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RESEARCH ARTICLE

Voluntary modulation of human stretch reflexes

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Abstract It has been postulated that the central nervous system (CNS) can tune the mechanical behavior of a joint by altering reflex stiffness in a task-dependant manner. However, most of the evidence supporting this hypothesis has come from the analysis of H-reflexes or electromyogram (EMG) responses. Changes in overall stiffness have been documented but, as yet, there is no direct evidence that the CNS can control reflex stiffness independently of the intrinsic stiffness. We have used a novel identification algorithm to estimate intrinsic and reflex stiffness and feed it back to subjects in real-time. Using this biofeedback, subjects could learn to control reflex stiffness independently of intrinsic stiffness. At low torque levels, subjects could vary their reflex stiffness gain by a factor of 4, while maintaining elastic stiffness and torque constant. EMG measurements confirmed that the contraction levels of the ankle muscles remained constant. Further experiments showed that subjects could change their reflexes rapidly on command. Thus, we conclude that the CNS can control reflex stiffness independently and so has great flexibility in adjusting the mechanical properties of a joint to meet functional requirements.

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Introduction

Joint stiffness describes the relationship between the position of a joint and the torque about it (Kearney and Hunter 1990); hence it is a key property in the control of movement and posture. Joint stiffness is composed of two components:

1. Intrinsic stiffness, which is generated by the viscoelastic properties of the joint, muscles and connective tissue, as well as the inertia of the limb.
2. Reflex stiffness, which is generated by active muscle contraction in response to afferent feedback.

Previous studies have shown that intrinsic stiffness varies with the activation level of the associated muscles, either with contraction of the agonist alone which results in a change in the mean level of torque, or with co-contraction of the agonist and the antagonist leading to no net change in torque (Sinkjaer et al. 1988; Weiss et al. 1988; Carter et al. 1990; Kearney and Hunter 1990; Zhang et al. 1998; Mirbagheri et al. 2000). Intrinsic stiffness also varies with the position of the joint (Weiss et al. 1986a, b; Zhang et al. 1998; Mirbagheri et al. 2000). Reflex stiffness has been shown to depend on multiple factors including amplitude and velocity of the stretch (Stein and Kearney 1995), initial position of the joint (Mirbagheri et al. 2000) and background torque (Sinkjaer et al. 1988; Carter et al. 1990; Mirbagheri et al. 2000). It has also been shown that reflex stiffness varies cyclically during periodic tasks such as imposed motions with the same trajectory as normal walking (Kearney et al. 1999).

In addition to studies, which measured reflex stiffness, many other studies have examined the electromyographic (EMG) stretch reflex activity of the muscle. The reflex EMG response has been shown to vary with activation

level (Cathers et al. 2004), joint position (Weiss et al. 1986c), and velocity (Ogiso et al. 2002). It has also been shown to vary depending on the task, such as walking, pedaling and standing (Grey et al. 2002), as well as the phase of cyclic tasks such as cycling (Grey et al. 2001). Other studies have shown that H-reflexes are modulated during walking (Capaday and Stein 1986; Brooke et al. 1991), running (Capaday and Stein 1987) and pedaling (McIlroy et al. 1992; Brooke et al. 1993; Collins et al. 1993).

It has been postulated that the central nervous system (CNS) can tune the mechanical behavior of the joint by altering reflex stiffness in a task-dependant manner. There is evidence in support of this hypothesis. The reflex EMG response has been reported to be greater in a "maintain position" task than in a "maintain torque" task (Akazawa et al. 1983; Doemges and Rack 1992a, b; Dietz et al. 1994). Other studies have shown that, given feedback of their reflex activity, subjects can control their reflexes (Neilson and Lance 1978; Neilson and McCaughey 1982; Evatt et al. 1989; Wolf and Segal 1990, 1996; Segal and Wolf 1994). However, there is doubt as to whether these changes represent true voluntary control of the reflex or rather simply result from varying activation levels of the associated muscles (Crago et al. 1976; Rothwell et al. 1980; De Serres and Milner 1991; Capaday et al. 1994). More recent studies have indicated that the level of arousal and sympathetic activity can alter the reflex response (Hjortskov et al. 2005; McIntyre et al. 2004). Furthermore all these studies have focused on the EMG activity of the reflex response, which does not always map directly to mechanical changes (Kearney et al. 1999). Thus, whether or not the CNS can control reflex and intrinsic stiffness independently remains unknown.

One reason for this is that it is difficult to distinguish the mechanical contributions of intrinsic and reflex stiffness, which occur together and vary simultaneously. Previous work from our lab addressed this issue using a parallel-cascade identification method that produces quantitative, dynamic estimates of intrinsic and reflex stiffness (Kearney et al. 1997). This method uses system identification methods to separate intrinsic and reflex mechanisms on the basis of delay. For small perturbations about a fixed operating point, intrinsic stiffness is described well by a linear dynamic model having three components: inertial, viscous and elastic. Reflex stiffness has been modeled by a differentiator followed by a delay, a static non-linearity and linear low-pass dynamics of second or third order (Kearney et al. 1997; Mirbagheri et al. 2000). Using this model we examined how intrinsic and reflex stiffness vary with joint position and contraction level (Mirbagheri et al. 2000). We also used it to study abnormalities of the intrinsic and reflex mechanisms associated with spinal cord injuries and strokes (Mirbagheri et al. 2001; Galiana et al. 2005). The parallel-cascade method was originally developed for off-line analysis. Recently, we extended the algorithm to produce estimates of intrinsic and reflex stiffness in real-time (Ludvig and Kearney 2006, 2007). In this paper we use this new algorithm to provide subjects with real-time feedback of intrinsic and reflex stiffness.

We examined the ability of human subjects to control reflex stiffness at the ankle when provided with real-time feedback of elastic stiffness, reflex stiffness gain, and ankle torque. We show that using this biofeedback, human subjects can modulate their reflex stiffness over a wide range, thereby altering the mechanical characteristics of the joint while maintaining intrinsic stiffness constant. This demonstrates that the CNS can control reflex stiffness independently and so has great flexibility in adjusting the mechanical properties of a joint to meet functional requirements.

Methods

Subjects

Two males and two females, between the ages of 23 and 46, with no history of neuromuscular disorders participated in the study. All subjects gave informed consent to the experimental procedure, which was approved by the McGill University Research Ethics Board.

Apparatus

A schematic diagram of the experimental apparatus is shown in Fig. 1. Subjects lay supine with their left foot attached to an electrohydraulic actuator by a custom-fitted fiberglass boot. Movement of the foot was restricted to plantarflexion and dorsiflexion with the axis of rotation of the ankle aligned with that of the actuator. The left leg was immobilized with a leather strap and supported with sand bags under the knee, preventing any upper limb muscles from contributing to the torque measured at the ankle. The toe section of the boot was cut out preventing the toe muscles from contributing to the torque measured at the ankle. Mechanical and hydraulic safety stops built into the actuator prevented movement of the ankle beyond its voluntary range of motion.

Ankle position was measured with a potentiometer (BI Technologies 6273), and ankle torque was measured with a torque transducer (Lebow 2110-5K). Both position and torque were defined to be positive for dorsiflexion and negative for plantarflexion. EMGs were measured using a 4-channel EMG system (Delsys Bagnoli-4 EMG System) with a bandwidth of 20–2,000 Hz and a gain of 1,000.

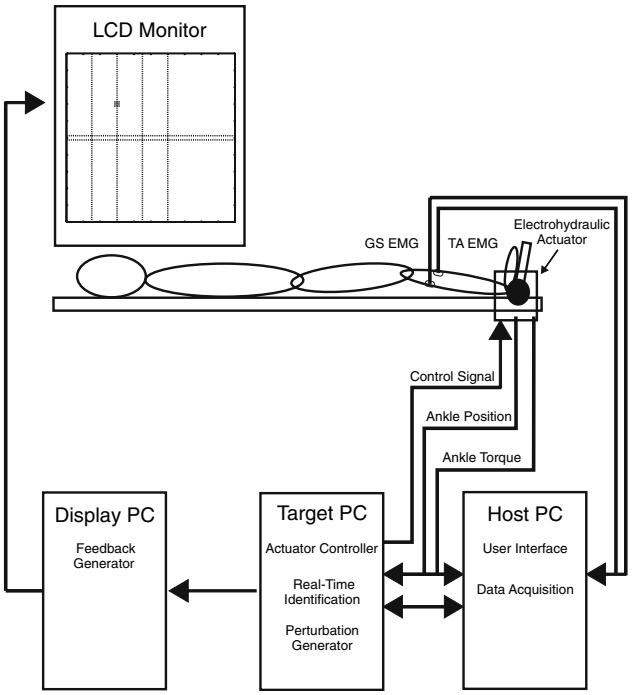

Fig. 1 Schematic of the experimental apparatus. An example of the visual feedback is shown in the LCD monitor. Subjects control the position of a small square in two-dimensions. The *x*-axis shows the reflex stiffness gain, while the *y*-axis shows torque. The two horizontal dotted lines show the target torque, while the multiple vertical dotted line show different reflex stiffness gain targets

Surface electrodes (Delsys DE-2.1) were placed on the lateral head of the gastrocnemius (GS) as well as on the belly of the tibialis anterior (TA). A disposable self-adhesive Ag/AgCl electrode (3M Red Dot) placed on the knee was used as the reference. In some trials the EMG activity of the different muscles of the gastrocnemius-soleus were also recorded. In these cases, electrodes were placed on the lateral head of the gastrocnemius (LG), the medial head of the gastrocnemius (MG), and over the soleus (Sol) at the musculotendinous junction of the Achilles tendon just inferior to the gastrocnemius.

Position, torque and EMG activity were sampled at 1 kHz using an NI-4472 data acquisition card in the Host PC (AMD Athlon 1.33 GHz, 1 GB RAM). Anti-aliasing was performed by the card, which oversampled the data and then applied a digital brick wall filter with a 486.3 Hz cut-off frequency prior to storing the data.

Actuator control and the real-time identification were carried out using xPC Target (The Mathworks inc.) on the Target PC (AMD Athlon 1.6 GHz, 256 MB RAM). Position and torque were low-pass filtered with 8-pole, 6-zero, linear phase, constant delay filters with a cut-off of 400 Hz (Frequency Devices 9064) and sampled at 1 kHz (ComputerBoards PCIM-DAS1602/16). The control signal to the actuator servo-valve was provided by a Computer-Boards PCIM-DDA06/16 Digital-to-Analog Card.

Visual feedback was generated using a custom display built using Simulink (The Mathworks Inc.) on the Display PC (Intel Pentium III 500 MHz, 256 MB RAM). Real-time estimates of intrinsic and reflex stiffness and average torque were computed on the Target PC and sent to the Display PC using the UDP network protocol, every 0.02 s. This machine generated the feedback display on a 15 inch LCD monitor (NEC) mounted above the subject's head.

Real-time stiffness estimates

A detailed description of the algorithm and studies used to validate it are presented in (Ludvig and Kearney 2006, 2007) and so it will be described only briefly here.

The algorithm assumes that the overall torque can be described as

$$\mathrm{TQ} = \mathrm{TQ_I} + \mathrm{TQ_R}, \tag{1}$$

where

$$\mathrm{TQ_I} = I\frac{d^2\theta}{dt^2} + B\frac{d\theta}{dt} + K\theta, \tag{2}$$

and

$$\mathrm{TQ_R} = \mathrm{LP}\left[n\left[\frac{d}{dt}(\theta(\tau))\right]\right], \tag{3}$$

where TQ is total torque, $\mathrm{TQ_I}$ and $\mathrm{TQ_R}$ are the intrinsic and reflex components of the torque, $\theta(\tau)$ is the position with a delay of τ, n is a static non-linearity, LP is a linear low-pass filter, and K, B and I are elastic, viscous and inertial stiffnesses, respectively. This parallel-cascade structure has been demonstrated to describe ankle mechanics well for a wide range of situations (Kearney et al. 1997; Mirbagheri et al. 2000, 2001; Galiana et al. 2005).

First, form the zero-lag cross-correlation between position and torque

$$E[\theta \bullet \mathrm{TQ}], \tag{4}$$

where E is the expectation value. Under general conditions this will depend on both components of Eq. (1); however, by using an appropriate position signal, it is possible to eliminate the correlation between position and reflex torque. This input consisted of randomly distributed "pulses" and "steps". The "pulses" consisted of a 40 ms pulse in a 500 ms interval, while the "steps" consisted of a 460 ms pulse in a 500 ms interval. Both "pulses" and "steps" were 0.035 rad amplitude. Each 500 ms interval

was separated by a random delay of between 0 and 200 ms so that the resulting dorsiflexing stretches were not predictable. For this input

$$E[\theta \bullet \mathrm{TQ_R}] = 0, \tag{5}$$

therefore

$$\begin{array}{rcl} E[\theta \bullet \mathrm{TQ}] & \approx & KE\left[\theta^2\right] \\ E\left[\dot{\theta} \bullet \mathrm{TQ}\right] & \approx & BE\left[\dot{\theta}^2\right] \\ E\left[\ddot{\theta} \bullet \mathrm{TQ}\right] & \approx & IE\left[\ddot{\theta}^2\right] \end{array}, \tag{6}$$

which can be used to estimate K, B and I.

Using the estimates of Eq. (6), we estimate reflex torque as

$$\hat{T}Q_R = TQ - \hat{I}\ddot{\theta} - \hat{B}\dot{\theta} - \hat{K}\theta. \tag{7}$$

Assuming that the non-linearity is a half-wave rectifier, reflex stiffness can be found by computing the impulse response function (IRF) between half-wave rectified velocity and reflex torque. However, finding the IRF is computationally intensive, so cross-correlations were used instead. Based on the reflex stiffness IRFs found by (Mirbagheri et al. 2000), the maximum value of the IRF occurs at a lag of 100 ms, and thus the cross-correlation at this lag was used to estimate the gain of the reflex stiffness IRF. A cross-correlation at a second lag of 435 ms, corresponding to a point in the reflex stiffness IRF where the value has returned to zero, was also estimated and used to account for any offsets in the reflex stiffness IRF. Thus, reflex stiffness gain was estimated as

$$\hat{G} = A\left(\Phi_{\dot{\theta}^+\hat{\mathrm{TQ}}_\mathrm{R}}(100) - \Phi_{\dot{\theta}^+\hat{\mathrm{TQ}}_\mathrm{R}}(435)\right), \tag{8}$$

where $\Phi_{\dot{\theta}^+\hat{\mathrm{TQ}}_\mathrm{R}}(\tau)$ is the cross-correlation between half-wave rectified velocity and estimated reflex torque at lag τ ms; and A is an empirically determined gain.

This computation was implemented in the real-time algorithm outlined by the following steps:

1. Position and torque were high-pass filtered at 0.033 Hz to remove the mean.
2. Position was double differentiated, to obtain the acceleration, multiplied by the torque, low-pass filtered at 0.033 Hz, divided by the acceleration squared, and low-pass filtered to estimate the inertial stiffness. This estimate was multiplied by the acceleration to estimate the inertial torque; this inertial torque estimate was then subtracted from the original torque. A low-pass filter was used to perform the averaging of the expectation values.
3. Step 2 was repeated for the velocity, using the torque minus the inertial torque instead of the original torque, to estimate the viscous stiffness and torque.
4. Step 2 was repeated for the position, using the torque minus the inertial and viscous torques to estimate the elastic stiffness and torque.
5. Reflex torque was estimated by subtracting the estimated intrinsic torque from the total torque.
6. Reflex stiffness gain was estimated by multiplying the reflex torque by a delayed half-wave rectified velocity then low-pass filtering at 0.033 Hz and then dividing it by the half-wave rectified velocity signal squared and filtered. Two different delays were used, 100 and 435 ms, with the latter being subtracted from the former. Finally the signal was multiplied by an empirically determined gain of 45, so that the estimate of the reflex stiffness gain was in the same range as the actual gain.

Procedure

Subjects participated in three experiments each lasting approximately one hour. In Experiment 1, subjects were trained to modulate elastic or reflex stiffness at different torque levels. The perturbation was applied continuously and the subject was asked to explore the torque versus elastic stiffness versus reflex stiffness gain space with the aid of feedback of torque and elastic or reflex stiffness. When a novel state was found, the subject was asked to maintain it for 60 s. Co-contraction was permitted during this session.

In Experiment 2, subjects were provided with feedback of torque and reflex stiffness gain and instructed to modulate their reflex stiffness gain while holding their torque constant without co-contracting. Once subjects achieved a stable reflex stiffness gain they were asked to maintain it and data were recorded for 60 s.

In Experiment 3, subjects were provided with visual feedback of torque and reflex stiffness gain or elastic stiffness and asked to maintain torque and elastic stiffness constant while modulating their reflex stiffness gain to one of three states—low, medium and high—in response to a verbal command. Each state was held for 1 min and data were collected for 10 min.

Off-line analysis

The non-linear parallel-cascade identification described in (Kearney et al. 1997) was used to validate the real-time estimates.

Reflex EMG responses in the GS are known to be unidirectionally rate sensitive, associated with a delay of

40 ms, and to last no more than 100 ms (Mirbagheri et al. 2000; Lambertz et al. 2002). Thus, reflex EMG was calculated by finding the maximum rectified EMG in the first 100 ms following stretch onset. Background EMG was calculated by finding the average rectified EMG for the interval 0–40 ms preceding stretch onset. Reflex and background EMGs recorded during maximum voluntary contractions (MVC) were used to normalize the raw EMG.

Statistical analysis was performed on the EMG measurements to determine whether the EMG remained constant while the reflex stiffness gain varied. Since the rectified EMG measures were not normally distributed, a Kruskal–Wallis non-parametric one-way analysis of variance was performed. This test compares the medians of the groups and returns a χ^2 value and the P value for the null hypothesis, which is that all samples are from the same distribution. Furthermore, the distribution of the reflex EMG has a long tail, thus plotting the mean and standard deviation is misleading. Thus, box-and-whisker plots were used when plotting reflex EMG data. The box shows the lower quartile, median and upper quartile, while the dotted error bars show the largest and smallest values within 1.5 times the interquartile range. The interquartile range is defined as the range in values between the lower and upper quartile. Any values beyond 1.5 times the interquartile range from the upper or lower quartile are considered outliers and are demarcated by a plus (+) sign.

Results

Figure 2 shows a data segment from a typical trial. Figure 2a shows the position signal, with a dorsiflexing stretch shown by the arrow. Dorsiflexing stretches—positive going under our sign convention—caused a synchronized burst of activity in the GS at a lag of approximately 40 ms, indicated by the arrow in GS EMG trace of Fig. 2d. This burst of activity in the EMG led to a contraction of the muscle and production of reflex torque with a characteristic twitch-like shape, shown by the arrow in Fig. 2b. Bursts of activity were also present in the EMG of the TA (Fig. 2c), however since they were highly correlated to the bursts of GS activity, we believe these spikes to be the result of cross-talk from the GS (Rossignol 1975).

Reflex stiffness gain versus elastic stiffness versus torque space

In Experiment 1 subjects were asked to explore various regions of the torque versus elastic stiffness versus reflex stiffness gain space, and when a novel position was found to maintain it for 60 s. Figure 3 shows the space that one

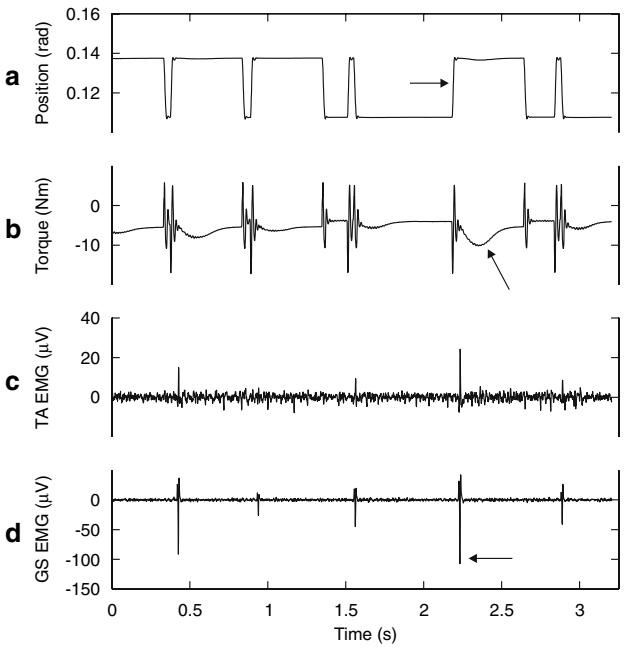

Fig. 2 Typical experimental trial, from Subject A, showing (**a**) ankle position, (**b**) torque and EMGs for (**c**) TA and (**d**) GS. Dorsiflexing ankle movements such as that shown by the *arrow* in the position trace, led to a reflex activation of the GS muscle, shown by the *arrow* in GS EMG trace, and resulted in a reflex contribution to ankle torque, shown by the *arrow* in torque trace

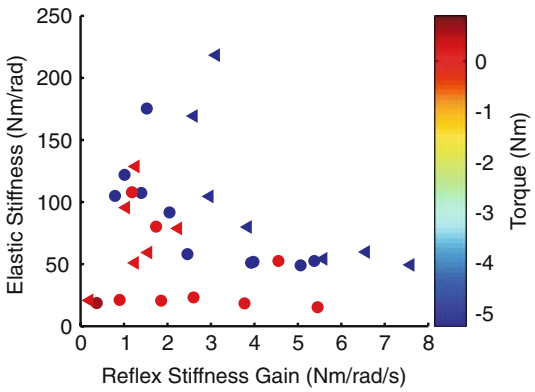

Fig. 3 Elastic stiffness-reflex stiffness gain-torque space for Subject A showing the many different combinations of elastic stiffness and reflex stiffness gains (estimated using real-time algorithm) at different torque levels. Note that there are many points with the same elastic stiffness and torque but different reflex stiffness. Torque levels are represented by the marker colors as defined by the *colorbar* at the right of the figure. *Triangles* indicate trials in which elastic stiffness and torque were used as visual feedback; *circles* indicate trials in which reflex stiffness gain and torque were fed back

subject was able to achieve; each marker represents the mean real-time estimate of reflex stiffness gain and elastic stiffness for a different state. Subjects were free to co-contract during this session, and the points with high elastic stiffness result from high levels of co-contraction. The

most important observation from this figure is that many different values of reflex stiffness gain were achieved for the same elastic stiffness and ankle torque. Thus, for example, the subject was able to generate reflex stiffness gains ranging from 0–6 while keeping the elastic stiffness (~20 Nm/rad) and ankle torque (~0 Nm) constant. Multiple values of reflex stiffness were also achieved elsewhere in the elastic stiffness-reflex stiffness space although the range of reflex stiffness values that could be achieved tended to decrease as elastic stiffness increased. All subjects were able to map out a similar space and this clearly demonstrates that reflex stiffness gain can be modulated independently of the background torque level and elastic stiffness of the joint.

Independent modulation of reflex stiffness

Figure 4 shows a typical data set from Experiment 2, where subjects were provided with feedback of torque and reflex stiffness gain and instructed to modulate their reflex stiffness gain while holding their torque constant without co-contracting. Figure 4a shows the real time estimates of reflex stiffness gain and elastic stiffness from one subject who modulated reflex stiffness gain by a factor of 5 while maintaining elastic stiffness nearly constant. The subject maintained an average torque level of approximately 0 Nm in all trials, as shown by the values above each set of points.

Validation of real-time estimates

To validate the real-time estimates of the reflex stiffness gain and elastic stiffness and provide a comprehensive description of the changes in intrinsic and reflex stiffness we performed a complete off-line identification for each state using a non-linear, parallel-cascade identification procedure (Kearney et al. 1997). Impulse response functions (IRF) for intrinsic compliance (the dynamic inverse of intrinsic stiffness) and reflex stiffness are shown for each trial in Fig. 4c and d, respectively. Data from the same trials are represented in the same colors in Fig. 4a, c and d. It is evident from Fig. 4c and d that the reflex stiffness IRF increased with increasing estimated reflex stiffness gain while the intrinsic compliance did not change in shape or size, confirming the conclusions made from the real-time estimates.

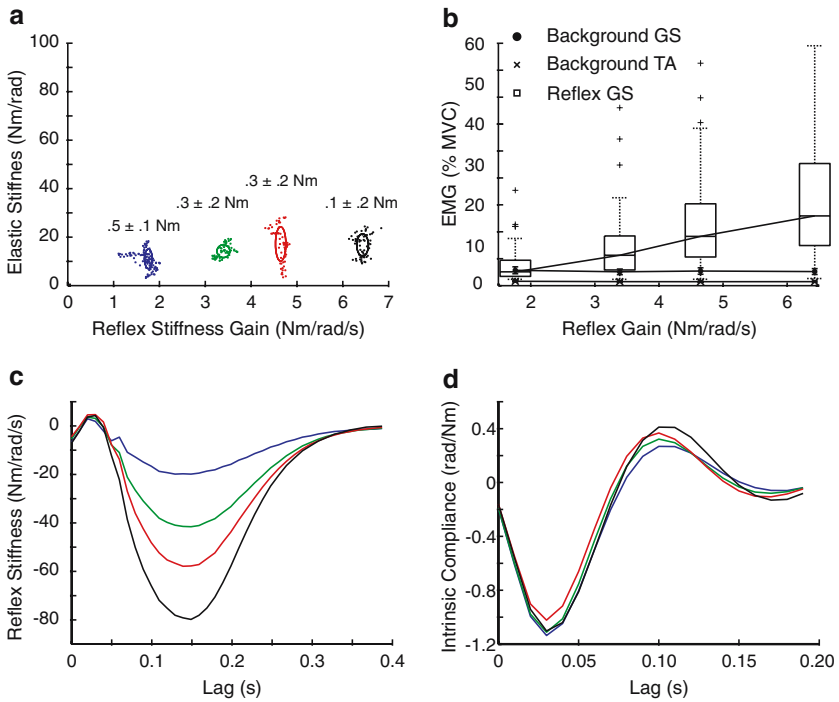

Fig. 4 Reflex stiffness is independent of intrinsic stiffness. Subject D was able to maintain states with different reflex stiffness gains but the same elastic stiffness and torque. **a** Real-time estimates of elastic stiffness and reflex stiffness gain for four different states maintained for 60 s and plotted at half second intervals with a superimposed ellipse centered on the mean and having axes lengths equal to the standard deviations in each direction. Mean and standard deviation of torque are given above each set of points. **b** Corresponding background TA and GS EMG, as well as reflex GS EMG. Reflex EMG increases with increasing reflex stiffness gain, while TA and GS background EMGs are invariant. **c** Reflex stiffness IRFs and **d** intrinsic compliance IRFs found using parallel-cascade identification. Colors of the curves correspond to those of trials shown in **a**

EMG recordings

In addition to measuring the mechanical properties of the joint, the EMG activity of the ankle muscles were also measured. Figure 4b shows the components of the EMG activity in GS and in TA. A non-parametric analysis of variance showed that the reflex GS ($\chi^2 = 192.8$, $P = 0$), background GS ($\chi^2 = 11$, $P = 0.01$) and background TA ($\chi^2 = 15$, $P = 0.002$) EMG activity were all non-constant. However, the changes in the background activity were small and there was no significant correlation between the reflex stiffness gain and the mean background activity in either the GS ($r^2 = 0.35$, $P = 0.40$) or the TA ($r^2 = 0.56$, $P = 0.25$). Thus, the EMG measurements confirm the mechanical measurements; reflex GS EMG increased with increasing reflex stiffness gain while background EMG activity and elastic stiffness remained nearly constant.

GS EMG activity was measured by placing a surface electrode over the lateral gastrocnemius; however it is possible that the reflex modulation was due to changing activation levels in the medial gastrocnemius or the soleus. For one subject the EMG activity was measured in both heads of the gastrocnemius and the soleus. Figure 5 shows the ensemble average of the rectified EMG activity recorded from both heads of the gastrocnemius and the soleus aligned on stretch onset. It is evident that the biggest differences amongst the different reflex states (denoted by the different colors) occurred between 40 and 100 ms after stretch onset. A non-parametric analysis of variance showed that the reflex activity was non-constant for all muscles, while background activity was non-constant in LG ($\chi^2 = 11$, $P = 0.01$) and MG ($\chi^2 = 22$, $P < 10^{-4}$). However, the changes were small and there was no correlation between the reflex activity and the background activity in either the LG ($r^2 = 0.004$, $P = 0.26$) or the MG ($r^2 = 0.009$, $P = 0.09$). Thus we conclude that even though the background activity of the muscle differed slightly among the different reflex stiffness gain states, there was no relationship between the EMG activity of the muscles in the 40 ms before stretch onset and the EMG of the resultant reflex response.

In addition to the experiments performed at zero torque, some subjects showed the ability to voluntarily modulate their reflex stiffness gain independently at torque levels, which corresponded to 5% of the maximum torque. Figure 6 shows the results of a series of trials where the subject maintained a constant torque of –2 Nm (5% maximal torque). The subject was able to change the reflex activity in the soleus ($\chi^2 = 42$, $P < 10^{-9}$) without changing the background activity ($\chi^2 = 0.38$, $P = 0.83$).

Reflex modulation on command

The first two experiments demonstrated that subjects could find states where reflex stiffness was different but intrinsic stiffness and torque were the same. Experiment 3 tested the

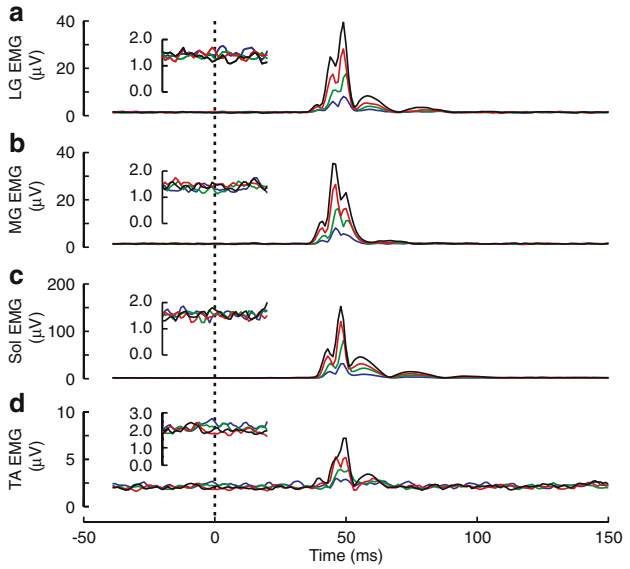

Fig. 5 Ensemble average of rectified EMGs. **a** lateral gastrocnemius (LG), **b** medial gastrocnemius (MG), **c** soleus (Sol), and **d** tibialis anterior (TA) EMGs for four different reflex stiffness gain states from Subject D. Colors correspond to the trials in Fig. 4. Background activity, shown in inset in each panel, was nearly constant for all muscles, while reflex activity was correlated with the reflex stiffness gain in all muscles

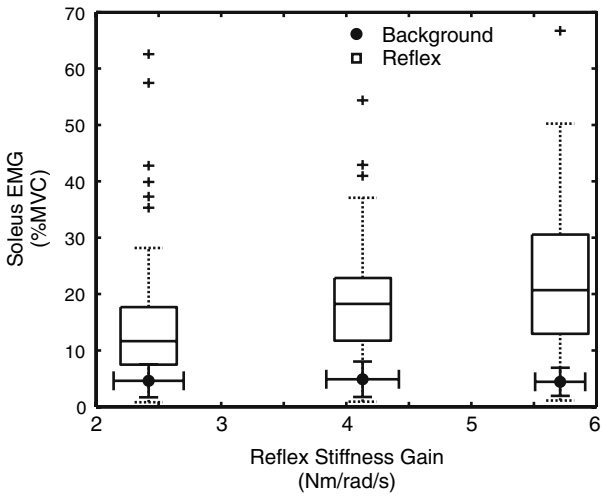

Fig. 6 Reflex modulation at 5% maximal torque. Subject D modulated her reflex stiffness gain while maintaining net torque constant at –2 Nm (5% maximal torque). The reflex EMG varied with the changing reflex stiffness gain while the background activity remained constant. The *solid error bars* show the standard deviation of the background EMG (*vertical*) and reflex stiffness gain (*horizontal*), while the box-and-whisker plot shows the reflex EMG activity

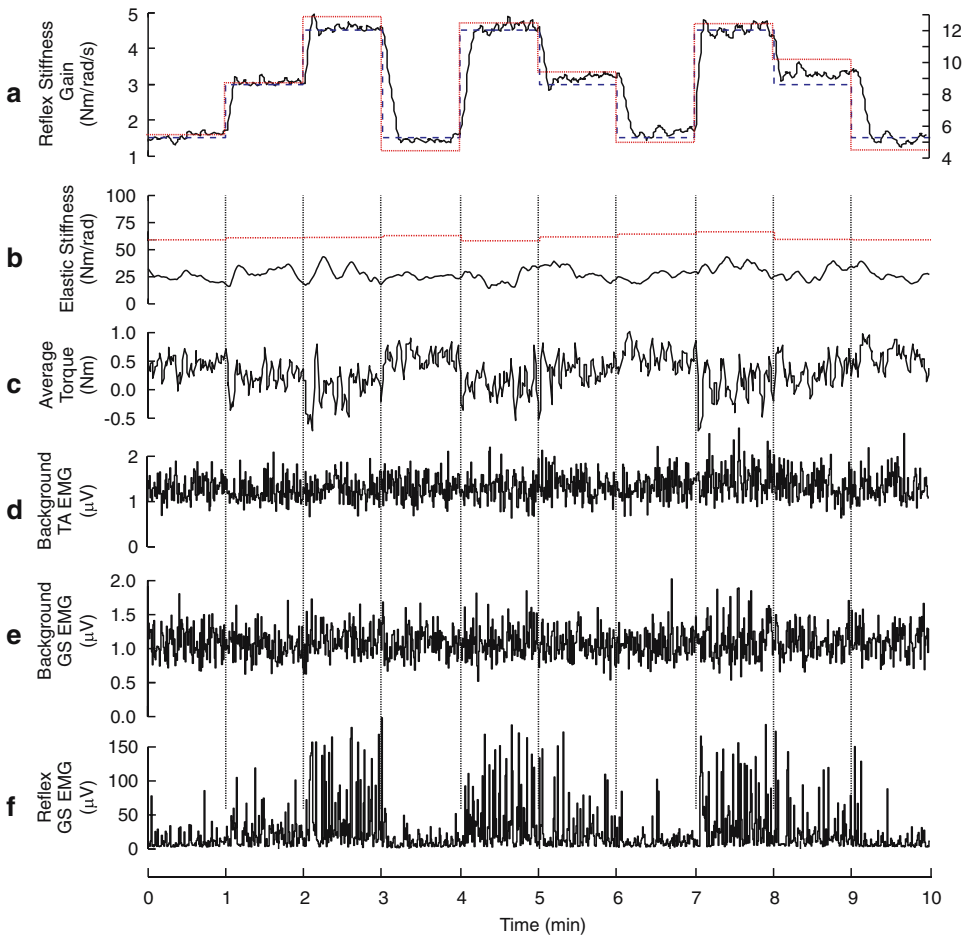

Fig. 7 Voluntary modulation of reflexes on command. **a** Subject D modulated her reflex stiffness gain (*black-solid line*) in response to a verbal command (*blue-dashed line*) while maintaining (**b**) elastic stiffness and background (**d**) GS and (**e**) TA EMG constant. There was a strong correlation of (**f**) reflex GS EMG with the reflex stiffness gain, and a weaker correlation of (**c**) torque with reflex stiffness gain. Parallel-cascade estimates (*red-dashed lines*) confirm real-time estimates as (**a**) the parallel-cascade reflex stiffness estimate (scale on the right) co-varied closely with the real-time estimate, while (**b**) elastic stiffness estimate remained constant

ability of subjects to switch between the different states on command. Figure 7 shows a typical experimental trial in which the subject tried to match their reflex stiffness gain (solid-black line) to a target level (dashed-blue line). The corresponding elastic stiffness, average torque, background EMGs from GS and TA, and GS reflex EMG activity are also shown. The vertical dotted lines demarcate the onset of a new reflex stiffness gain target level, which occurred every minute. It is evident that the subject was able to increase or decrease the reflex stiffness gain to different levels on command. The sluggish, low pass nature of the response is due at least in part to the real-time estimation algorithm, which required around 20 s to respond fully to a change in stiffness. The elastic stiffness was somewhat variable ($K = 28 \pm 6$ Nm/rad) but this variability was similar in magnitude to the variability seen when the reflex stiffness gain was held constant at 4.5 ($K = 36 \pm 5$ Nm/rad), and was not correlated with the changes in reflex stiffness gain ($r^2 = 0.33$, $P = 0.08$). As would be expected, there was a strong correlation between the mean reflex GS EMG and the mean reflex stiffness gain at each state ($r^2 = 0.97$, $P < 10^{-5}$), but neither TA ($r^2 = 0.03$, $P = 0.65$) nor GS ($r^2 = 0.24$, $P = 0.18$) background EMG levels were correlated with the reflex stiffness gain.

In addition to the real-time estimates, parallel-cascade estimates were also computed (dotted-red line). However, the real-time reflex stiffness gain estimates are relative estimates; hence the absolute magnitude of the two estimates may differ. Thus to compare the two, the real-time and parallel-cascade estimates were plotted on two different scales. The scale at the left shows the real-time scale, while that on the right shows the parallel-cascade scale. Figure 7a shows that the parallel-cascade and real-time estimates of reflex stiffness gain strongly co-vary ($r^2 = 0.97$, $P < 10^{-6}$). Furthermore there is no correlation between the reflex stiffness gain and the elastic stiffness ($r^2 = 0.001$, $P = 0.92$) as estimated by the parallel-cascade algorithm.

Figure 7 shows that the reflex stiffness gain and the torque co-vary ($r^2 = 0.89$, $P < 10^{-4}$). To examine the origin of this covariance, we aligned segments of data to the onset of dorsiflexing position changes and computed ensemble averages of the torque. Figure 8 shows the ensemble averages obtained for different reflex stiffness gains. It is evident that the torque traces were identical for latencies

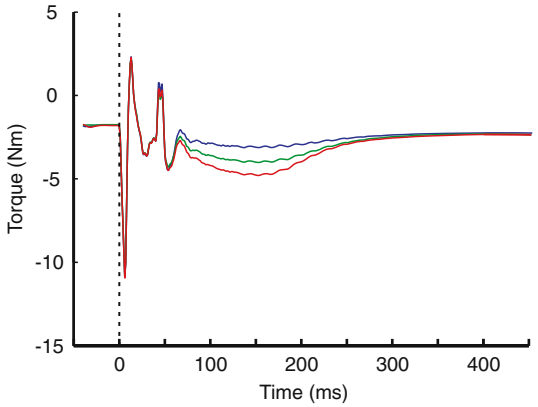

Fig. 8 Voluntary modulation of reflexes. Ensemble average of torque responses from data shown in Fig. 7 aligned on stretch onset (*dotted line*) for the three different reflex stiffness gains (*blue* = low, *green* = mid, *red* = high). Note that the curves only deviate at latencies >50 ms and therefore correspond to differences expected as a result of reflex responses

<50 and >300 ms but differed in the 50–300 ms interval where the mechanical effects of the reflex response would be expected. Furthermore, after segmenting the data into three time windows—0–40 ms prior to, 80–120 ms following, and 415–455 ms following the perturbation—it was determined that only the 80–120 ms segment was correlated with the reflex stiffness gain ($r^2 = 0.99$, $P < 10^{-8}$), while the 40 ms prior to the perturbation ($r^2 = 0.10$, $P = 0.37$) and 415–455 ms segment ($r^2 = 0.33$, $P = 0.08$) were not correlated to the reflex stiffness gain. This demonstrates that the change in average torque was in fact a result of increased reflex stiffness gain and not a change in background activity.

Inter-subject variability

While the results for each experiment are illustrated with data from one subject, all subjects were able to perform the three experiments, though some were more proficient than others. Using the data obtained in Experiment 2, Table 1 compiles the reflex stiffness gain (G), elastic stiffness (K) and torque (TQ) of each subject from the states where reflex stiffness gain was minimal and maximal. Though the range of reflex stiffness gain and elastic stiffness differed amongst the subjects, all subjects showed the ability to increase their reflex stiffness gain by a factor of at least 4 without appreciably altering their elastic stiffness. Additionally all subjects were able to modulate their reflex stiffness gain on command, though some were able to do so more quickly and with less variability than others (Fig. 9).

Discussion

These results demonstrate that with the aid of real-time feedback of reflex stiffness gain, elastic stiffness and torque, subjects can control their reflex stiffness gain and elastic stiffness independently. In Experiment 1 subjects were able to map out a three-dimensional space of reflex stiffness gain, elastic stiffness and mean torque level. In Experiment 2, where subjects maintained a constant torque, they were also able to modulate their reflexes without changing their elastic stiffness. Finally, in Experiment 3, subjects were able to set their reflex stiffness gain to a desired level on command, without correlated changes in either their background torque or elastic stiffness.

Real-time estimation of intrinsic and reflex stiffness

A key component of this study was the use of an algorithm that could produce real-time estimates of intrinsic and reflex stiffness. These estimates were needed to provide feedback to the subjects, so that they could modulate their reflex and intrinsic stiffness independently. The ability to view their stiffness values in real-time may be the reason the subjects were able to modulate their reflex stiffness on command despite previous failed attempts (Crago et al. 1976; Rothwell et al. 1980; Pearce et al. 2003). While others have separated intrinsic and reflex stiffness (Kearney et al. 1997; Zhang and Rymer 1997), neither algorithm operates in real-time. The algorithm used in the present

Table 1 Reflex stiffness gain, elastic stiffness, net torque and percentage of variance accounted for (VAF) of the reflex torque for all subjects from each end of the range of their reflex stiffness gain

Subject	Maximal torque (Nm)	Minimum				Maximum			
		Reflex stiffness gain (G) (Nm/rad/s)	Elastic stiffness (K) (Nm/rad)	Net torque (Nm)	Reflex torque VAF (%)	Reflex stiffness gain (G) (Nm/rad/s)	Elastic stiffness (K) (Nm/rad)	Net torque (Nm)	Reflex torque VAF (%)
A	–106	0.9 ± 0.2	21 ± 2	0.3 ± 0.2	<1	5.5 ± 0.3	15 ± 5	0 ± 0.2	16
B	–36	1.6 ± 0.1	44 ± 3	0.4 ± 0.2	9	5.9 ± 0.1	46 ± 11	–0.8 ± 0.3	43
C	–115	0.1 ± 0.1	52 ± 1	–0.2 ± 0.3	<1	5.3 ± 0.3	68 ± 18	–0.3 ± 0.4	10
D	–47	2.2 ± 0.6	28 ± 4	–0.3 ± 0.2	16	8.6 ± 0.7	37 ± 12	–0.7 ± 0.3	53

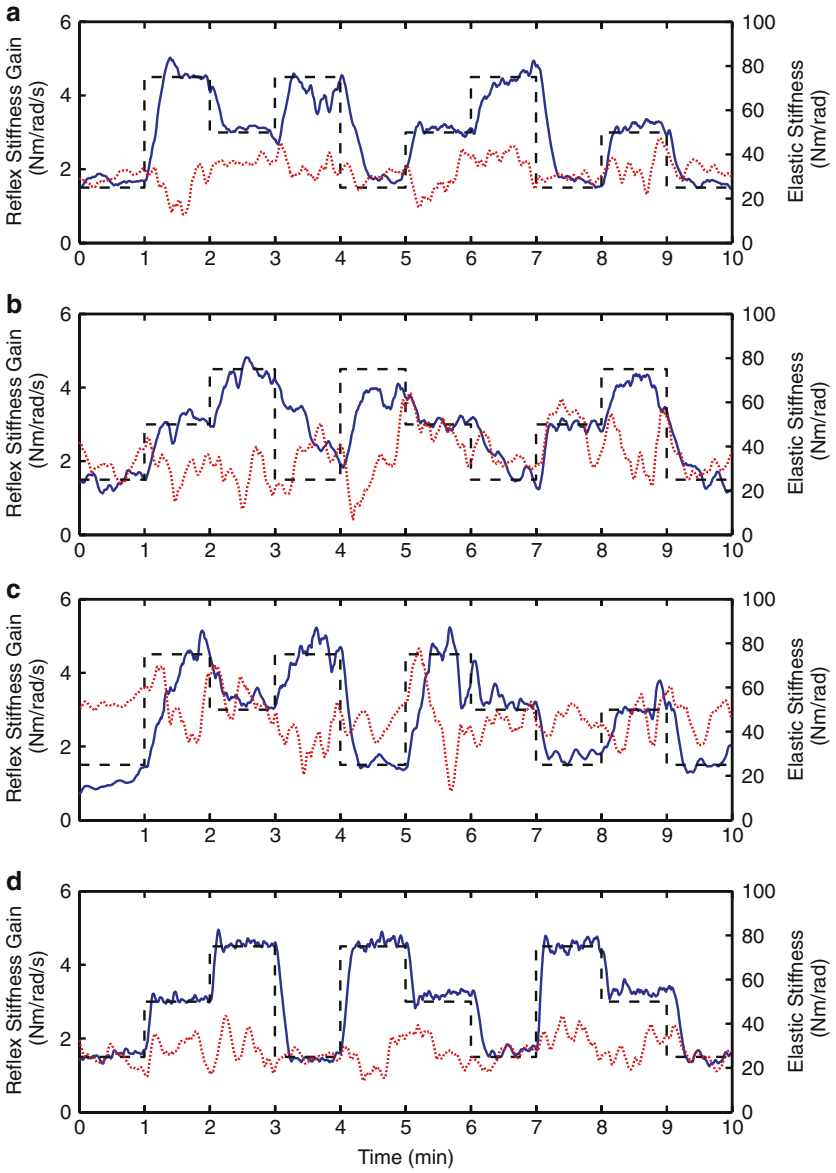

Fig. 9 Modulation on command for all subjects. Real-time estimate of reflex stiffness gain (blue-solid) and elastic stiffness (red-dotted) for all subjects when instructed to match a reflex stiffness gain target on command (black-dashed). All subjects were able to match the reflex stiffness gain target, albeit with different proficiencies

study was a simplified version of the real-time estimation algorithm discussed in detail in (Ludvig and Kearney 2006, 2007).

We are confident that the algorithm gives an accurate indication of changes in reflex intrinsic stiffness for two reasons. First, as demonstrated in Fig. 4, the results of the real-time algorithm were consistent with those obtained using our off-line identification algorithm, which has been validated extensively (Kearney et al. 1997). Secondly, the results are consistent with the analysis of individual steps as demonstrated in Fig. 8. The deviations of these responses only occurred between 50 and 300 ms following the stretch, thereby indicating that only the reflex stiffness varied, in agreement with the real-time estimates. Had intrinsic stiffness been different, there would be differences between the traces at all times including the first 50 ms before the reflex exerted a mechanical effect.

One potential application of the real-time estimation algorithm is the diagnosis and treatment of spasticity. Studies have shown that reflex stiffness is increased in spastic spinal cord injured patients (Mirbagheri et al. 2001) as well as some spastic stroke patients (Galiana et al. 2005). A number of studies have attempted to train healthy and spastic patients to control reflex stiffness using EMG as feedback (Neilson and McCaughey 1982; Evatt et al. 1989; Wolf and Segal 1990, 1996, Segal and Wolf 1994). These studies found that extensive training was required—including for normal subjects—to gain control over reflex responses. We found that subjects could learn to modulate their reflex stiffness gain over a four-fold range,

within 1 h training. It would seem, therefore, that the procedure used in our study may be more efficient for reflex training and may also prove to be more effective for certain spastic patients.

Independent and voluntary control of stretch reflexes

These experiments demonstrated that reflex stiffness gain can be altered up to a factor of four with no change in joint position, elastic stiffness, or background activity in the muscle or its antagonist (Figs. 3, 4). The small correlated changes in torque at the different reflex stiffness gains were shown to result from the varying reflex stiffness gain (Fig. 8). Furthermore, subjects were able to control reflex stiffness gain on command (Fig. 7). While it has been shown that stretch reflexes are modulated in many different contexts, it has been widely believed that this modulation is only produced as a consequence of other actions, such as changing background levels of torque or co-contraction (Crago et al. 1976; Rothwell et al. 1980; De Serres and Milner 1991; Capaday et al. 1994). Indeed, it is well established that reflex stiffness as well as the reflex EMG activity do vary with background level activity and joint position (Weiss et al. 1986a, b; Sinkjaer et al. 1988; Carter et al. 1990; Mirbagheri et al. 2000; Cathers et al. 2004). A number of studies have shown some voluntary control of reflexes (Neilson and Lance 1978; Neilson and McCaughey 1982; Akazawa et al. 1983; Evatt et al. 1989; Wolf and Segal 1990, 1996; Doemges and Rack 1992a, b; Dietz et al. 1994; Segal and Wolf 1994). However, these studies measured only the reflex EMG activity in response to a perturbation; other studies have shown that EMG activity does not map directly to mechanical changes (Kearney et al. 1999). Furthermore, many of those studies did not account for the reflex modulation with joint position and activation level. The current study is the first to systematically address these issues. However, whether subjects are able to achieve this independent and voluntary control of reflex stiffness under more natural tasks remains unknown.

Sources of stretch reflex modulation

How is this voluntary modulation of the reflex achieved? There would seem to be a number of possible mechanisms, including: α-motor excitability, long loop pathways, muscle spindles, pre-synaptic modulation and interneuronal gain.

One important factor affecting stretch reflex response is α-motoneuron excitability. Descending inputs from the CNS could excite the α-motoneurons, causing them to be more excitable and fire action potentials in response to smaller stimuli (Matthews 1986; Stein and Kearney 1995). This may be the source of activation level modulation of stretch reflexes (Mirbagheri et al. 2000). However, if this were the mechanism acting in the present study, we would expect to see a general increase in the background EMG of that muscle. Since the background EMG levels remained invariant, α-motor excitability is likely not the source of modulation in our experiments. Capaday et al. (1994) suggested that sub-threshold activation of α-motoneurons could lead to changes in reflex EMG with no associated change in background levels. However, they only observed this phenomenon at torque levels around 0 Nm, and thus cannot explain the phenomena seen in Fig. 6, where the subject was able to modulate her reflex stiffness gain at a torque corresponding to 5% maximal torque.

Long-loop and transcortical pathways (Petersen et al. 1998) can be discounted as the mechanism for the stretch reflex modulation seen in the current study. The reflex related activity in the GS EMG occurred between 40 and 60 ms following stretch onset (Fig. 5), longer pathways to higher centers could not contribute at such short latencies.

It is well established that γ-motoneurons can modulate reflex feedback (Hulliger et al. 1989; Ribot-Ciscar et al. 1991). Furthermore, recent studies showing reflex modulation with sympathetic activity have suggested that changes in γ-motoneuron activity are responsible for the modulation (Rossi-Durand 2002; Hjortskov et al. 2005; McIntyre et al. 2004). Thus the voluntary reflex modulation seen here could be achieved by γ-control.

Another possible source of reflex control is pre-synaptic modulation. This mechanism is mediated by interneurons innervated by primary afferents, flexion reflex afferents and neurons descending from the CNS (Jankowska 1992; Katz 1999). Thus pre-synaptic modulation would increase or decrease the activity in the primary afferent for a given stretch. A number of studies have shown that H-reflexes in the soleus were inhibited by an increase in pre-synaptic inhibition, which was generated by stimulation of the common peroneal nerve (Stewart and Brooke 1993; Capaday et al. 1995). Capaday (1995) found a decrease in the cat soleus stretch reflex when pre-synaptic inhibition was induced by injection of baclofen. Furthermore it is believed that the stretch reflex modulation caused by the Jendrassik maneuver is mediated through pre-synaptic inhibition (Zehr and Stein 1999).

Reflex modulation can also take place through interneuronal pathways. Not only is there a direct synapse between primary afferents and the α-motoneurons, but there are pathways where the primary afferents connect to the α-motoneuron through interneurons. Furthermore, it is known that these interneurons receive inputs from neurons descending from the CNS (Jankowska 1992). These polysynaptic pathways can be expected to contribute at slightly longer lags than the monosynaptic response.

Based on the evidence collected in this study we cannot conclusively determine the source of modulation. We can

eliminate α-motoneuron and long-loop reflexes as sources of modulation but we cannot distinguish between γ-control, pre-synaptic inhibition and polysynaptic pathways.

Significance of stretch reflex modulation

We have shown that the stretch reflex can be controlled voluntarily, and we have proposed a number of different possibilities for the origin of the modulation—but are the changes significant mechanically?

To assess the significance of this stretch reflex modulation, we estimated the percentage of the total torque accounted for by the reflex stiffness, using the parallel-cascade identification algorithm (Table 1). For Subject B, at the lowest level of reflex stiffness gain, the reflex stiffness accounted for only 9%, while at the highest level it accounted for 43%. This shows that this subject could modulate her reflex stiffness from negligible levels up to almost half of total joint torque. All subjects showed this ability to alter their reflexes in a manner, which greatly increased the percentage of torque, which can be attributed to reflex stiffness. Such increases in joint stiffness via increases in reflex response may have greater energy benefits than merely increasing background levels of muscle contraction.

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