe fatigue indicated
that fusimotor adjustment could compensate for fatigue and
make reductions in EMG response and in dynamic reflex gain
much less sensitive to fatigue than the corresponding reduction
in intrinsic stiffness. In short, to reach the same levels of
torque, dynamic reflexes contributed relatively more and in-
trinsistiffness contributed relatively less after fatigue.

It is worth noting that the intrinsic and reflex changes asso-
ciated with muscle fatigue were assessed at comparable levels
of submaximal muscle torque before and after fatigue. This
experimental protocol is different from that used in some other
fatigue studies in which fatigue-induced changes were investi-
gated under sustained MVCs before and after fatigue (Bon-
giovanni and Hagbarth 1990; Garland and McComas 1990; 
Woods et al. 1987). Despite the difference in protocols, similar
segmental motor regulatory mechanisms may be involved in
both sustained MVCs and submaximal contraction (Bigland-
Ritchie et al. 1986a–c; Garland and Kaufman 1995). The
inhibitory reflex in response to fatigue-induced muscle changes
reported in previous studies appears consistent with the reduc-
tion in static reflex gain observed in the present study. The
maximal effort used in previous studies left little room for
compensation by recruiting new motor units and increasing
dynamic reflex activity (Garland and McComas 1990; Woods
et al. 1987). In contrast, the submaximal contraction used in
the present study provides us with a tool to evaluate the compen-
satory roles of intrinsic and reflex components for muscle
fatigue in tasks involved frequently in daily activities.

For submaximal contractions, the observed intrinsic and
reflex changes associated with muscle fatigue were consistent
with the findings of a recent study on fatigue-induced changes
for submaximal contractions in which the authors reported that
triceps surae muscle fatigue was associated with a decrease in
ankle joint stiffness and increases in joint viscosity and dy-
namic reflex gain for comparable levels of muscle torque (Qita
and Kearney 2000). Static reflex gain was not assessed in the
preceding study.

It is also worth noting that both the intrinsic and reflex
parameters estimated might depend on the perturbation used
because different perturbations may cause the neuromuscular
system to assume different states. The band-limited “white-
noise” perturbation used in this study was designed to elicit
both reflex and intrinsic components of the system. Unlike a
“step” perturbation that invokes a dynamic stretch reflex re-
response, the white noise perturbation invoked continuous reflex
and intrinsic contributions to joint torque. The identification
procedures gave a simultaneous estimation of the intrinsic and
reflex parameters averaged over a trial. The reflex activities
could be affected by the perturbation signals (bandwidth, am-
plitude, etc.) considerably (Zhang and Rymer 1997).

Generally, very wide bandwidth perturbations tend to sup-
press reflex contributions, while low bandwidth perturbations
tend to promote them. The perturbations used in this study
were not necessarily optimal to address all relevant hypotheses.
Ideally, different perturbation protocols are needed to manifest
or suppress certain reflex or intrinsic actions of neuromuscular
systems affected by muscle fatigue and evaluate them appro-
priately. In addition, further work can be done to modify the
NDDE model used in this study to include force feedback as
well as spindle-mediated position and velocity feedback
(Zhang and Rymer 1997).

The authors thank P.B.C. Matthews for helpful comments.
The authors gratefully acknowledge the support of the National Institutes of
Health, the Whitaker Foundation, and the Falk Medical Research Trust.

REFERENCES

Allen DG, Westerblad H, and Lännergren J. The role of intracellular
acidosis in muscle fatigue. In: Fatigue: Neural and Muscular Mechanisms,

Balestra C, Duchateau J, and Hanaut K. Effects of fatigue on the stretch
reflex in a human muscle. Electroenceph Clin Neurophysiol 85: 46–52,

Bigland-Ritchie B, Cafarelli BE, and Vollestad NK. Fatigue of submaxi-

Bigland-Ritchie BR, Dawson NJ, Johansson RS, and Lippold OJ. Reflex
origins for the slowing of motorneuron firing rates in fatigue of human

Bigland-Ritchie BR, Furbush F, and Woods JJ. Fatigue of intermittent
submaximal voluntary contractions: central and peripheral factors. J Appl

Bigland-Ritchie B, Johansson R, Lippold OJ, and Woods JJ. Contractile
speed and EMG changes during fatigue of sustained maximal voluntary

Bigland-Ritchie BR and Woods JJ. Changes in muscle contractile properties
and neural control during human muscular fatigue. Muscle Nerve 7: 691–

Bongiovanni LG and Hagbarth K-E. Tonic vibration reflexes elicited during
fatigue from maximal voluntary contractions in man. J Physiol (Lond) 423:
1–14, 1990.

Cook R, Franks K, Luciani GB, and Pate E. The inhibition of rabbit
muscle skeletal muscle contraction by hydrogen ion and phosphate. J Physiol

De Luca CJ. Myoelectric manifestations of localized muscular fatigue in

Deborde L, Emonet-Defand F, Harker DW, Jam L, and Laporte Y.
Glycogen depletion elicited in tenuissimus intrafusal muscle fibres by stim-

Dolmage T and Cafarelli E. Role of fatigue during repeated submaximal
contractions of human quadriceps muscle. Can J Physiol Pharmacol 69:

Edman KAP and Lou F. Changes in force and stiffness induced by fatigue and
intracellular acidification in frog muscle fibers. J Physiol (Lond) 424:
133–149, 1990.

Edman KAP and Lou F. Myofibrillar fatigue versus failure of activation
during respective stimulation of frog muscle fibers. J Physiol (Lond) 457:

Edman KAP and Mattiacci AR. Effects of fatigue and altered pH on
isometric force and velocity of shortening at zero load in frog muscle fibers.

Enoka RM and Stuart DG. Neurobiology of muscle fatigue. J Appl Physiol

Enoka RM, Trayanova N, Lagoudis Y, Bevan L, Reinking RM, and Stuart
DG. Neurobiology of muscle fatigue-related changes in motor unit action

Garland SJ, Garner SH, and McComas AJ. Reduced voluntary electromyo-
graphic activity after fatiguing stimulation of human muscle. J Physiol

Garland SJ and Kaufman MP. Role of muscle afferents in the inhibition of
motoneurons during fatigue. In: Fatigue: Neural and Muscular Mecha-

isms, edited by Gandevia SC, Enoka RM, McComas AJ, Stuart DG, and

Garland SJ and McComas AJ. Reflex inhibition of human soleus muscle

J Neurophysiol • VOL 86 • SEPTEMBER 2001 • www.jn.org